Diagnostic Lumbar Puncture and Associated Risk Factors in Children with Acute Lymphoblastic Leukemia

Hussien Naji Abdullah
College of Medicine, Babylon University, Hilla Iraq.

Abstract
A study used to determine the risk factors for spontaneous (Bloody) and procedure related (Traumatic) hemorrhagic complications in diagnostic lumbar punctures (LPs) of children with acute lymphoblastic leukemia (ALL).

In our study age of the patient and platelet count at time of diagnostic LPs are important risk factors for hemorrhagic problems related to the procedure. In the age less than 1 year, 25 procedure performed traumatic and bloody LPs (52%, 36% respectively). With the low platelet count < 100 x 10^9/L, high incidence of traumatic and bloody LPs (33.3%, 25.5% respectively), and the majority seen in cases with severe thrombocytopenia (platelet count < 25 x 10^9) were traumatic and bloody LPs are (72%, 27.9% respectively).

Introduction

Lumbar puncture (LP) also called spinal tap, is the procedure doctors use to obtain sample of cerebrospinal fluid (CSF), the liquid that surround the brain and spinal cord, for tests. Cerebrospinal fluid is formed in special areas of the brain called choroidplexus in the ventricles. It flow down from the ventricles into the area around the spinal cord. CSF is usually clear and contain small amount of protein and sugar (glucose). During Lumbar puncture you either lie on your side (Horizontal) or sit upright position (1,2) and the site thoroughly cleaned. Your back is scrubbed with local anesthetic medicine on the surface of the skin used. When the skin is numb from local anesthetic, a small needle is inserted into your back at the level of the hip bones below the bottom of the spinal cord, in the intervertebral space between vertebrae L4-L5. The needle pushed forward gently until the CSF is found(3). For testing 3-5 milliliter of fluid are removed and put into special sterile tubes. Lumbar puncture is easier to perform if the patient follows positioning instructions completely(2).

Although LP is generally safe, there is a risk of trauma and blood can be introduced into the cerebrospinal fluid(4,5,6). The mechanism of bleeding into the CSF at the
Time of LP is not known with certainty, over insertion of the LP needle can lead to CSF contamination with blood, through laceration of vertebral venous plexus or soft tissue trauma (7).

Blood in the CSF alter the cell count, increase the protein level and can cause false positive cytological and culture results thereby cause diagnostic confusion (8,9,10). Further more circulating leukemic(11,12,13) cells and bacteria(14) can introduced into the CSF and worsening the patients prognosis.

The objective of the study to identify the risky hemorrhagic complications of diagnostic (LP) in children with acute lymphoblastic leukemia.

**Material and Methods**

Three hundred seventy-eight pediatric patients with newly diagnosed Acute Lymphoblastic Leukemia (ALL) with circulation lymphoblast at the period, February 1998 and October 2006, underwent a diagnostic lumbar puncture (LP) for central nervous system leukemia. For each LP, the patients age, sex, platelet count and number of RBCs per microliter of CSF were recorded.

Traumatic lumbar punctures defined as those in which CSF contained at least 10 RBCs per microliter because this degree of blood contamination of CSF is associated with a worsened prognosis in pediatric patients with ALL and circulating lymphoblast (15).

Bloody lumbar punctures defined as those in which the CSF contained at least 500 RBCs per microliter, this degree of blood contamination causes diagnostic confusion for patients with suspected meningitis and possibly increased risk of introducing bacteria into the CSF when LP is performed on patients with bacteremia (16,17).

Age categories were younger than 1 year and 1 to 18 years because of obvious differences in risk of study outcomes below and above the age of 1 year for both sex (male and female).

Platelet counts from $1 \times 10^9$/L to $100 \times 10^9$/L were categorized in increments of $25 \times 10^9$/L and considered as a risk factor because of associated abnormal bleeding time and other hemostatic measures (18,19).

Platelet count higher than $100 \times 10^9$/L comprised a single category because bleeding time and other measures of hemostasis are normal when the platelet count is above this value (18).

**Results**

The cerebrospinal fluid findings of diagnostic Lumbar punctures (LPs) performed on 378 pediatric patients with newly diagnosed acute lymphoblastic leukemia (ALL) with thrombocytopenia were studied.

Sex, age and platelet count were considered possible risk factors for traumatic and bloody lumber puncture.

Of the 378 (LPs) studied traumatic and bloody LPs (26.4%, 19.31% respectively) table (1). Male patients 192 (51%) and female patients 186 (49%), range in age from 1 month to 18 year (median 4.9 years) table (1).

The relation-ship of age to hemorrhagic complications of LPs in patients with ALL presented (in figure 1) . Age less than one year was associated with high incidence of both traumatic and bloody LPs (52% traumatic and 36% bloody) than other pediatric age groups (childhood and adolescence) table (1) and figure (1).

All platelet count of $100 \times 10^9$/L or less were associated with increased incidence of traumatic and bloody LPs compared to LPs performed at platelet count of $100 \times 10^9$/L or more. However all hemorrhagic complications of LPs were more frequent if the procedure was performed on patient with platelet count $<25 \times 10^9$/L (72 % traumatic and 27.9% bloody) table (2).
Discussion

The study evaluated an important problem with a common procedure, traumatic and bloody LPs, that may indirectly lead to poor outcome in pediatric patients with newly diagnosed ALL with circulating lymphoblast and thrombocytopenia (15). Moreover, bloody cerebrospinal fluid (CSF) obscure the diagnosis of central nervous system leukemia at the presentation of ALL. Therefore, attempts should be made to reduce the risk of traumatic and bloody LPs (20).

The high proportion of traumatic and bloody LPs observed in this study (26.4, 19.3 respectively) is more than the range reported in other studies (6-19%) (15,21,22). The increased risk of bloody LPs in infants may be due to technical difficulty in performing the LP that results from smaller intervertebral spaces and the shallow depth of needle insertion required to reach thecal space. Sex had no effect on the procedure (23).

Platelet count is strong predictor of traumatic and bloody LP. Patients in all categories with platelet count of 100x10⁹/L or less were associated with increased risk. Of the 378 patient with diagnostic LPs, 43 procedure performed at < 25x10⁹/L platelet count with (72% traumatic and 27.9% bloody) 69 procedure performed at platelet count 26-50x10⁹/L with (10.5% traumatic and 17.3% bloody), 86 at platelet count 51-75x10⁹/L with (3.7% traumatic and 13% bloody), 72 performed at count 76-100x10⁹/L with (13.8% traumatic and 19.4% bloody), and 108 procedure performed at platelet count > 100x10⁹/L with (9.2% traumatic and 4.6% bloody). High incidence of traumatic and bloody LP consistent with other studies (15,19,23). Furthermore the risk was elevated with sever thrombocytopenia (count <25x10⁹/L, for both traumatic and bloody (72% and 27.9% respectively). A higher platelet count is needed to reduced such risk in patient with circulating leukemia cells or bacteriemia (23).

In the patients with platelet count 100x10⁹/L or more there is low incidence of both traumatic and bloody LPs, consistent with the normal bleeding times found in patients with platelet count higher than 100x10⁹/L.

Conclusion

Cerebrospinal fluid examination is a common procedure for the diagnosis of central nervous system leukemia in pediatric patients with newly diagnosed acute lymphoblastic leukemia with circulating lymphoblast.

The data emphasize the importance of a properly performed LPs particularly at time of diagnosis when low platelet count. Diagnostic LPs in ALL should only be done by an experienced physician preferably by the oncologist and this is not the time to teach LPs to our students or residents.

References

7- Craig F. Stroabant J. Depth of insertion of a lumbar Puncture needle. Arch Dis child 1997; 77: 450.
Table (1) Effect of Sex and age on traumatic and bloody Lumber punctures (LPs) of Pediatric patients with acute lymphoblastic leukemia.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients</th>
<th>Traumatic</th>
<th>Bloody</th>
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<tbody>
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<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>total</td>
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<td>100</td>
<td>26.4%</td>
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<tr>
<td>Sex</td>
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<tr>
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<td>54</td>
<td>28.1%</td>
</tr>
<tr>
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<td>186 (49%)</td>
<td>46</td>
<td>24.1%</td>
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<tr>
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<td>&lt; 1 year</td>
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<tr>
<td>1 – 18 year</td>
<td>353</td>
<td>87</td>
<td>24.6%</td>
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Table (2) Effect of platelet count on traumatic and bloody Lumbar Punctures (LPs) of pediatric patients with acute lymphoblastic leukemia.

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Traumatic</th>
<th>Bloody</th>
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<tr>
<td>Platelet count</td>
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<td>1-25x10⁷/L</td>
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<td>31</td>
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<td>Total</td>
<td>378</td>
<td>100</td>
<td>26.4%</td>
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Peroxidase enzyme activity in gingival tissues associated with aggressive periodontitis: Histochemical investigation

*Lehadh M. Al – Azzawi, **Khalid B. Mirza
* Department of Oral Pathology, College of Dentistry – University of Baghdad, Baghdad – Iraq.
** Department of Periodontics, College of Dentistry – University of Baghdad, Baghdad – Iraq.

Abstract
Background: Cytochemical studies on peroxidase have contributed significantly to understanding of the movement of lysosomal enzymes and secretory protein through the various compartments of secretory pathway. The peroxidase in leukocytes (myeloperoxidase) could help in determining the severity of inflammation.
Aim: To determine the severity of inflammation in gingival tissue associated with aggressive periodontitis by histochemical method and to determine peroxidase enzyme activity semiquantitatively.
Material and Method: Five gingival biopsies and five blood smears, three with aggressive periodontitis and two from healthy gingiva. Histochemical method for peroxidase activity using the technique described by Deimann et al (1991) was used.
Results: sections clearly show a wide and intense distribution of the enzyme activity in gingival tissue with inflammation specifically in the subepithelial connective tissue, while a discrete low activity was obtained in the epithelial tissue. Control section showed small or few amounts of enzyme activity. In blood smears from aggressive periodontitis and control showed similar peroxidase activity in the section.
Conclusion: PMNs dysfunction observed in periodontal lesions may be a localized phenomenon caused by plaque bacterial products not found in healthy sites.

الخلاصة
تثبت الدراسات الكيميائية الخلوية أن إنزيم البيروكسيداز يساهم بشكل ملحوظ في حركة إنزيمات اللايوزوم والبروتينات الإفرازية خلال مختلف الممرات الإفرازية.
إنزيم البيروكسيداز الموجود في خلايا الدم البيضاء قد يساعد في تحديد شدة الأنتهاب.
عدم فاعلية كريات الدم البيضاء الموجودة في مناطق الالتهاب الثانوي يعود إلى منتجات البكتيريا الموجودة في الصفحات الجرثومية الغير موجودة في المناطق الخالية من الالتهاب.
Introduction

Aggressive periodontitis is seen most commonly in young adults. During the active phase, the gingival tissues are extremely inflamed and there is haemorrhage, proliferation of the marginal gingiva and exudation. Destruction is very rapid with loss of much of the alveolar bone occurring within a few weeks to months. This phase may be accompanied by general malaise, weight loss and depression, although these symptoms are not seen in all patients. The disease may progress, without remission to tooth loss. Most patients with aggressive periodontitis have serum antibodies specific for various species of Bacteroids, Actinobacillus, or both and manifest defects in either neutrophil or monocytes chemotaxis, phagocytosis or both.\(^1,2,3\)

At the present time it is not possible to distinguish prior to treatment which individuals will respond to therapy and which will not. So far studies have found no clinical features which permits identification of these patients prior to treatment.\(^3\)

Several indices have been reported which attempt to record the presence and extent of periodontal inflammation.\(^3,4\) These indices depend on clinical and visual assessment of inflammation and have several disadvantages. They allow only semiquantitative measurement of the degree of inflammation and are prone to considerable variation between examiners.\(^5,6\)

The measurement of gingival fluid volume has been widely used although there is poor correlation between the amounts of fluid and the extent of inflammatory infiltrate in the tissue. PMN leucocytes are present in gingival tissue and fluid and their numbers increase concurrently with the severity of inflammation.\(^2,4,6\) The PMN leucocytes contain peroxidase, which could provide a measure of the severity of the inflammatory process. It has been observed that the peroxidase activity in gingival tissue and exudates resembles that of leucocytes and that there is an increase in activity with certain inflammatory changes in the periodontium.\(^6,7\)

Aim of the study

The purpose of this study is to determine semiquantitatively the peroxidase activity in the gingival tissue associated with aggressive periodontitis.

Materials and Methods

Five gingival biopsies (3 aggressive periodontitis and 2 clinically healthy) and five smears of peripheral blood films from the thumb were obtained from volunteers and patients attending the Periodontal and Oral Surgery Department, College of Dentistry, University of Baghdad.

None of the subjects had contributing systemic disease or received antibiotics or medication in the past six months known to affect the results of this histochemical investigation. Patient from either sex were 20 – 32 years old. Both diseased and clinically healthy sites, when available, were selected from each patient.

The selection of clinically healthy gingiva was chosen when no signs of inflammation were present and didn’t bleed on probing. Aggressive periodontitis was diagnosed on clinical and radiographic basis. The clinical features are florid, highly acute inflammation with bleeding and proliferation of marginal gingiva. The amounts of associated microbial plaque vary greatly and pus may or may not ooze from the deep pockets (more than 7 mm). Radiographic evidence shows destruction of alveolar bone. Gingival sections of both diseased and normal were stained for H&E for general histopathological morphology.

Fresh frozen tissues block (0.5, 1, 1 cm) were immediately transferred to the cryostat (Slee Medical Equipment Ltd, Lanier works Hither Green Lane S. E., 13, London). After placed on a piece of cork with a drop or two of 10% gum acacia (BDH chemicals Ltd.,...
Poole England). The cork with tissue on top were placed on the cryostat chuck with a drop or two of distilled water underneath, and then quenched in liquid nitrogen. Fresh frozen sections of 6 – 8 µ thickness were received on clean cover slips, left for 15 minutes at room temperature for dryness and consequent adherence.

**Histochemical demonstration of Peroxidase:**
The method followed in this study was that of Deimann et al., (1991) 8, which in principle depends on the sequential oxidation of benzidin to a blue and to a brown reaction product.

Accordingly fresh frozen sections and blood smears were incubated for 8 minutes at 15 – 20 ºC in the dark medium consisting of 1ml saturated (42 g in 100 ml), ammonium chloride (BDH, Analar), 1 ml 5 % EDTA (Fluka AG, Buchs SG) and one drop of 3 % H₂O₂ (BDH, Analar), at pH 5.0 and containing 7.5 % sucrose (May and Baker Ltd, England). After incubation sections were post fixed for 6 minutes in formalin vapour, rinsed briefly with distilled water, counterstained for 1 – 2 minutes in 1 % neutral red and mounted in PVP (BDH, Lab reagent).

**Results**

**Histopathology:**
H & E stain used in figure 1 (A & B) show inflammation with increasing number of leucocytes and macrophages these two cell types are widely distributed throughout the section, but mainly concentrated towards the epithelium. In comparing this picture with a section from healthy gingival, the latter shown minimal number of PMNs and macrophages in both epithelium and connective tissue (figure 2).

**Gingival histochemistry of Peroxidase activity:**
Figure 3 (A & B) show intense inflammation the enzymatic stain is widely distributed in both connective tissue and epithelium. These sections show tissue destruction and loss of architecture the stain has concentrated in the area of severe inflammation, it has leaked from the connective tissue towards the epithelium. Increase in stain density is seen in area of inflammation. The gingival epithelium show elongated rete pegs indicating the presence of inflammation.

**Blood cytochemistry and Peroxidase:**
The blood from all patients with aggressive periodontitis show similar picture to blood from healthy control (figure 4 A & 4 B). The reaction product is brown; this has been transferred from the blue due to a function of time in the laboratory preparation procedure.

Granulocytes show strong coarse granules that is evenly distributed through out the cytoplasm, the nucleus show no peroxidase activity. Lymphocytes show no peroxidase activity neither in the cytoplasm nor in the nucleus, the dots of dark stains in the RBC represent pseudoperoxidase.

**Discussion**
Many authors have reported that several pathogens isolated from periodontal lesions have the potential to cause PMNs dysfunction or even to kill PMNs. However, PMNs were found in higher numbers in periodontal lesion as compared to gingivitis sites12. In aggressive periodontitis the viability of PMNs collected from diseased sites was to be lower 9. The reasons for the decreased PMN viability are not known, but it has been suggested that local factors may alter cell viability as well as cell functions.

