

is rising steadily. This can be explained by the improvement in the training of eye doctors as well as the reasonable prices of the intraocular lens Yemeni patients are getting. Moreover, the introduction of the memorandum issued by the Ministry of Health for the routine use of intraocular lenses in cataract surgery help in putting this technique as the standard for every cataract surgery. Unfortunately, the number of glaucoma filtration surgery (trabeculectomy) is very small and is falling over the years compared to the predicted affected patients with glaucoma. There are number of explanations for this low surgical intervention: 1. Most glaucoma patients in our community were presented late with advanced pale cupped discs and at this stage there are few that can be offered. 2. Many eye surgeons throughout Yemen avoid doing glaucoma filtration surgery (trabeculectomy) for lack of training. 3. The fear of complications of trabeculectomy especially in advanced cases, made experienced eye doctors to avoid surgical intervention. 4. The introduction of new generations of anti-glaucoma therapy with better hypotensive effect.

We need to tackle these problems by educating our patients and introducing screening programs within the Yemeni community; hence those glaucoma patients can be presented earlier and get treated safely. We also need to train more doctors to perform trabeculectomy filtration surgery and to know how to manage the complications of this procedure. This will decrease the number of blind people due to a reasonably treatable disease.

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References

1. Thylefors B. The WHO program for the prevention of blindness and cataract in developing countries. *Doc Ophthalmol* 1992; 81: 339-344.
2. Shields MB. Textbook of Glaucoma. 3rd ed. Baltimore (MD): Williams and Wilkins; 1992.
3. Cairns JE. Trabeculectomy: Preliminary report of a new method. *Am J Ophthalmol* 1968; 66: 673-679.
4. Al-Raei M, Al-Shabooti AA, Bamashmus MA. Ophthalmic surgical experience in Al-Thawra Hospital in Sana'a. *Yemeni Journal of Medical Sciences* 2001; 1: 15-19.
5. Whittaker KW, Gillow JT, Cunliffe IA. Is the role of trabeculectomy in glaucoma management changing? *Eye* 2001; 15: 449-452.

Is methotrexate safe in the treatment of psoriatic patients?

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Psoriasis is a common genetically determined, chronic, relapsing and remitting, inflammatory skin disease, with great physical and social impact.¹ Accelerated epidermal cell replication, with abnormal pattern of keratinocyte differentiation and the presence of dermal and epidermal inflammatory cell infiltration have been considered to be the main pathological events in psoriasis.^{1,2} Topical applications of tar, steroids or calcipotriol are therapies of choice for patients with mild to moderate severity of psoriasis.³ However, in patients with severe psoriasis, systemic therapy is an established alternative, such as photochemotherapy (PUVA), retinoids, cyclosporine and methotrexate (MTX).^{1,3} Methotrexate is considered as a cytotoxic agent. It is an antimetabolite that mediate its antimetabolic effects through inhibition of DNA synthesis by blocking dihydrofolate reductase and thymidylate synthetase enzymes.^{4,5} It also has anti-inflammatory effects through inhibition of leukocyte chemotaxis. These 2 principle actions explain its clinical effect in controlling psoriasis.^{4,5} Methotrexate is an effective treatment for severe psoriasis. It is particularly useful in controlling erythrodermic and generalized pustular psoriasis (GPP) form, where it may be a life saving drug.^{1,5} The most serious toxic effect of the drug is hepatotoxicity.⁵ The tendency to a liver damage may be related to multiple risk factors, such as advanced age, diabetes, alcohol intake, obesity and impaired renal function.⁵ Reported signs of MTX toxicity also include, bone marrow suppression with leukopenia and thrombocytopenia, gastro intestinal ulceration, pneumonitis, oligospermia and nephrotoxicity.⁵ Due to these reported toxic effects, many dermatologists limit its uses, although it is available and inexpensive as compared to other systemic drugs for psoriasis. Therefore, the present study was arranged to investigate further, the effects of long term, low dose MTX therapy, in the management of severe psoriasis in Iraqi patients.

One hundred and thirty-two patients with severe psoriasis consisting of 22 patients with erythrodermic form, 29 patients with GPP and 81 patients with widespread plaque psoriasis were selected from the Department of Dermatology and Venereology, Baghdad Teaching Hospital, Baghdad, Iraq to receive MTX therapy during the period October 1998 to September 2000. They were 79 females and 53 males with female to male ratio of 1:49.¹ Their ages ranged from 18-66 years (mean 42.3 ± SD 10.2 years). All patients were informed

