Original Article

Frequency of Hyperuricaemic Uveitis in patients taking Antituberculus Therapy in Bahawal Victoria Hospital Bahawalpur

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Objective: To determine the frequency of hyperuricaemic uveitis in tuberculous patients taking antituberculus therapy ATT at Bahawal Victoria Hospital Bahawalpur.

Duration of Study: The **study was conducted in Pulmonology department, Bahawal Victoria Hospital and Ophthalamology Department, in collaboration with Pathology department, Quaid-e-Azam Medical College Bahawalpur from May 2008 to January 2010.**

Study Design: **Observational study.**

Materials and Methods: 850 patients (750 males and 100 female aged 20 - 60 years) recieving 4 standard drugs as ATT (Rifampicin, PZA, Ethambutol, and isoniazid) were included. We used approved and fixed dose combination of 4 drugs of proven bio equivalence.Serum Uric acid levels and serum creatinine at 8 - 12 weeks after commencement of ATT were measured . Serum Uric acid and creatinine specimens were done on fully automated chemistry analyzer SELECTRA - E (Merck Diagnostics) using Merck reagents. All the patients were examined by slit lamp examination to diagnose uveitis by an ophthalamologist.

Results: All study subjects had hyperuricemia and normal creatinine. Keratic precipitates and posterior synechae were found in few percent of the patients. Band keratopathy with refractile, yellow crystals in the deep corneal epithelial cells and at the level of Bowman membrane were seen in one patient.Conjunctival nodules containing needle like crystals were also seen within the intrapalpaberal areas, associated with a mild marginal keratitis in one patient.

Conclusion: Hyperuricaemic uveitis starts almost after 8 weeks of commencement of ATT in tuberculous patients. If it is left undiagnosed sight –threatening effects can occur

Key Words: Hyperuricaemia, Uveitis, Tuberculosis

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Introduction

Tuberculosis is a common disease in developing countries, rather its incidence is increasing again in developed countries.[1] Treatment is with standard therapy of 3 or 4 drugs in the initial eight weeks.[2] Drugs commonly used as antituberculosis therapy (ATT) are pyrazinamide (PZA), rifampicin, isoniazid (INH), ethambutol, and streptomycin.[3] Many drugs needed in the treatment of TB are known to stress the kidneys and liver.[4] Clearance of uric acid (UA) is also affected when kidney functions are impaired. Clearance of UA also varies in different conditions. It has been observed that tubular secretion of UA negatively encountered with basal metabolic index (BMI). PZA is a well known modulator of UA transport via the proximal tubules.[4]

Hyperuricemia is defined as a serum UA concentrtion

in excess of urate solubility, which is about 420 micromol/l in men and 360 micromol/l in women.[5] People with elevated uric acid but without the symptoms of gout, nephropathy, or kidney stones are classified as having asymptomatic hyperuricemia.[6] If the gouty symptoms do not occur, people with asymptomatic hyperuricemia are usually unaware of their condition and the possible consequences such as hypertension, diabetes mellitus, renal disease, cardiovascular diseases and uvietis may occur.[6, 7]

Increased urbanization, westernization and economic development have already contributed to a worldwide substantial rise in UA level both in developed and developing countries. The prevelence of hyperuricemia has been reported to be increasing recently.[5]

Sign and symptoms of hyperuricemic uveitis in ocular tissue, secondary to elevated levels of UA salts in the serum and resulting deposition of these salts within uveal tissue can cause serious sight threatening effects. Rarely gout can produce significant ocular findings. The incidence of age-related-macular-degeneration (ARMD) is higher in patients with gout.[7]

Acute uveitis is characterized by sudden onset of unilateral pain, photophobia and redness which may be associated with lacrimation. Chronic uveitis has insidious onset and many patients are asymptomatic until the development of complications.[7]

Materials and Methods

We conducted a prospective and observational study in Pulmonology department, Bahawal Victoria Hospital and Ophthalamology department, in collaboration with Pathology department,Quaid-e-Azam Medical College Bahawalpur, from May 2008 to January 2010. 850 patients (750 males and 100 female aged 20-60 years) recieving 4 standard drugs as ATT (Rifampicin, PZA, Ethambutol, and isoniazid) were included. All drugs were given in fixed dose combination according to the weight as recommended by WHO.[8] We used approved and fixed dose combination of 4 drugs of proven bio equivalency[9]. Only those patients were included in the study, who were found to have normal serum UA, creatinine and no uvietis on slit lamp examination and had no sign of uvietis, after being examined by an ophthalamologist.