In this context, it should be recalled that specific bacteria such as Actinobacillus actinomycetemcomitans, which has the potential to kill human PMNs, might alter PMN viability in the sulcus 6. In contrast with these observations, a study showed no difference in crevicular cell viability between periodontitis and healthy patients 2. Since in general the literature there is certain confusion in the nomenclature of
juvenile and aggressive periodontitis, it is possible that the clinical criteria of selection were not uniform between their various studies.

In vitro phagocytic function of sulcular PMNs has been shown to be impaired in aggressive periodontitis 3, 9, 11. In addition, in juvenile and aggressive periodontitis as well as in other patients with periodontal disease, it was found that the phagocytic capacity of PMNs from periodontal lesions was decreased when compared to the function of the cells isolated from healthy sites 9, 11. This could suggest differences in the number of receptors for immunoglobulins present on PMN membranes between the two cell populations 12.

It is also possible that PMN dysfunction observed in periodontal lesions might be a localized phenomenon caused by plaque bacterial products not found in healthy sites. This hypothesis is supported by the fact that several oral pathogens are able to produce functional abnormalities in PMNs 11 and that PMN phagocytic function can be modulated by factors from Gram – ve bacteria 13, 14. Their findings are in contrast with the data of the longitudinal study which did not show any significant variations in PMN functions during the experimental gingivitis period 12, 15, 16. These observations may reflect the differences in the clinical gingivitis and periodontitis situations. Gingivitis is a clinical entity which differs from periodontitis, not only in its bacterial etiology, but also in its histopathologic features. It is generally thought that gingivitis progress with time to periodontitis but the conditions for the progression is not fully understood.

It appears that in gingivitis, when there is a balance between the host and the bacteria, PMNs are functionally competent. Could it be possible that the progression from gingivitis to periodontitis may be due to factors impeding on PMN functions with bacterial proliferation as a consequence? This hypothesis remains to be proven.

References
Figure 1. Photomicrograph of aggressive periodontitis showing severe inflammation with high number of PMN leukocytes.
A. H & E (X 40).
B. H & E (X 100).

Figure 2. Photomicrograph of healthy gingiva.
Figure 3. Histochemical reaction of peroxidase enzyme in tissue section of aggressive periodontitis, brown to blue colour fine granules stain final reaction product. (A & B X 40).
Figure 4. Blood cytochemistry of peroxidase activity showing the final reaction product granules in the cytoplasm of PMN (X1000).

A. Blood from healthy person
B. Blood from patient suffering from aggressive periodontitis
Histological Changes in Liver Associated with Administration of Hydroxyurea in Male Albino Mice

Maysaa Adil Hadi, Nadia Hamid AL-Taii, *Hussein Naji Abd-Alla
Dept. of Biology/College of Science - University of Babylon
*College of Medicine/ Babylon University

Abstract

Hydroxyurea (HU) have been used for treatment of a variety of tumors. It becomes standard therapy for chronic myelogenous leukemia, polycythemia and sickle cell disease. Numerous studies have been published about their side effects but less studies has dealt with HU effect in histological structure of liver, therefore these experiments were designed to study the effect of HU on hepatic tissue. We concluded that HU had negative side effect in the liver.

Introduction

Hydroxyurea (HU) was first synthesized in the 1860s. After that it was found to be active against a variety of tumors. It is an antineoplastic drug that reduceS the synthesis of deoxyribonucleic acid (DNA) [1] by inhibiting ribonucleotide reductase [2, 3]. Therefore HU used for inhibition of human immunodeficiency virus (HIV) replication [4]. Hydroxyurea has become standard therapy for chronic myelogenous leukemia, polycythemia, and other myeloproliferative disorders [5] such as essential thrombocythemia [6]. Also it is used for treatment of sickle cell disease [3, 7, 8, 9]. Hydroxyurea is readily absorbed after oral administration, reaches peak blood level in 2-4 hr, and is excreted in the urine with a half-life of less than 8 hr. It enters cells by passive diffusion and is distributed throughout body fluid [4]. The hepatocytes are the main target of the cytotoxic drugs. The liver is the most active organ in metabolizing foreign compound as HU and generate metabolites nitric oxide (NO) throughout three hours after the injection [10]. Nitric oxide not only more reactive but also more cytotoxic than parent compound [11].

Materials and Methods

Adult albino male mice Mus musculus were used throughout the experiment. All mice were given water and pellet ad libitum. They divided into two groups, each group consisted of 5 animals and treated as following :-
1- The first group of mice were injected intraperitoneal (i.p) with 1 ml of Phosphate Buffer Saline and considered as a control group.

2- The second group were injected intraperitoneal with 1 ml of hydroxyurea (Samadroxyurea) which manufactured by the state company for drugs industry and medical appliance Samarra – Iraq was diluted with Phosphate Buffer Saline to prepare, the dosage used in this experiments was (1.02g/kg) [10].

Body weight was taken before and after the experiments then the animals killed by spinal dislocation after 24 hours. The liver was removed , weighted , fixed for 24 hours in formalin 10% solution, processed and the paraffin sections (5 micron thickness) were prepared and stained with Hematoxylin & Eosin (HE) method [12 ] for light microscopical study.

The liver / body weight ratio was calculated as follow:-
Liver/ body weight ratio = \frac{liver weight (gram)}{body weight (gram)} × 100

Analysis of variance (ANOVA) was used for statistical analysis of data and standard error was calculated [ 13 ].

**Results and Discussion**

First: Body and Liver Weight:-

This study indicated no significant differences in body weight and liver/ body weight ratio (Figure -1- and figure-2- respectively) in hydroxyurea treated group as compared with control group.

Second :- Histopathological study:-

A:- Hydroxyurea group :-

Some parts of hepatic lobules had normal architecture such as normal size of hepatocytes and normal nucleus ( figure 3) . Another hepatic lobules had some histological changes which we can summarized as follow:-

1- Cloudy swelling and intracellular odema which reflect failure of membrane ion pumps because of lack of cellular ATP allowing the cell to accumulate fluid [ 14 ]. The earliest light microscopic evidence of cellular injury is loss of normal staining intensity of the cytoplasm owing to swelling of membrane – bound organelle , swelling of endoplasmic reticulum and mitochondria and described as cloudy swelling [ 15 ] as seen in figure (4). This may be due to the effect of HU in vasodilation which results from the HU – derived nitric oxide [ 3, 11 ].

2- Necrosis :- Small areas of nicrosis was seen in figure (5) which results from exposure to HU . Necrosis was light eosinophilic [15].

3- Vascular congestion (figure 4 A&6A,B) and infiltration of inflammatory cells (figure 6C). The focal accumulation of inflammatory cells usually seen in relation to the site of necrotic hepatocytes .This inflammatory cells migrate by chemotactic agents from tissue debris. [ 15 ].

The hepatocytes with their high degree of metabolic activity are disturbed by many substances and demonstrate the histological and cellular responses known such as cloudy swelling , necrosis and fatty change [ 15 ].

All previous histological changes may be due to in vivo formation of nitric oxide (NO) after three hours of administration of hydroxyurea and then exhibits its
biological effects [3, 8, 10, 11]. These previous studies revealed that there was ability of liver tissue to convert HU to NO and provided in sight into the metabolism of this drug. The liver is one organ that is clearly influenced by NO as inflammatory mediator [2, 17, 18] which plays an important role in endothelium-derived relaxation and inflammation [12].

B. control group:- Normal architecture of liver was seen (Figure :7 ) which is similar to those described by [19].

References


Figure-1-Changes in body weight in treated groups
Fig -3- Hepatic tissue of mice treated with hydroxyurea show normal hepatocytes & normal hepatic architecture (HE: 600X).

Figure-2-Changes in in liver/ body weight ratio in treated groups
Fig-4- Hepatic tissue of mice treated with hydroxyurea show cloudy swelling and vascular congestion (VC).
K: kupffer cell, B:binucleated hepatocytes. (HE: 600X)
Fig-6- Hepatic tissue of mice treated with HU show vascular congestion (VC), infiltration of inflammatory cells (In) & binucleated hepatocytes (B). (HE: A: 150X, B&C: 600X).

Fig-7- Hepatic tissue of mice treated with pbs (control group showed normal architecture of hepatic lobules & hepatocytes. (HE A: 150X, B: 600X) CV: central vein.
the protection of liver by fenugreek seeds from the effects of prostaglandin $f_2\alpha$
in male albino mice
Maysaa Adil Hadi
Dept. of Biology, College of Science, University of Babylon, Iraq

Abstract

Prostaglandins (PGs) have been used for many medical aspects such as parturition, blood pressure control and another. Numerous studies have been published about their effects on the kidney, thyroid gland, male and female reproductive system. But no previous studies has dealt the possibility of minimizing their effect or even repair the damaging structure has been reported. These experiments were designed to study the effect of PGF$_2\alpha$ on hepatic tissue and then use fenugreek seeds to overcome the PGF$_2\alpha$ effects on hepatic tissue. We concluded that fenugreek seeds could inhibit the negative side effects of PGF$_2\alpha$ in the liver especially by using six dose of fenugreek after PGF$_2\alpha$ injection in similar doses.

Introduction:

Prostaglandins (PGs) play diverse and important roles in human health and disease states and regulate abroad range of physiological processes such as pregnancy, labor (parturition) (1, 2, 3), blood pressure control (4), modulation of inflammation and immune response (5), liver protection and damage (6). In many malignant tumours including some liver tumours increased
levels of PGs, most notably PGE$_2$ and PGF$_2\alpha$, have been detected (7). PGs stimulate tumour growth and they presumably act in most of carcinogenesis (8).

Most PGs exert their actions by binding to specific cells surface receptor, PGF$_2\alpha$ may act on it's G Protein-Coupled receptor (FP) (9,10,11). Receptors for PGs have been identified in various tissues (12) such as liver (13,14). PGF$_2\alpha$ may be imported intracellular via a transporter which has high affinity for PGF$_2\alpha$ which increases intracellular cyclic AMP (15).

Previous studies have been showed some PGs have effect on protein and lipid metabolism (16). Also have effect on carbohydrate metabolism, the studies about effects of PGs on glycogenesis revealed that PGE$_2$ (10µg/ml) significantly inhibited incorporation of glucose into glycogen pool. PGE$_2$ at (1-10 µg /ml) stimulated incorporation of glucose into non-glycogen macromolecules and these results indicated that PGE$_2$ and PGF$_2\alpha$, in physiological concentration, directly influence the metabolism of glucose (17). Also PGs have inhibitory effect on insulin secretion which in turn effect on carbohydrates, lipids and protein metabolism (18) especially PGF$_2\alpha$ at (5µg/Kg body weight) which cause degenerative changes in beta cells of pancreas including vacuolation, decreasing or losing of secretory granules of insulin and increasing apoptotic beta cells (19).

Fenugreek seeds have been used as a food spice and in traditional medicine for numerous indications including labor induction, aiding digestion and as a general tonic to improve metabolism and health. Many animal and human trials suggest possible hypoglycemic and antihyperlipidemic properties of oral fenugreek seeds powder (20,21).

Present interest in fenugreek focuses on its potential benefits for people with diabetes or high cholesterol. Fenugreek seeds which rich in proteins contain the unique major amino acid 4-hydroxyisoleucine which has been characterized as one of the active ingredients in fenugreek for blood glucose control (22,23).

**Materials and Methods:**

Three groups of albino male mice *Mus musculus* (12-18 weeks old) were used in this study. The temperature in animal house was 22-30°C with a system of (12 hours light :12 hours dark). All mice was given water and pellet *ad libitum*, 20 mice were used and divided into equal groups (five for each) as the following :-
1- The first group of animals were injected subcutaneously daily for 6 days with 0.1 ml normal physiological saline (0.9% NaCl) and considered as a control group.

2- The second group was injected subcutaneously daily for 6 days with 0.1 ml prostaglandin F₂α (5µg/Kg body weight) . PG₂α (Veteglan) from Spanish Calier company was diluted with sterilized normal physiological saline to preparation the concentration used in this experiments (19).

3- The third group was given PGF₂α as the second group then was given watery solution of fenugreek seeds orally with a dose (1.6 mg/gm body weight) daily for 6 days. This group subdivided into two groups:

a- First group was given fenugreek after 30 minutes from PGF₂α injection.

b- Second group was given six doses of fenugreek after injection with six doses of PGF₂α.

Body weight was taken before and after the experiments then the animals killed by spinal dislocation after 24 hours from the last dose of treatment. The liver was removed, weighted, fixed in formalin 10% solution, processed and 5 micron thickness paraffin sections were stained with Hematoxylin and Eosin (HE) methods and glycogen stain(Periodic Acid Shiff(PAS))(24) for light microscopic observation and examined. The liver / body weight ratio was calculated as follow:

\[
\text{Liver/body weight ratio} = \frac{\text{Liver weight (gram)}}{\text{Body weight (gram)}} \times 100
\]

The results statistically analyzed by using analysis of variance (ANOVA) and standard error was calculated (25).

**Results & Discussion:**

**First : liver weight:**

(a) **Animals group treated with PGF₂α:**

There was no significant decrease in liver /body weight ratio in PGF₂α treated group (Table -1- ).The cause of decreasing although it was not significant may be due to the degeneration of many hepatocytes or because the PGs inhibited incorporation of glucose into glycogen which showed in this study.Glycogen stained with PAS appear as purple patches (24) was few in this group compared with control group (figure-1-).The decreasing of glycogenesis occur by directly
influence of PGF2α on the metabolism of glucose (17) through the inhibitory effect on insulin secretion by causing degenerative changes and apoptosis of beta cell (19).

(b) Animals treated with PGF2α and fenugreek seeds:
There was no significant differences in animals treated with PGF2α and fenugreek seeds solution. This may be due to administration of PGF2α decrease the liver weight compared with control group but when treated with fenugreek seeds (especially 6 doses of fenugreek solution after 6 doses PGF2α injection) enhanced the liver weight because fenugreek seeds increasing insulin secretion and increase glycogenesis (20,21) and then increase glycogen storage in liver as seen in figure-1-which appear abundant and then effect on liver weight. Our results agree with (26) who reveals that fenugreek seeds boiled extract caused a significant increase in liver glycogen levels and liver / body weight percentage.

Second : - Histopathological study:-
- Animals group treated with PGF2α :-
  Most hepatocytes showed marked degenerative changes in both nucleus & cytoplasm, only few hepatocytes remained with normal appearance. We can summarized histological changes of follow:-

1- The most characteristic changes in the liver were increase in the size of most hepatocytes and their nucleus (cellular hypertrophy), while another hepatocytes contain irregular nuclear envelope (figure: 2 A,B). Hepatic lobules contain many hepatocytes with vacuolated cytoplasm (Figures 2,3,4). Some Hepatic lobules occasionally had few atrophied cells which reveals to necrosis. The nucleus of each necrotic cell was smaller, condensed and intensely stained with hematoxylin (figure: 2B, 4A). These changes might be due to the presence of PGF2α receptors on hepatocytes (13,14) or might be due to the effect of PGF2α on membrane permeability (27) who revealed that gap junction permeability between hepatocyte doublets was strongly inhibited by prolonged (2h) treatment with PGF2α which may enhance or diminish the propagation of Ca^{2+} signals which is important for certain hepatic functions including biliary flow and glucose output.

2- Some sinusoids were enlarged (figure: 2C,2D,4B) because degeneration of most hepatocytes while another sinusoids were normal.

3- Increasing of Kupffer cells number as seen in (figure :2) may due to activation
of Kupffer cells which have been documented to play an important role in the early events of liver injury and regeneration by releasing biologically active mediators such as Interleukin-6 (IL-6) (28).

4- Vascular congestion (figure:3C,D), infiltration of inflammatory cells at periphery of central vein (figure:3) and edema within hepatic lobules was frequently observed as signs of inflammatory process (figure:4, 2D). These results indicate PGF$_2$$\alpha$ is mediator of inflammation (5) through its role in vasodilatation which first cause increased blood flow then stasis of blood flow and increased capillary permeability then accumulation of fluid into tissues and second neutrophils migrate to site of tissue damage by chemotactic agents from tissue debris (29).