to avoid the drugs that may interact with MTX or may cause bone marrow suppression, nephrotoxicity or hepatotoxicity and instructed carefully to use contraceptive precautions during and after a minimum of 3 months of cessation of therapy. Pregnant women and nursing mothers, diabetic, alcoholic or patients with laboratory evidence of bone marrow, hepatic or renal impairment were not included. The starting dose of MTX for each patient in the study was 15-25 mg/week as a single intramuscular injection or triple oral doses (with 12 hours intervals), until adequate response was achieved, then, the doses were reduced gradually to 10 mg/week. Clinical response was assessed at week 1, 2, 4, 8 and then once monthly. Remission was considered as satisfactory when there is improvement (clearance) in more than 50% of the lesional surface area, with reduction in the severity of erythema, scale and elevation for individual psoriatic plaques, on a score from 0 to 4 as follows: 0 for absent, 1 for mild, 2 for moderate, 3 for severe and 4 for extremely severe. The side effects faced during the treatment intervals were also recorded. Serial laboratory evaluations for each patient in the study were performed, including complete blood count, liver function test and serum albumin were performed every 2-3 months of therapy. Liver enzymes were assessed 7 days after the last dose of MTX, to avoid the transient elevation that may occur during first few days of MTX intake. Renal function tests were performed every 2-3 months of therapy. Other investigations included chest x-ray, seminal fluid analysis, sperm counts, motility and morphology were analyzed every 2 months of therapy for 24 patients. Ultrasound (US) scanning of the liver were performed prior to therapy for 60 patients and repeated after 6 months of therapy. Liver biopsies were obtained from all patients with abnormal liver US scanning. The body weight of the patients ranged from 50-105 kg (mean 78.3 ± SD 14.7 kg). The duration of the disease ranged from 8 months to 32 years (mean 15.2 ± 8.4 years). Total duration of MTX therapy varied from 16-72 weeks (mean 41.1 ± SD 14.3 weeks) and total cumulative dose ranged from 240-960 mg (mean 604 ± SD 172.8 mg). Remission was achieved in 59 (44.6%) after 2 weeks of therapy, 83 (62.8%) after 4 weeks of therapy and 104 (78.8%) patients after 8 weeks of therapy. Similar responses as achieved after 8 weeks of therapy were observed after further therapy. A number of side effects were noticed in our study. The main cutaneous side effect was the intense itching on 55 (41.5%), loss of appetite in 40 (30.3%) and nausea in 40 (30.3%) patients. Headache and malaise were noticed in 19 (14.3%) patients, while menstrual disturbances, mainly, oligomenorrhea were observed in 14 patients (which constitute 17.7% of female patients). Serial laboratory evaluations for our patients showed a decrease in hemoglobin level in 4 (3%) patients, the lowest hemoglobin level recorded in one patient was

10 g/dl after 5 months of therapy. Ten patients (7.6%) had slight decrease in white blood cell counts and absolute neutrophil counts after 5-6 months of therapy. Liver enzymes, mainly, serum glutamate pyruvate transaminase and serum alkaline phosphatase were elevated in 8 (6%) patients after 16 weeks of therapy, but returned to normal level after discontinuation of therapy. Repeated seminal fluid analysis showed a slight reduction in the sperm counts in 8.3% (2 out of 24) patients. Abnormal result of US scanning of the liver (enlarged liver with fatty changes) were detected in 5% of the patients (3 out of 60 patients). Fortunately, their liver biopsies resulted in mild histological changes (septal inflammatory infiltrate with mild fatty changes). This study showed that MTX is an effective therapy for controlling severe psoriasis, as remission was achieved in 78.8% of patients. Transient subjective discomforts, such as nausea, vomiting, headache, itching, loss of appetite and dizziness were experienced in some of our patients (5-40%). These results are similar to other reported literature,^{4,5} that are transient and reversible with cessation of therapy. Ultrasound scanning is a safe and quick method for the detection of liver diseases. Previous literature suggest that patients with normal U/S scan prior or during MTX therapy, could be spared from liver biopsies, as mortalities and morbidities of these invasive procedures are not negligible. Methotrexate, in this study, unlike other published literature,^{4,5} resulted in low incidence of liver damage and associated with few laboratory abnormalities. This could be due to proper selection of patients and absence of risk factors, mainly alcohol intake.

It can be concluded that, MTX is an effective drug for severe psoriasis and is relatively safe therapy if patients are carefully selected and regular monitoring for side effects is performed regularly during therapy.

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References

1. Camp RD. Psoriasis. In: Rook A, Wilkenson DS, Ebling FJG, Champion RH, Burton JL, editors. Text book of Dermatology. 5th ed. London (UK): Blackwell Scientific Publication; 1992. p. 1391-1459.
2. Toussaint S, Kamino H. Noninfectious Erythematous Papular and Squamous Disease of the skin. In: Edler D, Elenitsas R, Jaworsky C, Johnson B, editors. Lever's Histopathology of the skin. 8th ed. Philadelphia (PA): Lippincott Raven; 1997. p. 151-184.
3. Farber EM. History of treatment of psoriasis. *J Am Acad Dermatol* 1992; 27: 640-645.
4. Olsen EA. The pharmacology of Methotrexate. *J Am Acad Dermatol* 1988; 19: 145-156.
5. Zachariae H. Methotrexate side effects. *Br J Dermatol* 1990; 122: 127-133.