After taking a baseline value of serum UA and creatinine, the value were repeated at 8-12 weeks after commencement of ATT. Serum UA and creatinine specimens were done on fully automated chemistry analyzer SELECTRA - E (Merck Diagnostics) using Merck reagents. All the patients were examined by slit lamp examination to diagnose uveitis by an ophthalamologist. All the patients with renal diseases, liver diseases, on chemotherapy were excluded from study.

Statistical analysis was done by independent sample't' test.

Results

850 subjects (750 males: 100 females), aged 16 - 60 (mean= 41years) were included in the study. All study subjects had hyperuricemia and normal creatinine. Results shown in Table 1.

Table I: Serum Mean Uric Acid and Creatinine levels.

Age(years)	Uric acid (mg / dl) Mean SD	Creatinine (mg / dl) Mean SD
20-30	18.5 ±0.57	0.87 ±0.11
31-40	21.1 ±0.81	0.61 ±0.10
41-50	16.8 ±0.45	0.94 ±0.20
51-60	20.5 ±0.22	0.75 ±0.20

Table II: Ocular manifestations in the eye secondary to Uric Acid crystals within the ocular tissue.

	Keratic precipitates	Posterior synechae
Males	1%	0.2%
Females	0.5%	0%

In few patients'eyes band keratopathy with refractile, yellow crystals in the deep corneal epithelial cells at the level of Bowman membrane were seen.

Conjunctival nodules containing needle like crystals were also seen within the intrapalpaberal areas, associated with a mild marginal keratitis in one patient.

Visual blurring from the corneal haze or foreign body sensation due to epithelial breakdown was treated with scrapping of the epithelium and removal of crystals.

Scleritis and tenovitis were not seen in any patient. Uric acid nodules called Tophi was seen in two patients.

Discussion

Urates filtered (8-12 %) by glomeruli is excreted in the urine as uric acid. After filteration, 98-100% of the urates is reabsorbed; about half the re absorbed urate is secreted back into the proximl tubules, and about 40% of that is again reabsorbed.[6]

Our study shows that ATT significantly increased the level of UA in blood during the course of study which is similar to another study[4] in which hyperuricemia occurred after the commencement of anti-TB treatment.

Another study conducted on children taking PZA showed different results regarding uric acid levels in blood after ATT as compared to our study.[10] The reason is that we used fixed dose combination tablets for treatment while in the study mentioned above, PZA was used in split dose. That might be the reason that the level of UA in the blood was very high in our study. Another reason of high UA in our study as compared to above mentioned study may be that in our study adult population was studied as compared to children in this study.

When compared to another study[11] our study also had almost the similar results, except for the fact that percentage of keratic precipitates was high in our study. This may be due to the fact that latest and better diagnostic and sensitive opthalmological slit lamps allow better visualisation.

In one such study[5] 50% of the patients between 6th and 8th weeks of treatment developed progressive hyperurecemia while in our study 100% of patients developed hyperurecemia. This difference may be due to the fact that the number of study subjects (n= 850) was much higher in our study as compared to the comparative study (n= 50) and only PZA was used as monotherapy. The percentage of ocular tissue manifestations associated with raised UA was also found to be higher as compared to the study mentioned above.[5] This may be due to the reason that we studied a larger population and used combination therapy for treatment of TB.

The study results regarding hyperuricaemic and creatinine levels in blood after ATT are almost the same when compared with study conducted in Nigeria.[12] Our study also shows similar results as a study conducted recently.[13]

Conclusion

Combination therapy remains a useful treatment in the management of patients with pulmonary tuberculosis, despite the relatively minimal side effects as hyperuricemic uveitis which must be timely diagnosed in order to prevent sight- threatening side effects.

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