**b- Animals treated with PGF$_2$$\alpha$ & Fenugreek seeds:**

There was histological changes in hepatic tissue of animals group treated with fenugreek seeds after 30 minutes from PGF$_2$$\alpha$ injection but they were less than in animals group treated with PGF$_2$$\alpha$ alone. These changes include increased proliferate hepatocytes, some enlarged sinusoids, congestion & infiltration of inflammatory cell (figure: 5 A,B) but many parts of another lobules had normal architecture (figure: 5C). While animals group which treated 6 doses of fenugreek seeds after 6 doses of PGF$_2$$\alpha$ demonstrate hepatic architecture like normal hepatic tissue (figure:5D).

These results may be due to the presence of several compounds in fenugreek seeds or may be because fenugreek seeds increasing the sensitivity of tissue to available insulin (30).

**C- Control group:** light microscopic examination of the liver revealed the presence of normal morphology of hepatocytes and normal architecture of liver (figure:6). These finding are similar to those described by other authors (31).

**Conclusion:**

The present study conclude that the PGF$_2$$\alpha$ had negative effect in histological structure of liver and fenugreek seeds could inhibit this negative effect in liver especially by using 6 doses of fenugreek after 6 doses of PGF$_2$$\alpha$ injection. We advise to use fenugreek seeds in future studies to inhibit PGs & other hepatotoxic drugs side effects by using fenugreek seeds in longer time than 6 days.

**References**


### Table -1- Liver / body weight ratio changes in treated groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Liver/ body weight ratio (Mean ± S.E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.56 ± 0.76</td>
</tr>
<tr>
<td>PGF$_2\alpha$</td>
<td>4.75 ± 0.16</td>
</tr>
<tr>
<td>PGF$_2\alpha$ + fenugreek seeds</td>
<td>5.20 ± 0.41</td>
</tr>
<tr>
<td>PGF$_2\alpha$ (6 doses) + fenugreek seeds</td>
<td>5.45 ± 0.07</td>
</tr>
</tbody>
</table>

S.E: Standard Error  N= 5
Figure-1:- Hepatic tissue of mice stained with PAS stain showed glycogen (▲)
A: control group
B: PGF₂α treated group
C: Fenugreek & PGF₂α treated group
(PAS: 600X)
Figure-2: - Hepatic tissue of mice treated with PGF$_2\alpha$ showed:
A: Hypertrophic heptic cells with irregular nuclear envelope (H), vacuolation of cytoplasm (V), increasing of Kupffer cell number (K).
B: Necrotic hepatocytes (N).
C, D: Enlarged sinusoids (ES).
(HE: 600X)
Figure-3:- Hepatic tissue of mice treated with PGF$_2$$\alpha$ showed:

A,B: Infiltration of Inflammatory cells (In) at periphery of central vein (CV) . (HE:A 150X, B 600X)

C,D: Central vein congestion (CVC) (HE: 600X)
Figure-4- Hepatic tissue of mice treated with PGF$_2\alpha$ showed edema (od ) , some enlarged sinusoids (ES) and necrotic hepatocytes (N).

( HE: 600X ).
Figure-5:-Hepatic tissue of mice treated with fenugreek seeds and PGF$_2$$\alpha$ injection showed:
A: Binucleated hepatocytes (B) , some enlarged sinusoids (ES). (HE: 600X).
B: Central vein congestion (CVC) and Infiltration of Inflammatory cells (In) (HE: 150X) .
C,D: Normal architecture of many parts of hepatic lobules , CV: central vein (HE:C150 X,D600X)
Figure-6:- Hepatic tissue of mice treated with normal physiological saline (control group) showed normal architecture of hepatic lobules and hepatocytes, CV: central vein (HE: A150 X, B 600X)
The humoral mucosal immunity of urinary tract kelbsiella infections in menopausal women

*Shnawa i.m.s., **Hamza h.j
*Babylon university. college of science department of Biology, **college of nursing

ABSTRACT
Seventy – one menopausal women patient (MWP) with urinary tract infections (UTI), thirty - two adulthood women patients (AWP) with UTI and twenty normal women subjects (NWS) were the study groups. Pyuria but not haematuria via examination of urine sediments. Kelbsiella like colony morphotypes were noted on blood agar and Mac (on key agar, in single and mixed infection patterns. K. pneumoniae and, K. oxytoca, were identified as uropathogens.

Klebsiella antigenic epitopes can be of B cell and of the Th2 dependent types activating mucosal humnal immmal immune responsce in the urinary tract during Klebsiella infections. Lower mucosal antibody titers (4-16) were noted among MWP than that of AMP (16-64). This may attributed to local costimulatory signals, activation of suppresser T cells and disturbance of the Th1/Th2 activities leading to production of low activity and affinity antibodies.

Introduction

The humoral mucosal immunity of urinary tract kelbsiella infections in menopausal women
The normal function of urinary tract have mucosa associated lymphoid aggregates (1,2) such aggregates forms the basis for mucosal immunity in both their humoral and cellular arms (2,3). Ascending, haematogenous and / or lymphogenous routes of infections are primarily combted by urine voding mechanisms mucosal trapping, mononuclear cell system, polymorphonuclear cells and urinary mucosal immunoglobulin (UMIG) (4,5). Imbalance, however, between The virulence factors of The uropathogen and the elements of mucosal immune system of the host lead to clinical infection (5) in the present work the possible effects of menopause on urinary mucosal immunity during women infection was being investigated.

Materials and methods
1. urine samples
   Seven milliliters amounts of clean catch midstream urine samples were collected aseptically from 71 menopausal women and 32 adulthood women with urinary tract infections as a test group and 20 normal women subject as control group in Hilla maternity and childhood hospital.
2. urinary mucosal immunoglobulin separation: The urine samples were filtered through whatman no.1 filter paper, then mixed with equal amount of Polyethylene Glycol (PEG) 6000 6% and precipitated as in (6,7) then partially characterized as in (8).
3. uropathogens
   The Klebsiella and the coexisting species were identified from primary plate cultures as in (9) using classical biochemical tests and API 20 E for conformation of isolate identification. Whole cell antigens were done as in (10).
4. serology:
   Slide and tube agglutination studies were done as in (10)
5. Biometry: statistical analysis was made as in (11)

Results
1-Infection
   The MUP, AWP and NUS urine samples were deposited and wet mount prepared significant grades of pyuria rather than haematuria were noted among AWP and MWP but not NWS single monomicrobial infections were higher than dimicrobial infections. Intact uropathogens were found in higher rates than injured uropathogens Klebsiella – like clony morph types on blood and MacConkey ager plates K. pneumoniae and K. oxytoca were identified from MWP in higher rates than AWP and NWS. (Table 1) In dimicrobial infection The coexisting organisms were E.coli, Eerobacter, S. epidermidisermidis and St. pyogenes.

1- Urinary Mucosal Immune Responses ,
2-1 Urinary Mucosal Immunoglobulins,
   The solution that were obtained using PEG 6000 6% precipitation and redisolution, were found to biurate positive, 2ME resistant and rected specifically with whole cell antigens of the corresponding uropathogens were considered as UMIG, one case from each of klebsiella species, the titer dropped to zero upon 2ME treatments indicating serum fraction (8 to zero, 4 to zero). Two UMIG negative cases noted among K. pneumoniae cases.

2-2.: specific mucosal antibody titres, most of the mucosal antibody titres were within 8 in MWP in contrast to the most noted titres 16 or more among AWP (Table 2)
2-3 : The Klebsiella specific urinary humoral mucosal immune responses in MWP.
2-3-1 : K. pneumoniae:-
Twenty- two and seven cases of \textit{K. pneumoniae} of urinary tract infections were noted among MWP and AWP. The age ranges in MWP were 47-49 while for AWP were 18-29 years. The means, medians, and ranges were 1.69, 0.89, and 16.22 g/L for MWP, while they were 1.49, 0.90, and 4g/L for AWP. The mucosal specific antibody titre means, medians and ranges were 7.5, 8 and 28 respectively for MWP while they were 24, 16 and 56 for AMP.

2-3-2: \textit{K. oxytoca}:
Ten and three cases of \textit{K. oxytoca} urinary tract infection among MWP and AWP respectively. The age ranges were 47-49 for MWP and 22-30 for AWP. The concentration means, medians and range of UMFO for MWP were 2.33, 1.67, and 10.2 g/L while for AWP They were 1.11, 0.90, and 0.7 g/L respectively. The titre means, medians and ranges of UMI of for MWP were 7.6, 8 and 8 for MWP while They were for AWP as, 37.3, 32, and 48 respectively.

2- Biometry :-
3-1: Regression Analysis :
The correlation between UMFG connection and titles were of simple linear type with significant r in both \textit{K. pneumoniae} and \textit{K. oxytoca}. It was positive in the two former cases and negative for the third cases (table 3).

3-2: Paired observation t statistics:
The paired observation analysis t statistics for the differences between mucosal antibodies in AWP and AWP were significant at \textit{K. pneumoniae} and \textit{K. oxytoca} (table 4).

4- Mucosal Immunology of Mixed Infection:
Six \textit{K. pneumoniae} and three \textit{K. oxytoca} were noted in mixed infection states with other uropathogens. The Klebsiella specific UMI titre were ranging among 4-16 and for the coexisting pathogen were 4-8 (Table-5).

Discussion
Klebsiella species can be the causals for descending from of an infections foci spreading through blood or lymph reaching bladder through glomerular filtration or ascending from the gut micro flora resident in perineum reaching urethral orific, urethra then bladder (6,12,13).

Aging and/or menopause in women are associated with lack of estrogen that lead to atrophic changes in urethra, vagina causing atrophic urthritis and atrophic vaginitis. Together with ulceration of B lymphocyte and T lymphocyte function (15,16,17).

Such changes may predispose the bladder, urethra to colonization with Klebsiella. Through the action of virulence factors such as capsule, siderophores, pilis, serum resistance and lipo poly saccharine (17,18,19).

\textit{K. pneumoniae} and \textit{K. oxytoca} were with higher infection rates among MWP than AWP (table 1).

Such finding may be due to the lack of estrogen in urethra and vagina which could be terminated by colonization of these areas with Klebsiella (15).

Klebsiella may contained B cell or Th2 dependent antigenic epitopes associated with urinary tract or the antigen primed B cells migrates to an effector sites producing antibodies proximately to urinary tract (1,20).

The suppressive effect of menopause on mucosal immune response may be due to one or more of the followings: 1- an alteration in antigen uptake ,antigen reception by effector immune cells (21,22), 2- production of low affinity or low avidity antibodies, 3-lack of co stimulation signals 4- activation of suppressor T cells, 5- disturbance of Th1/ Th2 activities, 6- there
may be presence of peptide antigen T antagonizes (4,23,24).

There were 2ME sensitive fractions of mucosal antibodies among klebsiella UTI (table 1,2,3) can be serum transcudated fraction (7).

*K. pneumoniae* UTI in MWP, tow cases were with lack of UMIG may be due to ; 1-high catabolic rate of UMIG due to combat infection 2- Real lack of UMIG due to suppression of synthesis, 3-UMIG conc. too low to be precipitated by PEG 6000 6% (25,26,27).

Thus, on conclusion of this study one may state the followings:
1. Higher rates of klebsiella infections among MWP than AWP.
2. Low UMIG titres found among MWP than in AWP this may be due to ultred B and T cell functions.
3. 2 ME sensitive serum fraction was noted among some of cases.
4. Among, MWP, two cases with lack of UMIG were noted.

**References**


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12- O'Connell, C.J. 1980 Laboratory diagnosis of Infectious diseases 2nd ed. USA Medical examination Publication Co.


Table 1: Urinary tract Infection among Menopause, adulthood and normal subject women.

<table>
<thead>
<tr>
<th>I Parasite</th>
<th>K. Pneumoniae</th>
<th>K. oxytoca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uropathogen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram Reaction</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>motility</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Capsule</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>String test</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Shape</td>
<td>OR</td>
<td>OR</td>
</tr>
<tr>
<td>Growth on MA</td>
<td>LFC</td>
<td>LFC</td>
</tr>
<tr>
<td>Growth on BA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indole</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Citrate</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Vp</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Urea</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>II Host-Parasite Interaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyuria</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Haematuria</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Injured Parasite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MWP</td>
<td>2:71(2.816%)</td>
<td>1:71(1.40%)</td>
</tr>
<tr>
<td>m</td>
<td>1:71(1.40%)</td>
<td>0:71(0%)</td>
</tr>
<tr>
<td>AWP</td>
<td>0:32 (0%)</td>
<td>0:32 (0%)</td>
</tr>
<tr>
<td>Intact parasite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20:71 (28.169%)</td>
<td>9:71(12.676%)</td>
<td></td>
</tr>
<tr>
<td>7:32 (21.675%)</td>
<td>3:32 (9.275%)</td>
<td></td>
</tr>
<tr>
<td>III Infection Rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single MWP</td>
<td>22:71(30.985%)</td>
<td>10:71(14.1%)</td>
</tr>
<tr>
<td>AWP</td>
<td>7:32 (21.875%)</td>
<td>3:32 (9.275%)</td>
</tr>
<tr>
<td>NW</td>
<td>1:20 (5%)</td>
<td>0:20 (0%)</td>
</tr>
<tr>
<td>Mixed MWP</td>
<td>8:71(11.267%)</td>
<td>3:71(4.225%)</td>
</tr>
</tbody>
</table>

OR: Oval Rods
LFC : Lactose Fermenting Colonies
MA : MacConkey Agar
BA : Blood Agar

Table 2: Urinary Mucosal Immunoglobulin
titres specific for Klebsiellae.

<table>
<thead>
<tr>
<th>Titre</th>
<th>K. Pneumoniae</th>
<th>K. oxytoca</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M  A</td>
<td>M  A</td>
</tr>
<tr>
<td>2</td>
<td>-  -</td>
<td>-  -</td>
</tr>
<tr>
<td>4</td>
<td>7  3</td>
<td>3  -</td>
</tr>
<tr>
<td>8</td>
<td>11 6</td>
<td>1  -</td>
</tr>
<tr>
<td>16</td>
<td>1  1</td>
<td>1  1</td>
</tr>
<tr>
<td>32</td>
<td>1  -</td>
<td>1  -</td>
</tr>
<tr>
<td>64</td>
<td>-  1</td>
<td>-  1</td>
</tr>
<tr>
<td>128</td>
<td>-  -</td>
<td>-  -</td>
</tr>
</tbody>
</table>

M = Menopause
A = Adulthood

Table 3: Humoral Mucosal Immune Responses of Urinary Tract Infected Women.

<table>
<thead>
<tr>
<th>No.pt.</th>
<th>Age</th>
<th>MWP</th>
<th>Conc. g/L</th>
<th>Titre</th>
<th>No.pt.</th>
<th>Age</th>
<th>AWP</th>
<th>Conc. g/L</th>
<th>titre</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>47</td>
<td>Mean</td>
<td>1.69</td>
<td>7.5</td>
<td>7</td>
<td>18</td>
<td>1.49</td>
<td>24</td>
<td></td>
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<tr>
<td>49</td>
<td></td>
<td>Median</td>
<td>0.89</td>
<td>8</td>
<td></td>
<td>0.9</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Range</td>
<td>16.22</td>
<td>24</td>
<td></td>
<td>4.07</td>
<td>56</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>r= 0.5</td>
<td></td>
<td></td>
<td></td>
<td>r</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$\gamma^* = 146512 + 0.6X$</td>
<td></td>
</tr>
</tbody>
</table>

$\gamma^* = 0.5147 + 29.833X$
### Table 4: 't' statistic for the Menopausal effects.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Menopausal Titre</th>
<th>Adult Hood Titre</th>
<th>t statistic</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>cal.</td>
<td>tab.</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>7.5</td>
<td>24</td>
<td>2.261</td>
<td>0.025</td>
</tr>
<tr>
<td>K. oxytoca</td>
<td>7.6</td>
<td>37.3</td>
<td>2.101</td>
<td>0.05</td>
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</table>

### Table 5: Mucosal Immune Responses of Mixed infections.

<table>
<thead>
<tr>
<th>Mixed infection</th>
<th>UMIG g/L</th>
<th>Titre</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. pneumoniae and E. coli</td>
<td>0.3396</td>
<td>4.4</td>
</tr>
<tr>
<td>and S. epidermidis</td>
<td>0.5596</td>
<td>8.8</td>
</tr>
<tr>
<td>and S. epidermidis</td>
<td>0.6112</td>
<td>4.4</td>
</tr>
<tr>
<td>and S. epidermidis</td>
<td>0.6112</td>
<td>4.4</td>
</tr>
<tr>
<td>and St. pyogenes</td>
<td>0.3391</td>
<td>4.8</td>
</tr>
<tr>
<td>and Enterobacter</td>
<td>1.5923</td>
<td>8.4</td>
</tr>
<tr>
<td>K. oxytoca and E. coli</td>
<td>1.069</td>
<td>8.8</td>
</tr>
<tr>
<td>and S. epidermidis.</td>
<td>1.98</td>
<td>8.4</td>
</tr>
<tr>
<td>and St. pyogenes</td>
<td>11.153</td>
<td>16.8</td>
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</table>
Atrial Fibrillation in Acute Myocardial Infarction
Mohanad AL-Jashami

Abstract
The aim of this study is to assess the incidence and prognosis of atrial fibrillation (AF) during the first 72 hours among six hundred patients admitted to coronary care unit with acute myocardial infarction (AMI) in Diwaniyah Teaching Hospital from April 2004 to May 2006; and to determine the characteristics of the myocardial infarction – induced AF.

Full history and physical examination was taken and patients were followed in the coronary care unit (CCU) by monitoring and ECG facilities during the first 72 hours of onset. Atrial fibrillation was found in 96 patients (16%), 32 females and 64 males.

AF occurred in the first 24 hours in 56 patients (58%), recurrent in 24 patients (25%) and was transient (lasted less than 24 hours) in 80 patients (83%). Compared with patients without AF, those with this arrhythmia were older, had a higher frequency of heart failure (75% vs.50%) particularly in anterior myocardial infarction (94% vs. 54%) and of pericarditis (25% vs. 7%) and had a higher CCU mortality (38% vs. 15%).

As opposed to death rates close to (44%) among patients with anterior infarction, the presence of AF did not affect the mortality among patients with inferior infarction (17%).

Absence of heart failure, persistent arrhythmia (longer than 24 hours), ventricular rate (higher than 120 beats per minute) and recurrence of arrhythmia were not associated with increased mortality, while late onset AF after 48 hours were associated with higher mortality.

It is concluded that AF is not an uncommon arrhythmia after myocardial infarction and that its occurrence should signify a more guarded prognosis.

Introduction
AF is the most common sustained cardiac arrhythmia, with an overall prevalence of 0.5% in the adult population, rising to 10% or more in those over 75 years. In this arrhythmia the atria beat rapidly, chaotically and ineffectively; the ventricles respond at irregular intervals giving the characteristic irregularly irregular
pulse. The ECG shows normal but irregular QRS complexes; there are no P waves but the base line may show irregular fibrillation waves. The onset of AF can cause palpitation and may precipitate or aggravate cardiac failure in patients with abnormal heart.

Continuous ECG monitoring in acute myocardial infarction (AMI) has provided considerable information on the incidence of arrhythmias in this condition. AF is the most common atrial dysarrhythmia complicating myocardial infarction. Although the role of ventricular arrhythmias associated with AMI is well appreciated, controversy continues regarding the prognostic significance of AF. Some investigators found no increase in mortality related to the presence of AF, while other studies showed a greater overall early mortality rate in patients with anterior myocardial infarction.

In AMI atrial fibrillation frequently transient and may not require treatment. However, if the arrhythmia causes a rapid ventricular rate with sever hypotension or circulatory collapse, cardioversion by means of an immediate synchronized DC shock should be considered. AF is often a feature of impending or overt left ventricular failure, and therapy may be ineffective if heart failure is not recognized and treated appropriately. AMI often develops at rest or with normal activity. In many cases, it is the patient’s first clinical manifestation of coronary heart disease. Large databases have demonstrated a diurnal pattern of onset, with peak occurrence about 6 a.m. Clinical experience holds and evidence supports that vigorous physical exertion, especially in an otherwise sedentary individual, can contribute to triggering of AMI, as can emotional stresses such as anger.

**Patients and Methods:**

From April 2004 to May 2006 six hundred patients with AMI were admitted consecutively to CCU at Diwaniya Teaching Hospital. The diagnosis of AMI was based on the presence of at least two of the following three criteria:

1. Clinical history of chest pain, typically AMI results in severe chest pain lasting more than 30 minutes and unrelied by sublingual nitroglycerin.
2. ECG criteria of AMI or evolving infarction, the earliest ECG change is usually ST elevation, later on there is diminution in the size of the R wave, and in transmural (full thickness) infarction a Q wave begins to develop.
3. AMI causes a detectable rise in the plasma concentration of enzymes and proteins that are normally concentrated within cardiac cells, the most widely used enzyme in detection of MI is creatine kinase (CK), a more sensitive and cardiac specific isoform of this enzyme (CK-MB), and the cardio specific proteins troponins T and I (which were not available in our hospital), other enzymes are Aspartate aminotransferase (AST) and lactate dehydrogenase (LDH).

Anterior infarction was defined by the presence of ECG changes in leads 1, AVL, V1-V6 on the standard 12 lead ECG. Inferior infarction was defined by changes in lead 11,111,AVF, true posterior infarction defined by RS in lead V1 greater than 1.0 was included with inferior myocardial infarction. Combined referring to involvement of inferior plus anterior, lateral or septal wall. All patients were admitted within 24 hours of symptoms onset; the mean arrival time being six hours thirty minutes. Twelve lead ECG were recorded daily or whenever the patients had a new event or chest pain, in addition to continuous ECG monitoring for at least 72 hours and for 24 hours after the arrhythmia has stopped. A diagnosis of AF was made...
on the bases of a 12 lead ECG, by the absence of P wave and a variable degree of baseline fibrillary activity with the R-R intervals showing no ordered pattern. A clinical diagnosis of heart failure was established according to Framingham’s criteria with at least one major and two minor criteria. The major criteria include (paroxysmal nocturnal dyspnea, neck vein distention, rales, cardiomegaly, acute pulmonary edema, S3 gallop, increased venous pressure, positive heptojugular reflux). The minor criteria include (lower extremity edema, night cough, dyspnea on exertion, hepatomegaly, pleural effusion, vital capacity reduced by one third from normal, tachycardia).

Pericarditis was defined by the detection of a pericardial friction rub during hospitalization.

Patients who had AF on admission were included in this study but those known to have chronic AF were excluded as well as patients in whom AF was induced by DC shock for treatment of arrhythmias.

Statistical analysis was done using X^2 test with Yate's continuity correction to test the presence of association. Z test for the difference between two proportions was also used. Relative risk and confidence limit interval was calculated.

**Results**

A six hundred patients with AMI were included, their ages ranged between (33-85) years with a mean of (58.7+_9.8) years. Four hundred twenty two patients were male and 178 were females the male to female ratio was 2.8:1. AF was recorded in 96 patients (16%), their ages ranged between (48-70) years with a mean of (60.8+_6.3) years 64 of them were male and 32 of them were females making a male to female of 2:1. Table 1 shows that patients with an age of ≥ 60 years had a significantly 2.4 times risk of having AF than the younger ones (p < 0.05)

In 56 cases (58%) AF was either present on admission or began within 24 hours of the estimated time of infarct and 74 (77%) within 48 hours. Ten cases of AF occurred on the 3rd and 4th day after infarction. The cases lasted less than 24 hours were 80 (83%), out of them 56 (58%) lasted less than six hours. 16 cases had persistent AF (i.e.,> 24 hours). 61 patients (63%) had AF with a ventricular rate more than 120/min, 24 with a rate of 80-120/min and 12 with a rate less than 80/min. In 24 cases (25%) recurrent episodes of AF were recorded, twenty developed a second episode of AF within the first 24 hours. As shown in Table 2, there was no significant difference in the frequency of AF in relation to the location of AMI. Heart failure was more common among patients with AF than in remainder (75% vs. 50%), (p < 0.025). Heart failure was noted in almost all patients (94%) with anterior myocardial infarction and AF, as compared with those with out AF, the difference is highly significant (p < 0.005) while in those with inferior infarction and AF heart failure was less frequent (33%) an incidence comparable to those without AF. There was a significantly increased frequency of AF in patients with pericarditis compared to those without pericarditis (25% vs. 7%), (p < 0.005). Table 2 also demonstrates that the CCU mortality in patients with AF was significantly higher than those without AF (38% vs. 15%), (p < 0.01).

Relating the mortality rate to the location of infarction, we found that AF significantly increases the mortality rate in patients with anterior myocardial infarction (44% vs.16%), (p < 0.025) while on the contrary AF did not affect the mortality in patients with inferior myocardial infarction. Table 3 shows that AF in the presence of heart failure carried a significantly higher risk of death when compared to the patients with heart failure.
but without AF (p < 0.025), on the other hand AF did not significantly affect mortality in patients without heart failure.

Table 4: demonstrates the mortalities according to certain characteristics of the AF. It is obvious that the patients with late onset AF (> 48 hours) are significantly 3 times (p< 0.01) more liable to die than those with early onset AF. Although the patients with persistent AF (more than 24 hours) had a risk of death of 2.5 times, however, it is not significant statistically (p < 0.05). Ventricular rate more than 120/min, and recurrence of the arrhythmia did not affect the mortality.

Discussion

The incidence of AF of 16% in the present series of 600 patients admitted with AMI corresponds to the upper range of other reported series (7-20%) (1-3,8,13,18-22). AF is more common with increasing age.23 The present study reported a higher incidence of AF in the older age group, which is in accordance the results of previous studies.19,20,22

This is probably explained by the collagenous septa that develop in the atria with advancing age lead to no homogeneities in conduction and refractoriness which favor re-entry.23 The time of onset of AF in relation to onset of infarction is difficult to assess because it is difficult to determine precisely when the infarction occurs. When both occur before the patient reaches the hospital, it is difficult to determine whether the AF may have present before the infarction, but yet, the transitory nature of the arrhythmia suggested that previously undiagnosed chronic AF was unlikely. In this study 58% of the episodes began during the first 24 hours from the onset of symptoms with decreasing frequency throughout the next hours of monitoring.

These result were similar to the results found by Klass and Haywood18 and also agreed with Antman and Braunwald results.9 the higher incidence of AF during the first 24 hours could be explained by the fact that during the process of cell death there will be an increase in the release of catecholamine with electrolytes disturbances especially hypokalemia and hypomagnesaeemia; this process ceases with the maturation of infarction.24 Hod et al21 investigated the pathogenesis of AF in the early hours of an AMI in the population of patients who were admitted within three hours of the onset AMI. They suggested that acute left atrial ischemia is the path physiological mechanism of early AF. The majority of episodes (83%) of AF in our patients lasted less than 24 hours and usually less than six hours (58%), by this we concurred with Stannard1 and Klass18 who reported that AF complicating AMI is usually transient. In this study, there was no relation of AF to the site of infarction. Others1,4,13,18 have also demonstrated an equal distribution between anterior and posterior infarcts associated with AF. Robert and Kelly25 mentioned that atrial arrhythmias are more common with inferior infarction particularly with right ventricular involvement.

Others9,26 stated that AF occurs more frequently following anterior than inferior infarcts. Our data and previously reported studies8,10,26 point to the fact that AF is in most cases a pump failure arrhythmia. Left ventricular failure appears to be an attractive mechanism of AF in anterior myocardial infarction, as almost all patients (94%) with anterior myocardial infarction and AF having left ventricular failure, which in turn results in acute left atrial hypertension and distention.18,26 The increased atrial size would permit the coexistence many re-entrant circuits and is an important factor for the occurrence and maintenance of AF.23 From this we postulate that AF is secondary to failure rather than its cause, and the grave
prognosis of these cases is due to the homodynamic derangement.
The present study , however was unable to determine the temporal association of AF with congestive heart failure , and whether or not AF preceded or followed the development of heart failure . The observation that the appearance of AF during inferior wall infarction did not affect the prognosis supports the assumption that another , more benign mechanism may be responsible for the development of the arrhythmia in some cases .
The association between AF and pericarditis following AMI has been noted previously2, 12, 27. It is unclear whether pericarditis itself precipitates the arrhythmia or whether the associated large infarct size and chamber dilatation is responsible 12. In contrast to the generalized distribution of pericarditis of other etiologies, the pericarditis following infarction is typically localized to the site overlying infarction and thus unlikely to affect to affect the sinus or atrioventricular nodes 12.
The poorer prognosis of late onset AF (>48 hours) in the 25 cases reported in this study was attributed to other complications of myocardial infarction (shock and or sever congestive heart failure ) and the AF may have only been secondary to these insults.
We found that there was no correlation between the duration of AF and the prognosis ; a finding that differs from other previous reports 1, 18. The discrepancy noted between the relative risk (2.5) and the p value(> 0.05) in cases of persistent AF is due to a fewer number of patients involved .
Our data and previously reported studies 1, 8, 18-20 showed that patients with AF tended to have a higher mortality . Both Stanard and Stomman1, and Klass and Haywood 18 indicated that AF is in itself a Benign complication of myocardial infarction and that its prognostic significance relates to the severity of concurrent complications. Cristal

et al8 indicated that there is no cause and effect relationship between AF and the high mortality associated with it and the prognosis is related to the mechanism of production of AF and not to the arrhythmia itself. On the other hand , Helmers et al 19 considered AF an objective factor pointing to high risk patients

**Conclusion**

In our opinion AF is not an uncommon arrhythmia (16%) that complicates myocardial infarction early in the disease, and its development in the setting of acute anterior myocardial infarction or after the second day of infarction , predicts a poor prognosis and demands careful therapeutic intervention . Further study to assess the affect of therapeutic intervention on the mortality , in the above mentioned situations are recommended . Other associated complications of myocardial infarction were more common in the presence of AF , and their recognition can put the patients in a better clinical situations . So AF is not an uncommon arrhythmia after myocardial infarction and that its occurrence should signify a more guarded prognosis.

**References**

4. Julian DG, Vanlentine PA, Miller GG. Disturbance of the rate , rhythm and


Table 1: Incidence of AF according to age in 600 patients

<table>
<thead>
<tr>
<th>Age(years)</th>
<th>Total No.</th>
<th>AF%</th>
<th>RR</th>
<th>95% C.I.-RR</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>300</td>
<td>11.4</td>
<td>2.4</td>
<td>1.1-5.4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>300</td>
<td>4.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

RR: Relative risk
CI–RR = Confidence interval for the relative risk.

Table 2: Study subjects with and without AF (n = 600) according to the incidence, associated morbidity and mortality and to the site of AMI.

<table>
<thead>
<tr>
<th>Site Infarction</th>
<th>Anterior N=352</th>
<th>Inferoposterior N=192</th>
<th>Combined N=24</th>
<th>Non-Qwave N=32</th>
<th>Total N=600</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation</td>
<td>With</td>
<td>Without</td>
<td>With</td>
<td>Without</td>
<td>With</td>
</tr>
<tr>
<td>No. 64</td>
<td>%</td>
<td>%</td>
<td>No. 24</td>
<td>%</td>
<td>No. 168</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>60</td>
<td>94%</td>
<td>156</td>
<td>54%</td>
<td>8</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>16</td>
<td>25%</td>
<td>18</td>
<td>6%</td>
<td>8</td>
</tr>
<tr>
<td>C.C.U. Mortality</td>
<td>28</td>
<td>44%</td>
<td>50</td>
<td>17%</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 3: Mortality of 600 patients with AMI in relation to heart failure and AF.

<table>
<thead>
<tr>
<th>With Heart Failure</th>
<th>Total no.</th>
<th>Mortality rate (%)</th>
<th>RR</th>
<th>95% C.I.-RR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF + ve</td>
<td>72</td>
<td>44 %</td>
<td>2.5</td>
<td>1.2-5.2</td>
<td>&lt; 0.025</td>
</tr>
<tr>
<td>AF - ve</td>
<td>252</td>
<td>16%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Without Heart Failure</td>
<td>AF + ve</td>
<td>24</td>
<td>16%</td>
<td>1.4</td>
<td>o.3-6.8</td>
</tr>
<tr>
<td>AF - ve</td>
<td>252</td>
<td>12%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

N.S.=Non significant
Table 4: Mortality of 96 patients with AF according to the certain characteristics of the AF.

<table>
<thead>
<tr>
<th>Atrial Fibrillation</th>
<th>Total no.</th>
<th>Mortality rate (%)</th>
<th>R R</th>
<th>95% CI-RR</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset (Hours)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 48</td>
<td>25</td>
<td>80</td>
<td>3</td>
<td>1.18-1.1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>≤ 48</td>
<td>71</td>
<td>26.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Duration (Hours)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 24</td>
<td>24</td>
<td>75</td>
<td>2.5</td>
<td>0.8-7.5</td>
<td>N.s.</td>
</tr>
<tr>
<td>≤ 24</td>
<td>72</td>
<td>30</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ventricular Rate (bpm)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 120</td>
<td>58</td>
<td>40</td>
<td>1.2</td>
<td>0.6-2.2</td>
<td>N.s.</td>
</tr>
<tr>
<td>≤ 120</td>
<td>38</td>
<td>33.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No. Of Episodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recur.</td>
<td>24</td>
<td>50</td>
<td>1.5</td>
<td>0.6-4</td>
<td>N. s.</td>
</tr>
<tr>
<td>Single</td>
<td>72</td>
<td>33.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

b.p.m. = beats per minute
Abstract
Dental cares is epidemic modern disease, patients in mix-dention stage age (6-11) years old and this cause difficulty to continue their normal life, eating, social behavior and the higher cost in there treatment, we collect (221) child there age between (6-11) years old in Hilla town, random sample selection, our examination applied to this samples according to (MOH) roles and after teeth perishing and bit wing radiograph technical for diagnosis together with clinical examination, also we applied case sheet for each sample for statistic purpose. According to this study the samples had (41.7%) caries teeth within age (6-11) years old had seen with the condition of this study and Clinical examination about(58.3%) highly sensitive and effective in diagnosis of teeth cavitations decay stage in correlation with radiographic examination which is about (57%) effective in getting early diagnosis of initial teeth decay and the extension of the decay within tooth tissue and its relation to the tooth tissue changes.

Introduction:
Dental caries is epidemic modern disease, we directed our project to study in patient in mix-dention stage age (6-11) years old and this cause difficulty to continue their normal life, eating, social behavior and the higher cost in there treatment, in Iraq there are higher incidences for dental caries level in all childhood under 12years. Decay experience in a community is measured by evaluating the total effects of the carious process (past and present) up to the time of the examination. It is measured in terms of Decayed , Missing, or Filling Teeth or Surface, i.e. DMFT or DMFS , for permanent teeth capital letters are used while small letters are used for the primary dentition. These definitions (1) serve as reference for the following material. Epidemiological surveys indicate that the dental needs of young children are high. The results are presented by age groups. Before

Evaluation of Dental Caries and Diagnosis types in Mixdentin:
(In Vivo Study)
Ameer H.AL.Amiedy
any treatment is performed, a thorough examination including appropriate radiograph is necessary to obtain diagnostic records. Also included should be a medical, familial and dental history, an assessment of the child's cooperative ability, the occlusion, and the oral home care. From the epidemiological surveys the clinician should direct particular attention to those areas which are commonly decayed in the respective age groups.

**Aim of the study**

1- Evaluation of dental cares in the mix-dent ion age.

2- comparesme between different diagnose tool of the dental cares.

**Material and Method**

Case of study collection: we collect (221) child there age between (6-11) years old in Hilla town, random sample selection, our examination applied to this samples according to (MOH) roles and after teeth perishing and bit wing radiograph technical for diagnosis together with clinical examination, also we applied case sheet for each sample for statistic purpose, and than take the stander deviation to the number of decidue and permanent cares and filled tooth, with the number permanent teeth within the mouth sample as in table (1).

**Discussion**

Since the location and diagnosis of individual lesion are discussed in subsequent chapters, an outline only will be given here. Occlusal lesions in primary molars are more common than inter-proximal lesion in pre-school children (2). In these young children posterior contacts may not close until age 3 years, which may explain this observation: however, once posterior contacts close, the prevalence of inter-proximal lesions will increase. Second primary molars have more occlusal lesion than first primary molars, likewise the mandibular molars have more than the maxillary because of the depth and anatomy of the occlusal fissures. The labial and lingual surfaces of primary teeth seldom decay, except in the nursing bottle mouth syndrome. Mandibular primary incisors seldom decay, probably because of the spacing that occurs in the area and their close proximity to the duct of salivary sub- mandibular salivary gland, which means that they benefit from the diluting and buffering properties of saliva. The newly erupted first permanent molars and permanent incisors have morphologic areas which are susceptible to plaque retention and subsequent development of caries. These are the occlusal surface in
permanent molars, the lingual development pit and groove in mandibular permanent molars, and lingual pits in maxillary permanent incisors, notably the lateral incisor. Probably because of the depth and inclination of the occlusal fissure, the mandibular permanent molars decay more frequently than maxillary molars. In addition to these susceptible areas, the closing of posterior contacts will result in the development of class two lesions. At age seven years, there will be more molar inter-proximal lesions than occlusal lesions; this prevalence is reversed at age nine years (2).

For discus dental caries areas there are two reasons for this:

A-More permanent molars will exhibit occlusal decay at age nine, and secondly, some primary molars will be exfoliated to reduce the prevalence of posterior inter-proximal lesion. In the mixed-dentition the mesial surface of the first permanent molar is placed at risk if dental caries affects.

B- Primary molar. Also, the inter-proximal surface of maxillary incisors may be at risk in those children with closed anterior contacts and a high dental caries incidence.

The need for bite-wing radiographs to diagnose inter-proximal lesions cannot be overemphasized: Heennon et al. (1969) observed that 75% of these Class two lesions would be undiagnosed without bite-wing radiograph (3). When considering inter-proximal lesion in primary molars, the clinician must remember that the distance between external enamel surface and pulp is smaller in primary than permanent teeth. A Class two lesion into dentine on one primary molar surface is often accompanied by enamel decalcification on the adjacent primary tooth; such decalcifications, or radiograph etches of enamel, frequently exhibit histological carious penetration to the dentine (4). The presence of inter-proximal molar lesions in one quadrant should encourage the clinician to look critically for similar lesions in other quadrants (5). Even if they are not present, it is not uncommon for such lesions to become apparent clinically within a year if a truly effective preventive program is not implemented. When deciding on the need to restore incipient lesions, the clinician should assess the child's caries incidence (from previous
dental care), the anticipated response to preventive care, and the regularity of dental visits.

Analysis of these bite-wing radiographs are taken compared to the examination. I believe that many inter-proximal lesions therefore remain undiagnosed and that the real (dmft and DMFT indexes) would be higher than those reported in these publications. However, it can be said certainty that 75% of the school-age children will exhibit dental caries, although this figure may indeed be closer to 100 per cent in un fluoridated communities (6), while according to this study we have 58.3% non caries teeth while 41.7% decay teeth within age (6-11) years old in Hilla town as see with condition of this study as seen in diagram number (4).

Table (3) and Diagram (2-3-4-5) relation between clinical and radiographic dental decay diagnosis. as we can say that the correlation obtain in numbers of deep and cavitations decay during clinical examination (100+262), while the value of teeth number in radiographic examination (61+100) of this examine samples. So the clinical examination is more accurate and sensitive than radiographic examination. During clinical teeth cavitations decay examination in table number (4) the result was this study fined more sensitive than radiographic examination in diagnosis the distractive teeth decay.

From Table (4) the radiological view for all clinical stages in mixdention teeth and Table (3) and when we correlated between this tables and with exclude the normal diagnostic teeth (we use only clinical diagnose decay teeth only with radiographic diagnose normal and teeth decay), we found radiographic diagnose in early and initial dental decay is more perfect and sensitive. And diagram (4-5) we can conclude the perfect and effectiveness of the radiographic examination in diagnosis of the teeth decay than clinical examination especially initial teeth decay in relation to these diagrams and the table.

**Conclusions**

1- According to this study the samples had (58.3%) non caries teeth while (41.7%) caries teeth within age (6-11) years old had seen with the condition of this study.

2- Clinical examination helped in diagnosis of teeth cavitations decay
stage in correlation with radiographic examination which is more effective and sensitive in getting early diagnosis of initial teeth decay and the extension of the decay within tooth tissue and its relation to the tooth tissue changes than the clinical examination in early stage or initial dental decay.

References


Table (1) Sample Cause Selection.

<table>
<thead>
<tr>
<th>age</th>
<th>Samples number</th>
<th>dmft index</th>
<th>DMFT index</th>
<th>SD,Permanent teeth numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>32</td>
<td>1.1</td>
<td>0.6</td>
<td>4.2</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>5.8</td>
<td>0.5</td>
<td>7.1</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>5.1</td>
<td>1.3</td>
<td>9.8</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>4.1</td>
<td>1.5</td>
<td>11.9</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>5.1</td>
<td>1.7</td>
<td>13.2</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>4.5</td>
<td>1.9</td>
<td>16.4</td>
</tr>
</tbody>
</table>

Diagram (1) Child study samples
Table (2) values of examine teeth.

<table>
<thead>
<tr>
<th>X-Ray Examine</th>
<th>Clinical Examine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caries teeth</td>
<td>No carious teeth</td>
</tr>
<tr>
<td>161(18.5%)</td>
<td>707(81.5%)</td>
</tr>
<tr>
<td>Caries teeth</td>
<td>No carious teeth</td>
</tr>
<tr>
<td>362(41.7%)</td>
<td>506(58.3%)</td>
</tr>
</tbody>
</table>

Table (3) Relation between clinical and radiographic dental decay diagnosis in values.
*We find the percent of accuracy of cavitations and deep dental decay increase in clinical examination than that in radiographic examination.

<table>
<thead>
<tr>
<th>Clinical examine</th>
<th>X-Ray examine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>Decayed tooth</td>
</tr>
<tr>
<td>707 (81.5%)</td>
<td>262 (72.4%)</td>
</tr>
<tr>
<td>161 (18.5%)</td>
<td>100 (27.6%)</td>
</tr>
<tr>
<td>868 (100%)</td>
<td>362 (100%)</td>
</tr>
</tbody>
</table>

72.4%+27.6%=100%* Sensitivity of Clinical examination
12.1%+27.6%=39.7% Sensitivity of Radiograph examination

Diagram (2) clinical teeth samples examination
Diagram (3) Radiographic teeth samples examination

Diagram (4) Relation between clinical and radiographic examinations of the Dental cares of permanent molar in the samples
Table (4) Dental decay values variation in difference stages.
* High percent mean radiographic examination more active or more sensitive than clinical examination in early stage or initial dental decay samples.

<table>
<thead>
<tr>
<th>Clinical examine</th>
<th>Non caries teeth</th>
<th>X-Ray examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>262 (72.4%)</td>
<td>15 (50%)</td>
<td>362 (100%)</td>
</tr>
<tr>
<td>100 (27.6%)</td>
<td>15 (50%)</td>
<td>100 (27.6%)</td>
</tr>
<tr>
<td>362 (100%)</td>
<td>30 (100%)</td>
<td>362 (100%)</td>
</tr>
<tr>
<td>262 (44.8%)</td>
<td>0%</td>
<td>262 (44.8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulp decay invasion</th>
<th>Dentin or enamel decay cavitations</th>
<th>Enamel decay</th>
<th>Initial decay</th>
<th>Non caries teeth</th>
<th>Decay teeth</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 (50%)</td>
<td>24 (57.1%)</td>
<td>139 (76%)</td>
<td>84 (78.5%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>15 (50%)</td>
<td>18 (42.9%)</td>
<td>44 (24%)</td>
<td>23 (21.5%)</td>
<td></td>
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<tr>
<td>30 (100%)</td>
<td>42 (100%)</td>
<td>183 (100%)</td>
<td>107 (100%)</td>
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</tr>
<tr>
<td>0%</td>
<td>6 (14.2%)</td>
<td>95 (52%)</td>
<td>61 (57%)*</td>
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</tr>
</tbody>
</table>

Diagram (5) Clinical teeth decay dental in relation to radiographic examinations
Abstract

Non–melanoma skin cancers like basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are not uncommon skin diseases in Iraqi patients, so this study was conducted to shed light on various clinical and histopathological aspects of these cancers affecting the face, at Hilla city.

A total of 50 patients with non–melanoma skin cancers was seen. Their ages ranged between 10 – 85 years (mean ± SD, 54.9 ± 16.1 years), while their ages of onset ranged between 7 – 80 years (mean ± SD, 52.4 ± 15.5 years). The duration of the disease ranged from 1-7 years (mean ± SD, 2.9 ± 1.5 years). There were 28 males (56%) and 22 females (44%) with a sex ratio of 1.3 : 1.

Twenty–nine patients with basal cell carcinomas were seen (58%). There ages ranged between 30 – 85 years (mean ± SD 58.4 ± 13.9 years), while their ages of onset between 29 – 80 years (mean ± SD, 50.7 ± 18.4 years). The duration of the disease ranged between 1-7 years (mean ± SD, 3.4 ± 1.4 years). There were 16 males (55%) and 13 females (45%) with a sex ratio of 1.2 : 1. The clinical types of BCCs on the face were : nodulo–ulcerative (38%), pigmented (14%), morpheaform (4%) and cystic (2%). The sites of involvement of BCCs on the face were : nose (16%), cheeks (14%), forehead (12%), inner canthi of eyes (6%), upper vermilion lip (4%), retroauricular (4%) and inside the auricle of left ear (2%). The pathological types of BCCs were : nodular (40%), pigmented (14%) and morpheaform (4%). The clinical types of BCCs, the sites of involvement on the face and the pathological features were comparable to what has been reported.

Eighteen patient with squamous cell carcinomas were seen (36%). Their ages ranged between 10 – 70 years (mean ± SD, 48 ± 19 years) while their ages of onset between 7 – 68 years (mean ± SD, 54.6 ± 10.6 years). The duration of the disease ranged between 1 – 3 years (mean ± SD 1.5 ± 1.6 years). There were 9 males (50%) and 9 females (50%) with a sex ratio of 1 : 1. The sites of involvement of SCCs on the face were : cheeks (16%), lower lip (8%), upper lip (4%), forehead (4%), nose (2%) and pinna of left ear (2%). The pathological types of SCCs were : well differentiated (16%), moderately well differentiated (18%) and poorly differentiated (2%). The
clinical, histopathological and sites of involvement were similar to what has been reported. The study presented the first reported case of SCC arising from a scar of localized atrophic discoid lupus erythematosus on the upper lip, in Iraq.

Other non-melanoma skin cancers of the face reported in the study were: basosquamous (2%), mycosis fungoides (2%) and kaposi’s sarcoma (2%).

Introduction

Basal cell carcinoma (BCC) is a malignant tumor of skin composed of cells similar to those in the basal area of the epidermis and its appendages (1). Although a cancer, BCC is only locally invasive and rarely metastasizes (1, 2). Basal cell carcinoma is the most common form of skin cancer (3, 4). It crops up most commonly on the faces of the middle aged or elderly (3). BCC is generally a disorder of white individuals especially those with very fair skin (5). Men have a significantly higher incidence than women (6). The male : female ratio is approximately 3 : 2 (5). The tumor may occur at any age but the incidence of BCC increases markedly after age of 40 years. The incidence in younger people is increasing possibly as a result of increased sun exposure (7). Eighty – five percent of all BCCs appear on the head and neck region, 25 – 30% occur on the nose alone, the most common site (7). nodulo-ulcerative type is the most common type(3). The typical BCC runs a slow progressive course of peripheral extension which produces the thread – like margin, the nodule with a central depression or the expanding rodent ulcer (1). Other variants are cystic, cicatricial ( morpheic), superficial and pigmented (3). Lesions of pigmented BCC contain increased brown or black pigment and are seen more commonly in individuals with dark skin (8).
characteristic cells of BCC (basalioma) cells have a large oval or elongated nucleus (9). The nuclei resemble those of basal cells of the epidermis but basalioma cells differ from basal cells by having a larger ratio of nucleus to cytoplasm and by not showing intercellular bridges (9). The peripheral cell layer of the tumor masses shows a palisade arrangement of the nuclei (9, 10).

Squamous cell carcinoma (SCC) is a malignant tumor arising from the keratinocytes of the epidermis (1). SCC does not often arise from healthy looking skin. Commonly there are signs of damage from sunlight: solar elastosis of the dermis, hyperkeratosis, irregular pigmentation and telangiectasia of the skin or leukokeratosis and fissuring of the lip. The first evidence of malignancy is induration. The area may be plaque-like, verrucous, tumid or ulcerated, but in all cases, the lesion feels firm when pressed between the finger and thumb. The most common sites for SCC are those most exposed to the sun, they occur on the upper part of the face and especially in males on the lower lip and pinna of ear (1). The incidence increases rapidly with age and sun exposure and is approximately twice as high in men as in women (4). Cutaneous SCC that arise secondary to inflammatory and degenerative processes (previous x – radiation or thermal injury, chronic ulcers, chronic inflammation or Bowen's disease) have much higher rate of metastasis than those developing in sun-damaged skin (3, 9).

Squamous cell carcinoma is a true invasive carcinoma of the surface epidermis (9). On histological examination, the tumor consists of irregular masses of epidermal cells that proliferate downwards into the dermis. The invading tumor masses are composed in varying proportions of normal squamous cells and atypical (anaplastic) squamous cells. Atypicality of squamous cells expresses itself in such changes as: great variation in the size and shape of the cells, hyperplasia and hyperchromasia of the nuclei, absence of intercellular bridges, keratinization of individual cells and the presence of atypical mitotic figures (9). Differentiation in SCC is in the direction of keratinization. Keratinization often takes place in the form of horn pearls which are very characteristic structures composed of concentric layers of squamous cells showing gradually increasing keratinization towards the center (9).

Aim of study:

Non-melanoma skin cancers like BCC and SCC are not an uncommon skin
diseases in Iraqi patients, so the aim of this work was to shed light on various clinical and histopathological aspects of these cancers affecting the face; at Hilla city.

**Patients and methods:**

A total of 50 patients with non–melanoma skin cancers were studied in department of dermatology, Merjan teaching hospital during the period from July 2005 to December 2007.

A clinical history was taken from each patient including: name, age, sex, age of onset and duration of disease; symptoms related to the lesion like pain, itching, bleeding and tenderness were recorded; and predisposing medical conditions such as albinism, xeroderma pigmentosa, epidermo dysplasia verruciformis, organ transplantation and any immune compromised state.

A thorough physical examination was performed to determine general health, type of tumor, site on the face and number of lesions. Also by examination, we tried to exclude the presence or absence of lymphadenopathy. Shaving or incisional biopsies were obtained in all patients. The biopsies were kept in 10% formalin solution and sent for histopathological examination with hematoxylin and eosin staining methods.

**Results:**

A total of 50 patients with non–melanoma skin cancers (NMSCs) was seen, their ages ranged between 10 – 85 years with a mean ± standard deviation (SD) of 54.9 ± 16.1 years, while their ages of onset ranged between 7 – 80 years with a mean ± SD of 52.4 ± 15.5 years. The duration of the disease ranged from 1 – 7 years with a mean ± SD of 2.9 ± 1.5 years. There were 28 males (56%) and 22 females (44%) with a sex ratio of 1.3 : 1. Regarding the age of presentation, the bulk of the patients was between 40 – 80 years of age. Most of the cases were in the 6th decade of life forming about 30% (Figure I).

Regarding the age of onset, most of the cases started in the 6th decade of life forming about 40% (Figure II).

The types and numbers of cases of non–melanoma skin cancers seen in this study were shown in table (1).

Twenty-nine patients with basal cell carcinoma were seen (58%). Their ages ranged between 30 – 85 years with a mean ± SD of 58.4 ± 13.9 years, while their ages of onset between 29 – 80 years with a mean ± SD of 50.7 ± 18.4 years. The duration of the disease ranged between 1 – 7 years with a mean ± SD of 3.4 ± 1.4 years. There were
16 males (55%) and 13 females (45%) with a sex ratio of 1.2 : 1.

Clinical types of BCCs and sites of involvement were shown in tables (2) and (3) respectively.

The majority of patients (19) were in the form of nodular and noduloulcerative which was the classical presentation with a pink pearly shaped border, the surface of some was covered with a telangiectatic vessels figure (1). The size of lesions ranged from 0.5 – 3 cm in diameter.

Pigmented BCCs were seen in 7 patients. Clinically, it was the same of nodular type but with black color figure (2). Morphea form or sclerosing BCC was seen in 2 female patients, one on the nasal tip and the other on the right cheek. The lesions were firm yellowish with a waxy surface and ill-defined borders.

Cystic BCC was seen in one patient in left cheek of a 35 years old man as a smooth round pinkish cystic lesion with a telangiectatic vessels on the surface.

Nose, cheeks and forehead were the common sites of involvement of BCC on the face. Two cases of BCC, pigmented and noduloulcerated were seen on the vermilion border of the upper lip and a case of nodular lesion was seen inside the auricle of left ear figure (3).

The histopathological picture was corresponding with the clinical picture table (4). The classical picture was masses of basophilic cells (basalioma cells) invading the dermis with a palisading arrangement of nuclei at the periphery of these masses figure (4).

In pigmented BCC, in addition to tumor masses in the dermis, there was heavy deposition of brown pigment within melanophages surrounding these masses of basophilic cells. In morphea form BCC, small groups of closely packed tumor cells arranged in elongated strands and embedded in a dense fibrous tissue of the dermis.

Eighteen patients with SCCs (36%) were seen. Their ages ranged between 10 – 70 years with a mean ± SD of 48 ± 19 years, while their ages of onset between 7 – 68 years with a mean ± SD of 54.6 ± 10.6. The duration of disease ranged between 1 – 3 years with a mean ± SD of 1.5 ± 1.6 years. There were 9 males (50%) and 9 females (50%) with a sex ratio of 1 : 1.

Clinically, the patients with SCC presented as a hard indurated plaques or nodules, some were ulcerated. The majority arised from areas damaged by sunlight in actinic keratosis or solar cheilitis of lower lip especially. Cheeks and lower lip were the common sites of involvement table (5).
A 50 years old female patient with an old scar of localized atrophic discoid lupus erythematosus in a butterfly distribution on the face developed SCC on the part of the scar located on the upper lip (11) figure (5).

Two children female patients 10 years old with xeroderma pigmentosus which is a rare autosomal recessive disease in which there is a defect of repair of DNA damage by exposure to sunlight because of deficiency of an endonuclease enzyme which is responsible for this repair of DNA damage. Patient suffer from severe photosensitivity, hypo and hyper pigmentation, early aging process and skin tumors at an early age (12). These patients developed SCC on the cheeks and nose figure (6).

In one male patient, SCC presented as a hard circumscribed conical markedly hyperkeratotic lesion on the pinna of the left ear (cutaneous horn).

Pathological types of SCCs were shown in table (6). Nearly all the types may be in the form of well differentiated or moderately well differentiated. The dermis was invaded by masses of squamous epithelial cells, some were large and others were small in size with loss of polarity. Several horn pearls were present in the majority of cases figure (7). Others contain few horn pearls in addition to individual cell keratinization (dyskeratosis). Well differentiated carcinomas showed marked lymphocytic inflammatory infiltrate surrounding tumor masses. One poorly differentiated SCC showed no evidence of keratinization (no horn pearls or dyskeratosis) with absence of inflammatory infiltrate. There was only atypical tumor cells.

A 60 years old male patient presented with ulcerated lesion on the upper lip with a pearly shaped border. Clinically looking as BCC but on histopathological examination, had features of both BCC and SCC, so this type was called a basal squamous cell carcinoma or metatypical BCC (1). The cells were larger with a larger paler nucleus than in the classic BCC and have a more eosinophilic cytoplasm.

A 55 years old male patient with a hard pinkish ulcerated plaque 2 × 2 cm on the forehead. The patient also had tumid plaques and nodules, some were ulcerated affecting the trunk on the chest and back of 3 years duration. Histopathological examination revealed a diffuse inflammatory infiltrate of lymphocytes in the upper dermis in a band – like, many of the cells were atypical, some infiltrating the epidermis (epidermotropism) forming in
some sites a pautrier microabcesses. So this was a case of mycosis fungoides which is a type of cutaneous T–cell lymphoma.

A 70 years old male patient presented with multiple hard dark brown nodule involving both ears bilaterally symmetrical. These nodules coalesce together forming a cauliflower –like picture figure (8). The patient also had multiple violet nodules and plagues affecting upper and lower limbs with genitalia. The duration of the disease was about 1 year. Histopathology showed proliferation of spindle cells, protruding endothelial cells of capillaries and extravasation of red blood cells. These clinical and pathological pictures consistent with classical Kaposi sarcoma.

In all cases of non–melanoma skin cancers of the face, metastasis to regional lymph nodes was not noticed.

Discussion:

Basal cell carcinoma is the most common form of skin cancer, seen commonly on the faces of the middle age or elderly. Male to female ratio is about 3 : 2 and the incidence increases markedly after age of 40 years (5). In our study, BCC was the commonest type of non–melanoma skin cancers of the face forming about 58 % of the cases. Most BCC cases were between the ages 50 – 80 years. The male to female ratio was about 1.2 : 1. This finding was comparable to those reported in the literature (3,5).

Noduloulcerative was the commonest type of BCC. Nose, cheeks and forehead were the commonest sites of involvement. The clinical types of BCC and sites of involvement of the face, in the present study were comparable to what has been published (3,7). Regarding the sites of BCC in this study, 2 patients with BCC ( pigmented and nodulo ulcerative ) were seen on the vermilion border of the upper lip. This finding was also comparable to a study of 18 cases of BCC which involved predominantly the vermilion lip which include the vermilion border and the outer mucosal surface of the lip (13). These sites are rarely involved by BCC.

BCC was also seen in sites not exclusively with maximum exposure to sunlight like inner canthus of both eyes, behind the ears and inside the auricle of left ear (6 patients). This may indicate that regional factors perhaps related to the density and type of pilosebaceous follicles are important in determining the distribution of the tumor and distribution of the lesions on the face(1). The histopathological features of different types of BCC were similar to what has been reported (9,10).
Squamous cell carcinoma was the next common non-melanoma skin cancers of the face forming about 36% of cases with an equal male to female ratio 1:1. This contradicts to what has been reported in the literature which shows that men are twice affected as women with a sex ratio of 2:1. This probably because of a relatively small number of cases was taken during the study period (18 cases).

The clinical, histopathological and sites of involvement of SCC in our study were similar to what has been reported (1,3,9). The prevalence and distribution of lesions of SCC correlates well with the exposure to ultraviolet radiation. In the presort work, there was a first reported case of SCC arising from a scar of localized atrophic discoid lupus erythematosus on the upper lip, in Iraq (14).

Other non-melanoma skin cancers reported in this study were baso squamous, mycosis fungoides and Kaposi sarcoma (2%) for each one.

The biological significance of baso squamous carcinoma is that this pathological pattern is associated with a significantly higher incidence of metastatic spread (1).

The finding of hard indurated plaque on the forehead of our patient with mycosis fungoides was comparable to a previous Iraqi study of 20 patients with mycosis fungoides (1998) in which 3 patients (15%) with tumor stage, nodular lesions some fungating with ulceration were involving the face.

Ears involvement, bilaterally symmetrical in our patient with kaposi sarcoma was the first reported site of face involvement in Iraqi patients. In a previous Iraqi study, face was also involved and mucosal involvement was detected in 10% of the cases in the form of macules or papules on the hard palate and ulcerative lesions on the tongue (15).

References:


Figure I: Age of presentation for NMSCs of the face.
Figure II: Age of onset for NMSCs of the face.

Table 1: Types of NMSCs of the face:

<table>
<thead>
<tr>
<th>Type</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma</td>
<td>29</td>
<td>58%</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>18</td>
<td>36%</td>
</tr>
<tr>
<td>Baso squamous carcinoma</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Mycosis fungoides</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 2: Clinical types of BCCs on the face:

<table>
<thead>
<tr>
<th>Clinical type of BCC</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodulo – ulcerative (rodent ulcer)</td>
<td>19</td>
<td>38%</td>
</tr>
<tr>
<td>Pigmented</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Morpheaform</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Cystic</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>
### Table 3: Sites of involvement of BCCs on the face:

<table>
<thead>
<tr>
<th>Site of BCC</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Cheeks</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Forehead</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>Inner canthi of eyes</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Upper vermilion lip</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Retro auricular</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Inside auricle of left ear</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

### Table 4: Pathological types of BCC of the face:

<table>
<thead>
<tr>
<th>Pathology of BCC</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>Pigmented</td>
<td>7</td>
<td>14%</td>
</tr>
<tr>
<td>Morpheaform</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>

### Table 5: Sites of involvement of SCCs on the face:

<table>
<thead>
<tr>
<th>Site of SCC</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheeks</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Lower lip</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td>Upper lip</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Forehead</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Nose</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Pinna of left ear</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>
Table 6: pathological types of SCC of the face:

<table>
<thead>
<tr>
<th>Pathology of SCC</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well differentiated</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Moderately well differentiated</td>
<td>9</td>
<td>18%</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Figure (1): Nodular BCC involving the nose.*
Figure (2): Pigmented BCCs involving right cheek and the side of the nose.
Figure (3): Nodular BCC inside the auricle of left ear.
Figure (4): Histopathology of classical BCC showing masses of basophilic cells invading the dermis with peripheral palisading (H & E, x40).
Figure (5) : SCC involving the scar of atrophic discoid lupus erythematosus.
**Figure (6)**: SCC in xeroderma pigmentosa patient.
Figure (7): Histopathology of well differentiated SCC showing squamous cells invading the dermis with multiple horn pearls and dyskeratosis (individual cell keratinization) (H & E, x400).
Abstract
This work aims to study the infectious etiological agents of common bacterial pathogens associated with burn wound infections.

In this study, 56 samples were collected from patients with burn wound infections in Hilla Surgical Teaching Hospital. A total of 47 samples showed bacterial growth, identified as following: Pseudomonas aeruginosa (31 isolates), Staphylococcus aureus (6 isolates), Klebsilla spp. (4 isolates), E.coli (4 isolates), and Proteus spp. (2 isolates) whereas the reminder (9) samples showed no bacterial growth.

The effect of some antibiotics on these bacterial isolates was studied, and the results showed that Amikacin was the most effective antibiotic among them. The ability of \textit{Pseudomonas aeruginosa} to invade tissues depends production of extracellular enzymes(proteases).

Introduction
Burn injuries by fire and hot liquids and contact with hot surfaces have been recognized as a significant and major public health problem. \textit{Pseudomonas aeruginosa} is one of the most important and most common causes of serious infections in burn patients [1,2].

The invasive type burn wound infections is characterized by green pigment visible in subcutaneous fast, which is erythematous and later becomes (a black, necrotic, nodular lesion) ecthyma gangrenosum vesicular lesions and crusted serrated margins of partial– thickness facial burns are characteristic of burn wound infection of viral origin. [3,4]

Consequently broad –spectrum antibiotics are routinely used in the treatment of bacterial burn infections. The many antibiotics in use is the group of (Aminoglycosides) particularly amikacin [5].

Aminoglycosides groups were more effective in the treatment of burns infections than some other broad spectrum antibiotics e.g.
ceftaxime, carbencillin, Amoxycillin, and tetracycline[6]. This work was carried out to study the bacteriological agents of burn wound infection.

Materials & methods

* patients: -
Swabs of burn infections were obtained from fifty-six patients with age range from(2-70) years, who where attendants of burn unit in Hilla teaching hospital during the period of five months (October 2007-February 2008).

* Specimens: -
Swabs of bacterial cultures were collected from patients suffering from burn infections and the swabs were put into transport medium in the sterilized swab tube, then they were sent to the investigating laboratory within two hours of collection, where they were placed & inoculated onto medium [7].

Inoculating the swabs onto Blood agar enriched with 5% human blood and MaConky agar.

Laboratory Diagnosis:

According to the diagnostic procedures recommended by [8,9] The isolation and identification of bacteria were performed as follows:

**A single colony was taken from each primary positive culture and its diagnosis depended on the morphology properties and then colonies were selected and investigated by gram stain to observe a specific shape, color and aggregation. After staining specific biochemical test were done to reach the final identification such as (catalase test, Oxidase test).

Pseudomonas produce indophenol oxidase, an enzyme that renders them positive. This test frequently used in diagnosis to discriminate them from other gram-negative bacteria.

Colonies of Pseudomonas aeruginosa are distinguished from other bacteria of this genus by production of the water-soluble pigment pyocyanin and pyoverdin giving them a characteristic blue-green color on agar plates also the colonies have a characteristic fruity or grappa-like odor.[10,11]

**Antibiotic sensitivity test (Kirby-Bauer method).

It was performed by using a pure culture of previously identified bacterial isolate. A sterile swab was used to obtain an inoculum from standardized culture. This inoculum then was streaked on a Muller, Hinton plate [12].

***Protease:

One of the major virulence factor of Pseudomonas aeruginosa is the ability to produce extra cellular protease.

Results

In the tables

Discussion

Infection is one the most serious complication in burn patients and Pseudomonas especially Pseudomonas aeruginosa, is the most important resistant, and dangerous organism in burn wound infection[13].

In this study, Pseudomonas aeruginosa was found to be the commonest pathogens causing wound infection and bacteremia in burn patients.

Pseudomonas is notorious for its resistance to antibiotic, there fore aparticular dangerous and dreaded pathogen. The bacterium is naturally resistant to many antibiotics due to the permeability barrier afforded by its outer membrane LPS. Also, its tendency to colonize surface in a biofilm form makes the cells impervious to therapeutic concentration antibiotic.

The ability of Pseudomonas aeruginosa to produce two extracellular proteases have been associated with virulence that exert their activity at the invasive stage:

: elastase and alkaline protease. Elastase has several activities that relate to virulence. The enzyme cleaves collagen, IgG, IgA, and complement component. Alkaline protease interferes with fibrin formation and will lyse
Fibrin. Together, elastase, and alkaline protease destroy the ground substances of the cornea and other supporting structures composed of fibrin and elastin. Elastase and alkaline protease together are also reported to cause the inactivation of gamma interferon (IFN) and tumor necrosis factor (TNF). The use of penicillin led to the emergence of staphylococcus aureus as the commonest gram-positive early colonizer of burn wounds. As staphylococcus can be seeded into the circulation from an abscess, early diagnosis and prompt drainage can minimize or prevent haematogenous dissemination of staphylococcus infection. The subsequent development and use of broad-spectrum antibiotic effective against Staphylococcus led to the emergence of gram-negative organism, particularly Pseudomonas aeruginosa, as the predominant organism causing invasive burn infections in burn patients [14].

References


12- B alakit, H.A., clinical bacteriology and immunology of burn victims. 2007 (thesis)


Table 1: The number of percentages of bacterial burn infection in the cases.

<table>
<thead>
<tr>
<th>Type of result</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive culture</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Negative culture</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2: Distribution of bacterial species in the burn infection.

<table>
<thead>
<tr>
<th>Type of bacteria</th>
<th>Number of isolates</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td><em>Klebsiella spp.</em></td>
<td>4</td>
<td>7.3</td>
</tr>
<tr>
<td><em>E.coli</em></td>
<td>4</td>
<td>7.3</td>
</tr>
<tr>
<td><em>Proteus spp.</em></td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 3: Antibiotic profile of *Pseudomonas aeruginosa*
**All *Pseudomonas* isolates were able to produce extra cellular protease**

<table>
<thead>
<tr>
<th>Type of bacteria</th>
<th>Number of isolates</th>
<th>-</th>
<th>+</th>
<th>-</th>
<th>+</th>
<th>-</th>
<th>+</th>
<th>-</th>
<th>+</th>
</tr>
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<tbody>
<tr>
<td>Pseudomonas</td>
<td>1</td>
<td></td>
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</tr>
</tbody>
</table>

(-) sensitive
(+)Resistant
Concentration: CTX (30mcg), CIP (5mcg), CN (10mcg), AK (30mcg), AX (25mcg)
The Study of the effect of Helium – Neon Laser irradiation on the Albumin

Nadia Hussein Sahib , Khawla A. A. Shemran , Zina Abbas Ali
Hiba Rasheed Behayaa , Shimae Abd Al zahra Abbas
Babylon university,College of Medicine

Abstract
The aim of this research is to counting the absorption coefficient for several concentrations of Albumin solution (0.25 , 0.5 , 0.75 , 1 , 1.25 gm/100ml) before and after exposure to Helium – Neon laser irradiation with wavelength (632.8 nm) by light capacity (2 MW) which occurs within visible area (400 – 700 nm) by (Spectrophotometer.PD-303), it is also accounted the coefficient absorption for low concentration (0.25 , 0.5 , 0.75 gm/100ml) according to Beer - Lambert Law regarding the effect of Hydrogen bonding on coefficient of absorption whenever time increases.

INTRODUCTION
Albumin : the molecular weight of Bovine serum Albumin (BSA) has been published at 66.120 [1] or 66.267 [2]. but it was revised in 1990 to 66.430 [3]. All three values are based on amino acid sequence information available at the time. Albumins are a group of acidic proteins which occur in the body fluids seeds. Serum and plasma albumin is carbohydrate free and comprises 55-62 % of the total albumin in the body in the circulating plasma at one time with the rem which there is , in general , equilibration about every 24 hours.

Bovine albumin is a single poly peptide chain consisting of approximately 583 to 595 at PH 5-7 it contains 17 intrachain disulfide bridges and 1 sulphhydril group. [4]

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Laser Helium-Neon was studying the effect of irradiation on the Molecular Albumin, and the relationship between Laser irradiation and Absorption of monochromatic Light.

Absorption: The absorbance of a medium is defined as the ratio of absorbed and incident intensities. Absorption is due to a partial conversion of Light energy into heat motion or certain vibration of molecules of the absorbing material. The ability of medium to absorb radiation depends on a number of factors, mainly the electronic constitution of its atoms and molecules, the wavelength of radiation, the thickness of absorbing layer and internal parameters such as the temperature of the concentration of absorbing agents.

Absorption of monochromatic light. It can be expressed by the formula, known by Beer-Lambert Law: \[ I = I_0 e^{-cb} \]

\( I \) : transmitted Light
\( I_0 \) : Incident Light
\( C \) : concentration
\( b \) : thickness
\( \mu \) : Absorption Coefficient

Absorbance expressed in optical density (O.D), absorbed by the substance, according to the relationship:

\[ \ln \frac{I}{I_0} = -\mu C b = A = \text{O.D} \]
METHOD

1- Several concentrations were taken (0.25, 0.5, 0.75, 1, 1.25 gm/100 ml) from Albumin solution and exposed each concentration to Helium – Neon laser irradiation, then the absorption of each concentration was counted before and after exposure to irradiation by using (Spectrophotometer PD-303).

2- The lower concentrations were taken (0.25, 0.5, 0.75 gm/100ml) only from Albumin solution and exposed to Helium – Neon laser irradiation for (60 min, 30 min) for each concentration then the angular frequency was counted for each period of time.

\[ f = \frac{1}{t} \quad \text{Sec} \]

RESULTS:

Table (1) explains Albumin Absorption coefficient values for a different concentration.

<table>
<thead>
<tr>
<th>Wave Length (max)</th>
<th>Concentration Gm/100 mL</th>
<th>Absor.Coeff. Before irradiation a.u</th>
<th>Absor. Coeff. After Irradiation a.u</th>
</tr>
</thead>
<tbody>
<tr>
<td>632.8 nm</td>
<td>0.25</td>
<td>0.148</td>
<td>0.123</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.191</td>
<td>0.160</td>
</tr>
<tr>
<td></td>
<td>0.75</td>
<td>0.272</td>
<td>0.222</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.325</td>
<td>0.310</td>
</tr>
<tr>
<td></td>
<td>1.25</td>
<td>0.340</td>
<td>0.317</td>
</tr>
</tbody>
</table>

Table (2) explains Albumin Absorption coefficient values for low concentration with existence of variation of angular frequency.

<table>
<thead>
<tr>
<th>Concentration gm/100 mL</th>
<th>Angular freq. f=1 (sec) t</th>
<th>Absor.coeff. After (30)min a.u</th>
<th>Absor.freq. F=1 (sec) T</th>
<th>Absor. Coeff. After (60)min a.u</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration (mM)</td>
<td>Time = 30 min</td>
<td>Time = 60 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------</td>
<td>---------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.25 mM</td>
<td>$5.5 \times 10^{-4}$</td>
<td>0.238</td>
<td>$2.7 \times 10^{-4}$</td>
<td>0.249</td>
</tr>
<tr>
<td>0.5 mM</td>
<td>$5.5 \times 10^{-4}$</td>
<td>0.345</td>
<td>$2.7 \times 10^{-4}$</td>
<td>0.355</td>
</tr>
<tr>
<td>0.75 mM</td>
<td>$5.5 \times 10^{-4}$</td>
<td>0.495</td>
<td>$2.7 \times 10^{-4}$</td>
<td>0.505</td>
</tr>
</tbody>
</table>
Figure no. (2) shows laser pulse for lower concentration.

Discussion:
Figure (1) includes (A) and (B) shows the relation between absorption coefficient and the extents of Albumin solution concentrations (0.25, 0.5, 0.75, 1, 1.25 gm/100 ml) whereas many absorbed systems in light solutions follow Beer law [6], its text is that the line relation between absorption and concentration in the same size of solution and its inclination equals as shown in the following relation:

\[ A = b \cdot c \]

When concentration drawing in return to absorption is not linear, then the behaviour is called inclination of Beer Law and the reason of inclinations relates to mechanical or chemical factors and it might be positive when the inclination is to the upper or might be negative when the inclination is towards down. Figure no.(1) : B shows the drift in linear after concentration (0.75) and it is obvious from the drawing that the relation between absorption and concentration is linear in lower concentrations.[7]

While figure (2) shows the laser pulse for Albumin solution for lower concentrations (0.25, 0.5, 0.75, gm / 100 ml), it is obvious that the top of absorption increases with the increase of concentration of Albumin solution, the increasing of concentration leads to increasing the number of effected minutes in absorption.[8]

Conclusions:

1- The value of absorption increases with the increasing the concentration of Albumin solution with existing a drift on line. [9]
2- It is shown that the best extent from lower concentration, Beer Law will be applied on it. [10]

References:

Alcohol in the Breath and Blood."

المصادر العربية :
1- روربرت بكوسوك وأفرین ) 1988( – الطرائق الحديثة للتحليل الكيميائي ترجمة د. باسم محمد معدى ، د. مقداد
عبد السماحة مهدي دار开奖结果، بغداد - العراق.
Figure (1) shows the line relation between absorption coefficient and concentration (A) before & (B) after exposure to laser.
Abstract:

This study was prepared to study malignant tumors of urinary bladder in Babylon City in term of histopathological aspect.

Eighty one case of histologically proven primary urinary bladder tumor were collected during the period from 2005-2007, the results were as follow:

1. 71/81 case were transitional cell carcinoma, 8/81 case were squamous cell carcinoma, 1/81 was adenocarcinoma and 1/81 was undifferentiated carcinoma.

2. Male three times affected more than female.

3. Age distribution of bladder carcinoma was 25-80 year.

4. Regarding transitional cell carcinoma, most of the cases were from grade II (50/71) (70.45%).

5. Muscle invasion was present in 27.1% of the cases as follow:
   A. Muscle invasion was present in 18.3% of cases of transitional cell carcinoma.
   B. Muscle invasion was present in 100% of cases of squamous cell carcinoma.

Objective: The aim of the study is to know the most common and important tumors of urinary bladder in Babylon city and to identify its histological features.

Keyword:
- Tcc: Transitional cell carcinoma
- Scc: Squamous cell carcinoma

خلاصة البحث باللغة العربية:

تم إجراء هذا البحث لعرض عمل دراسة إحصائية لأورام المثانة في محافظة بابل ومعرفة أكثر أنواعها شيوعاً. وكانت النتائج كالآتي:

1. تم جمع 81 حالة لسرطان المثانة خلال الفترة 2005-2007 وكان عند حالات سرطان المثانة الطالبي الانتقال الحرجي 8 حالات، وحالة واحدة لكل من سرطان المثانة الغدي وسرطان المثانة الغير متميز.

2. كانت نسبة اصابة الذكور في حالة أضعاف اصابات الإناث.

3. كان معدل العمر لاصابة سرطان المثانة هو من 25-80 سنة.

4. بالنسبة لسرطان المثانة الطالبي الانتقال الحرجي فإن أكثر الحالات كانت من المريحة الثانية بنسبة 70.4%.

5. كانت نسبة اختراع الورم لجدار المثانة العضلي هي 27.1% من مجموع الحالات وهي كالآتي:
   A. نسبة اختراع ورم المثانة الطالبي الانتقال الحرجي لجدار المثانة العضلي هي 18.3%.
Introduction:-
Urothelial carcinoma are 3-4 times more common in male than female, the peak age of incidence is at 50-80 years. The most important risk factors are cigarette smoking, occupational exposure to aryl amines, chronic cyclophosphamide exposure, chronic inflammation such as chronic schistosomiasis heamatobium infection, stag horn calculus, recurrent infections, bladder extrophy (1)

The major prognostic factors depend on histological type of tumor ,degree of differentiation' of tumor (grade),depth of muscular invasion(stage),age of patient and mode of therapy.

Cellular CLASSIFICATION:
More than 90% of carcinoma bladder are transitional cell carcinoma (Tcc), about 6-8% are squamous cell carcinoma (Scc) & 2% are adeno carcinoma.(2)

A-Transitional cell carcinoma (urothelial Carcinoma):
Several grading system have been proposed for grading of Tcc. These are primarily based on cytological appearance of tumor rather than its architecture or invasiveness. The first widely used grading system in which the Tcc divided into four grades as follows (3).

Grade I: microscopically, it is composed of regular frond like papillae composed of a central fibro vascular core that is covered by a few layers of uniform transitional cells, mitosis are rare or absent.

Grade II: these characterized by more solid appearance and firmer consistency, microscopically, the papillary configuration persists, but there is more crowding and layering of cells, enlargement and hyperchromasia of nuclei, and more than an occasional mitotic figures.

Grade III: papillary areas may still be present but are irregularly distributed, the cell masses in small groups and mitotic figures are easily found.

Grade IV: papillary areas are scanty or absent, cellular atypia and pleomorphism are so marked that transitional cell nature of the tumor may be obscure, mitotic figure are frequent & a typical .the tumor are usually widely invasive.

Other classification according to world health organization international society of urological pathology (WHO/ ISUP)(4,5) is to divide the neoplastic lesion into flat and papillary and separate evaluation of papillary neoplasm for grades (based on architecture and cytology), the types of papillary neoplasm recognized in this classification are the following:-

-papilloma
-papillary neoplasm with low malignant potential
-low grade papillary carcinoma
-high grade papillary carcinoma

It is obvious that satisfactory classification of this tumor has not yet reached, it is believed that the original grading system is easy to be applied in practice and it is used in our study.

The grading of Tcc is of great prognostic value, thus the tumor at lower end of spectrum has low incidence of recurrence and negligible incidence of in situ and invasive carcinoma (6,7)

Stromal invasion by transitional cell carcinoma proceeded by two stage, invasion of lamina properia and invasion of muscular layer, the pathological staging is better prognostic indicator than histological grade.(8)

B-Squamous cell carcinoma:
Pure squamous cell carcinoma account for up to 10% of carcinoma of bladder, but in countries endemic for schistosomiasis, this rate is much higher.
Pre-existing squamous metaplasia with long standing chronic inflammation is typically give rise to tumor. Histologically, some are well differentiated exhibit obvious squamous differentiation with keratinization, others are poorly differentiated. Although clinical behavior is similar to Tcc, the prognosis is worse as the patients usually presented in advanced stage, and about 95% show muscle invasion at time of diagnosis.

**C-Adeno carcinoma:**
This is very rare & form less than 2% of tumors, they may arise in areas of glandular metaplasia, adeno carcinoma of bladder produce abundant mucin & tumor surface may be gelatinous. The histological features are similar to colonic carcinoma and range from well differentiated glands forming neoplasm to poorly differentiated signet ring carcinoma.

**D-Un differentiated carcinoma:**
These are tumors in which the neoplastic cells show neither transitional nor squamous or glandular differentiation, the cells range from large polygonal pleomorphic cells, to small cells to spindle sarcomatoid cells.

**Material & Methods:**
Between 2005-2007, eighty one case with histologically proven primary bladder cancer were collected from teaching hospital in Hilla city for 3 years duration.

- The tumors are assessed cystoscopically as there is bladder mass and surgical biopsy taken by cystoscope by Trans urethral resection.
- The biopsy is formalin fixed, paraffin embedded and stained by Heamatoxilin and Eosin and studied histopathologically.
- Clinical staging was done for all cases and the tumors were categorized and graded histologically.
- We use chi-square test ($x^2$) to analysis our data.

**Results:**
Eighty one patient with histologically proven carcinoma of urinary bladder were studied. The patients range in age from 25-80 year (mean 52.5 year) and there were 60 male and 21 female, male : female ratio was 3:1 (male is significantly affected more than female ($p<0.01$)).

- The frequency of Tcc were 71 case (87.6%), 53 of them were male and 13 were female, male : female ratio was 3:1 (male is significantly affected more than female ($p<0.01$), the mean age of Tcc was 52.5 year.
- Th frequency of Scc were 8 case (9.8%), 5 of them were male and 3 of them were female, male : female ratio was 5:3 (there is no significant difference between male and female ($p>0.05$), the mean age of Scc was 57.5 year.
- The frequency of adeno carcinoma was 1 (1.2%) and of undifferentiated carcinoma was 1 (1.2%).

In concern to Tcc, the frequency of grade I, II, III & IV were 8(11.2%), 50 (70.4 %), 11 (15.4 %) and 2 (2.8 %) respectively (there is significant difference between grades of Tcc ($p<0.01$)).

In concern to Scc, the frequency of well differentiated Scc was 3(37.5%) and of moderate differentiated Scc was 5(62.5%) and of poorly differentiated Scc was zero.

- Muscle invasion is present in 22 case(27.1%) (13 Tcc, 8 Scc and 1 adenocarcinoma).
- Acomparison was made between patients with Tcc and Scc in table number 2, in this series, the mean age of patients with Tcc is 52.5 year which is less than the mean age of Scc (57.5 year), the male to female ratio in Tcc was 3:1 while for Scc was 5:3 (Scc more common in female than Tcc).

- Muscle invasion was present in 13 case of TCC(18.3%) at time of diagnosis while all cases of SCC were muscle invading at time of diagnosis.

- Associated schistosomiasis was present in 1 case of TCC & 1 case of SCC.
Discussion:-

In the present study, the transitional cell carcinoma is the most common bladder tumor (87.6%) in Hilla city, while squamous cell carcinoma constitute only 9.8% of the cases seen over a period of 3 years duration. In countries endemic with schistosomiasis, the incidence of squamous cell carcinoma is much higher and may reach about 75% in Egypt (9) and 65% in south of Iraq (10).

- The mean age in this study was 52.5 years in Tcc and 57.5 years in Scc, the male: female ratio in Tcc 3:1 while it is 5:3 in Scc, the relatively younger age incidence and male predominance of Tcc are in agreement with other reports (9,11,12,13).

- Tumor grading show that Tcc grade I, II, III & IV frequency were 8 (11.2%), 50 (70.4%), 11 (15.4%) and 2 (2.8%) respectively, while for Scc the frequency of well differentiated was 3 (37.5%) & of moderately differentiated Scc were 5 (62.5%). These results may be slightly different from other studies, this discrepancy may be attributed to individual variation of interpretation of tumors grade (14).

- Muscle invasion is present in 13 cases (18.3%) with Tcc while all cases of Scc were muscle invading at time of diagnosis, this may be attributed that Scc are presented at advanced stage, this findings are in agreement with other reports (9,11,15,16).

- Histological grading and clinical staging were done for all cases and this is important in determination of mode of treatment and to know the prognosis of tumor.

- Superficial tumors were treated by transurethral resection with or without chemotherapy while for deeply invasive tumors with regional or distant metastasis, the standard treatment is radical cystectomy with or without radiation therapy or by combined chemotherapy-radiation therapy (17,18).

- Intravesical therapy with bacillus Calmette Guerin (BCG) is often used for treatment of patients with multiple tumors or recurrent tumors or as prophylactic measures in high risk patients after TUR (19,20).

In concern to schistosomiasis, it is found that only one case of Tcc and one case of Scc was associated with schistosomiasis, while in other studies, a close relation ship was found between schistosomiasis and bladder cancer and this was supported by many investigation (21,22) but rejected by others.

Conclusion:
Urinary bladder carcinoma is a common malignant tumor in Babylon city (it is the third malignant tumor in Babylon city) (23), mainly in male and its require complete evaluation and early detection as quick as possible in order to identify and treat the high risk patients in order to decrease the incidence of urinary bladder tumor.

Recommendation:-
It is important to try to reduce the incidence of bladder tumor by prevention and early detection.

Prevention is by public education
Early detection of localized early stages by different methods that have been focused on investigating tumor cells in urine and these include urine cytology, flow cytometry ABO (H) cell surface iso antigen or detection of tumor products in urine such as bladder tumor antigen test that detect the presence of basement membranes complex in urine (24,25).

Urine cytology is a specific, non invasive technique which can be useful in screening of high risk group (26,27).

References:


Picture (1)
Non-papillary carcinoma grade III.
Picture (2)
Squamous cell carcinoma with focal keratinization & necrosis.

Picture (3)
Adenocarcinoma of the bladder.
Undifferentiated carcinoma.

**Table No -1-**
Clinico – pathological Features in 71 patients with Tcc
- No. men / women 53 / 18
- Male to Female ratio 3 : 1
- Mean age at time of diagnosis 52.5 year
- Histological grade
  Grade I 8 (11.27%)
  Grade II 50 (70.45%)
  Grade III 11 (15.43%)
  Grade IV 2 (2.85%)
- Clinical Stage-
  Stage A (No muscle invasion) 58 (81.7%)
  Stage B (with muscle invasion) 13(18.3%)

**Table No - 2-**
A comparison between transitional and squamous cell Carcinoma.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Tcc</th>
<th>Scc</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>71 (87.61.)</td>
<td>8 (9.8%)</td>
</tr>
<tr>
<td>Mean age</td>
<td>52.5 year</td>
<td>57.5 year</td>
</tr>
<tr>
<td>Male : Female ratio</td>
<td>3 : 1</td>
<td>5 : 3</td>
</tr>
<tr>
<td>Tumor Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage A (No muscle invasion)</td>
<td>58 (81.7%)</td>
<td>0 (non)</td>
</tr>
<tr>
<td>Stage B (with muscle invasion)</td>
<td>13 (18.3%)</td>
<td>8 (100%)</td>
</tr>
<tr>
<td>Associated Schistosomiasis</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Figure No.1
Frequency of various histological type of primary CA bladder in 81 patients
Figure No.2
Frequency of histological grades of Tcc In 71 case

Grade II
70.45%

Grade I
11.27%

Grade III
15.43%

Grade IV
2.85%
Figure No.3
Age distribution & peak age of incidence of CA bladder in Babylon city.
Sex distribution of CA bladder in Babylon city

Figure No.4
Abstract

Treatment of plane warts is a problematic. Methods such as a combination of salicylic acid with lactic acid lotion, cryotherapy and cauterization are used but they are associated with high recurrence rate, risk of scar, pain and high cost. In addition, treatment with topical tretinoin lotion causes an irritant contact dermatitis that limited its use. Contractubex gel consists of heparin sodium 5000 I.U, extre cepa 10g, allantoin 1.0g in water-soluble, fat free gel, exerts a softening and smoothing effect on indurated, hypertrophic, painful and cosmetically disfiguring scar tissue.

In this study, the efficacy of contractubex gel in treatment of plane warts was evaluated and compared with 0.05% tretinoin lotion treatment. The results, after six weeks follow up revealed that up to 79.4% of the lesions in contractubex gel treated group diapered versus 20.6% of the lesions in tretinoin treated group. This modality of treatment seems to be superior to tretinoin lotion in the treatment of plane warts and even the common type, which is due to high efficacy of contractubex gel associated with low incidence of side effects. This is the first use for this drug in the treatment of viral warts.

الخلاصة

بعد علاج التاليل السطحية مشكلة علاجية يعالج بحلول خليط الابتراك والأنثيوستيك والأنثيوستيك باليركس بالرطوبة وكمية جداً تم استخدامه بشكل خاص عند المناطق تحتوي بالأنثيوستيك جيل على ألومنيوم الهيدروكسيد 5000 وحدة مسغغة بالتصل إلى 10 غرام بالانثيوستيك 1 غرم، وتشمل والأنثيوستيك تطورها الشعوبي. في هذه الدراسة تم اختبار تأثير الكورتيزول التنوبكس جيل على علاج التاليل السطحية مع مقارنة ذلك مع رعاية بحلول بالانثيوستيك 0.05% النتائج بعد المتابعة لمدة سنة ارتفاع وجدت أن 97.9% من التاليل التي عولجت بغاز الكورتيزول التنوبكس جيل قد اختلفت مقارنة بال وبالانثيوستيك بحلول بالانثيوستيك 0.05% هذا النوع من العلاج يعد فائقاً في تأثيره في علاج التاليل السطحية وحتى الشعوبي لمن تأثير كبير وسرع وبعض ضعيلة وهذا أول مرة تم فيها استخدام هذا العقار لمعالجة التاليل. 

Evaluation of The Efficacy of Contractubex Gel in Plane Wart Treatment

Kareema Amine Al-Khafaji

Babylon University, College of Medicine
Introduction

Warts are benign proliferations of the skin and mucosa that result from infection with human papilloma virus. Plane warts are smooth flat-topped papules most commonly found on the face, back of the hands and lower legs associated usually with skin colored or light brown coloration. They become inflamed as a result of an immunological reaction just before they resolve spontaneously (1, 2).

A variety of therapeutic modalities with different mode of action are available such as a combination of salicylic acid and lactic acid, trichloracitic acid, silver nitrate, potassium hydroxide, fluorouracil, interferon, retinoid, cimetidine, 5-aminolacvalinic acid, cryotherapy, Laser therapy electrocauterization and surgical excision (3, 4, 5). Mostly these modalities of treatment are associated with pain, inconvenience, risk of scarring and hypo or hyper pigmentation especially on the face. Cosmetic and psychosocial problems might be ended with some of these modalities of treatments (2). Retinoic acid may be applied topically in plane warts, although the best results are claimed for higher than usual concentration and associated with irritations as a common side effect (5).

Contractubex exerts a softening and smoothing effects on indurated hypertrophic, painful, and cosmetically disfiguring scar tissue. The water soluble gel base mediates the deep penetration of the active ingredient into the skin, there by affording an intensive local try to use it in the treatment of plane warts. To our knowledge, this is the first time that contractubex gel is used in the treatment of plane warts in comparison to 0.05% tretinoin lotion treatment.

Material and methods

During the period 2005-2007, seventy-five consecutive patients were examined in a private clinic as well as an out-patient clinic of the dermatological department in Mirjan-teaching hospital/Hilla. The diagnosis of plane warts was achieved. The patients involved in this study were chosen to have two sided body located plan warts and they were included in this double blind self-control comparison. Patients with systemic diseases such as diabetes mellitus, asthma, renal insufficiency, patients who were consuming immunosuppressive drugs (e.g. renal transplants..etc), pregnant and nursing women were excluded from this study. All patients were received full information on the purpose and design of this study. They were informed do not received any systemic or topical wart treatment within four weeks before entering the study. Detailed history sheet for every patient admitted to the study
was taken including number of the lesions in each area of the body as well as age, sex and address.

For each patient, lesions of one side of the body were treated by the application of contractubex gel and the other side by 0.05% tretinoin lotion (twice daily with each treatment). Solutions were applied on the lesions by a wood end of a cotton swab to minimize filtration of effective drug to the surrounding areas. For the children who were aged less than ten years, their parents were asked to apply the treatments. The side that was treated by intermittently selected for each patient should be fixed and registered in checklist.

Contractubex is a trade mark for an onion extract-containing gel preparation manufactured by Merz pharm GMbh&co.KGaA 60318 Frankhurt am Main, Germany, and designated for topical treatment of cicatrices (such as disfiguring scar tissue, contracture, etc). The preparation contain 10% Bulbus allii cepae extract, heparin sodium 5000 IU, allantoin 1g, and methyl-4-hydroxybenzoate 150 mg. The ether extract contain oils of allium cepae (0.005-0.15%), cyclo-alin-methyl-alein, propylalin, thiopropional-camphophelol, quartz derivatives, phloroglucin peptides, protocatechin acid, ferulic acid, amino acids, pectin phytohormones, vitamin C up to 33 mg, and vitamin B1 up to 60 mg. The gel is supplied in tubes of 20, 50, and 100g.

Duration of the treatment was planned to be six weeks and a control visits were arranged every three weeks intervals. The number of warts in the examined side of the body and any adverse effects related to the study preparation such as burning sensation, pruritus, erythema and contact dermatitis were recorded in each visit. Evaluation of the efficacy of the treatment was based on reduction of the number of warts. Statistical analysis was performed by the Chi-square test and value of $P < 0.01$ was considered significant.

**Results**

75 patients were participated in the entire study. Out of 75 patients 54 (72%) were females and 21 (28%) were males. The distribution of patients in different age groups was shown in (table 1). The peak incidence of plane warts was (30.7%) ranged between the age group 1-10 years. The over all number of the lesions were (1482); 752 lesions were treated by application of contractubex gel and 730 lesions were treated by 0.05% tretinoin lotion. In the first three weeks of treatment with contractubex gel 275 lesions (1st treats), and with 0.05% tretinoin lotion 65
lesions (2nd treats) were disappeared, In the second three weeks of follow up another 355 lesions in the first treats and 98 lesions in the second treats were disappeared, The total number of plane warts were 630 (79.4%) warts disappeared by contractubex gel versus the disappearance of 163 (20.6%) with 0.05% tretinoin lotion (table 2). The clinical significance of contractubex gel was (79.4%) and 0.05% tretinoin lotion (20.6%) was high, P.value is < 0.001. Regarding the time of improvement for each treatments have significant difference with time P.value is < 0.001. So both treatments have significant difference with 3 weeks, 6 weeks P.value is < 0.001. There is no significant side effects apart of mild dryness of skin. This treatment is also effective and can be used for common warts, milia, and syrengoma.

**Discussion**

Warts are benign, often spontaneously resolving, epidermal proliferations. Plane warts (juvenile) are caused by human papiloma virus (most often HPV-3 and HPV-10) and generally multiple, slightly elevated, smooth papules occurring most often on the face, hands, neck and legs of children and young adults (5,6). They may be in a group and linear arrangement implying a role of trauma (Koebner phenomenon). The nature of warts is unpredictable. They often fail to disappear with treatment or they recur after apparent cure. Some warts resolve spontaneously and thus the evaluation of treatment may be difficult. There is no way to prevent warts and both patients and physicians often become frustrated by an apparent endless appearance of new warts. Systemic medications are not successful and locally destructive methods are the mainstay of therapy.

The aim of treatment is to destroy the wart and to spare the normal skin with out causing distress to the patient or scarring as well as with minimal pain and inconvenience (7,8,9, 10.11).

Many researchers have studied about plane wart treatment. In a randomized controlled study of 25 children, 85% of warts disappeared with 0.05% tretinoin cream compared with 32% in controls (6). In this study, efficacy of tretinoin was less (53.7%) than contractubex gel. Retinoid are involved in the regulation of diverse biologic functions. They affect cell growth and differentiation, morphogenesis, tumor promotion and malignant cell growth, also exert immunomodulatory action and alter cellular adhesiveness (12).
Molluscum contagiosum, warts and various forms of ichthyosis may be improved by topical retinoids to a variable degree (12). It has been well-documented that Tretinoin (all-trans retinoic acid) increases proliferation of basal keratinocytes and also the number of cell layers expressing the differentiation markers involucrine, loricrine, fillagrin and epidermal transglutaminase (13). These epidermal changes collectively translate to clinical desquamation and peeling and mediated by nuclear receptors of retinoids(13). Induction of desquamation and immunomodulation may be the probable mechanism that explains the efficacy of tretinoin in plane wart treatment. In a randomized controlled study of 25 children, 85% of warts cleared with 0.05% tretinoin cream compared with 32% in controls(6), in other study the result was less(53.7%)(7), while in our study the result was lesser(20.6%).

The mechanism of action of contractubex gel in treatment of plane warts is proposed to be; 1-the active ingredients of contractubex gel has ability of penetration into the plane warts causing softening and inflammation of the lesions after which resolution and disappearance of the lesions and spare normal skin.

2-presence of vitamin C and vitamin B1 that proved to be effective in treatment of viral warts. Vitamin C is a powerful antioxidant that fights destructive, unstable molecules called free radicals. It strengthens cell walls in body tissues and boosts immunity, which helps the body fight viruses. It can be helpful against warts both as an oral supplement and as a topical treatment. And vitamin B Important in normal cell multiplication(12, 13,14, 15 ).

Conclusion :Contractubex gel appears as an effective, safe and cost-effective treatment in plane wart.

References