

BULLETIN ON THE ADVERSE DRUG EVENT (ADE) PROMPTED BY THE ANTI-TUBERCULAR THERAPY (ATT)**Mohd. Aqib Nizami*, Seema Tabassum and Naseha Iffath**

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ABSTRACT

Mycobacterium tuberculosis (MTB) is one of the major engenders of tuberculosis, it is preventable and curable though patient's compliance is the great challenge. Anti tubercular therapy (isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin) is most commonly used strategy in managing TB. The authors present a case of 23 years old female patient who was admitted in the emergency department with a history of consuming ATT from the past 3 months. Adverse drug event (ADE) associated with this ATT therapy is abundant, and is the major threat which leads to morbidity and even mortality if not recognized early, an equilibrium between management of ADE's and TB with ATT under the right diagnosis with the aid of professional knowledge helps in improving patient compliance and attaining fruitful outcomes of ATT in patients with TB.

INDEXWORDS: Mycobacterium tuberculosis (MTB), Anti tubercular therapy (ATT), isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin.

INTRODUCTION

Mycobacterium tuberculosis is the major culprit for infection Its effect extends not only to the lungs (pulmonary TB) but also effects other sites (extra pulmonary TB). This infection is communicable when people who are sick with pulmonary TB expel bacteria. Coughing is exemplar, Overall, a relatively small proportion (5.15%) of the estimated 1.7 billion people infected with mycobacterium tuberculosis will develop TB disease is much higher among people infected with HIV and also higher among people affected by risk factors such as under-nutrition, diabetes, smoking and alcohol consumption. For the past 5years, it has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS. This is despite the fact that, with a timely diagnosis and treatment, most people who develop TB disease can be cured.^[1]

Approximately 2.9 million people die from TB each year worldwide and about one fifth of them are Indigenous to India.^[2] With such fast spreading web of TB, India has adopted and enforced directly observed treatment short course (DOTs) strategy. The first line medicines included under DOTs include *isoniazid, rifampicin, pyrazinamide, ethambutol* and *streptomycin* are known to cause adverse effect such as gastritis, hepatotoxicity, skin allergies and visual disturbances. Out of these, hepatotoxicity is a potential serious adverse effect.^[3]

Gastritis usually represent specifically to the abnormal inflammation in the stomach lining. People who have gastritis may experience pain or discomfort in the upper abdomen, but many people with gastritis do not have any symptoms or other symptoms such as nausea, vomiting, bloating, loss of appetite and heart burn. The relationship between gastritis and symptoms is not clear.^[4,5] DOTs is usually well tolerated, however some patients may experience ADR's which can be major or minor therefore, for achieving better patient compliance, adverse effect of the drug should also be looked upon, rather than concentrating only on the treatment.^[5]

REVIEW OF LITERATURE

- Adverse effect of first line anti tubercular medicines on patient taking DOTs: a hospital based study, Majority of adverse effect were mild. Most commonly encountered symptoms were abdominal. Most patients reported ADE to be the most likely cause to stop the treatment. Special intervention to cure this mild adverse effect can lead to increased in patient compliance and hence better cure rate. Results also showed that family plays the important role as a support to combat the illness. (Amit kumar singh et al).
- Prevention or delay of gastritis through vestibular stimulation: A hypothesis, we have provided the possible mechanisms by which vestibular stimulation effects gastric secretin. Through animal studies are supporting our hypothesis, we suggest

the researchers to conduct human studies to provide scientific evidence for beneficial effects of vestibular stimulation as a supplementary treatment for gastritis. (Kumar sai sailesh et al).

- Cross sectional study for prevalence of NASID induced gastrointestinal, cardiac and renal complications in India; interim report, Results of the present interim analysis show that the prevalence of GI, cardiac and renal complications among patients is high due to exaggerated usage; however, the final analysis would provide the overall prevalence of this complication. (Suparna chatterjee et al).

CASE REPORT

A 23 years old female patient with a history of consuming ATT since past 3 months was brought to the tertiary care hospital, with the Grievance of Pain in the abdomen associated with nausea and 6-8 episodes of vomiting since 1 day. At the time of presentation patient was on ATT as a therapeutic strategy for the management of tuberculosis. On taking personal history,

it was revealed that the patient was non-alcoholic, non-smoker but gutka chewer. Patient doesn't have any other comorbidities and No significant family history was noted.

Physical examination showed that patient was conscious, cooperative and was responding properly. Patient was feeling weak with the blood pressure of 110/70 mmHg. On cardiac auscultation regular heartbeat with no murmur was heard and a heart rate of 89/min was recorded. Respiratory auscultation revealed symmetrical breath sounds, normal bronchial airway entry with a respiratory rate of 24 breaths/min. Her abdomen was soft, regular with normal bowel sounds.

Initial laboratory investigation showed 0.7 mg/dl of serum creatinine, 18 and 16 u/l of SGOT and SGPT respectively, 89 u/l of alkaline phosphatase, total protein; albumin; total bilirubin and direct bilirubin values of 6.7 gms/dl; 4.2 gms/dl; 0.6 mg/dl and 0.2 mg/dl respectively. Chest X-ray revealed air under diaphragm concluding hallow viscose perfusion.

Table 1: Her vitals in 4 consecutive days.

VITALS	DAY 1	DAY 2	DAY 3	DAY 4	UNITS
BP	100/60	110/70	110/80	120/80	mmHg
HR	92	121	94	90	Beats/min
R/R	22	20	18	24	Breaths/min
CVS	S1S2+	S1S2+	S1S2+	S1S2+	-
P/A	Soft, tender	Soft, tender	Soft, tender	Soft, tender	-
DRAIN	50ml	40ml	20ml	Nil	-
SPO2	80%	88%	86%	98%	-

She was given inj piptaz 4.5gm TID, inj metrogyl 500mg BD, inj tramadol 1amp in 100ml NS, inj zofer 4mg TID, inj pan 40mg BD and inj PCM 1gm SOS. Laparotomy was planned on next day of admission. On day 2, patient was advised for NBM and inj TT stat before surgery. Patient was also advised to have chest physio daily post operation. ATT of patient was stopped on admission. On day 3, patient complained of cough for which saline was give through nebulizer and ATT was reintroduced where it contains only isoniazid, rifampicin and ethambutol lacking pyrazinamide which was present in previous ATT. patient was discharged on 5th day with the following medications: ATT 3tab/day with an interval 30 min in morning, tab. Pantop 40mg OD and tab. Optineuron 1tab OD.

DISCUSSION

As per WHO report of 1999 one third of the world's population is infected with M. tuberculosis.^[6] According to **Peruvian national health strategy** for control and prevention of tuberculosis usually recommended treatment is based on DOTs strategy.^[7] First line drugs under DOTs strategy include multiple antitubercular agents such as isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin and they remain as a cornerstone of TB treatment. ADR to this regimen is common and is usually associated with significant morbidity and even some time causes mortality if not

detected early.^[8] ATT results in ADR of varying degree of severity Which include allergic reactions, GI disorder, hepatotoxicity, neurological disorders, arthralgia and many more.^[9,10,11,12]

According to this study conducted by *Chukanou et al* more than 5% of the patients on ATT experience ADRs.^[13] Mostly treatment of ATT induced ADRs are conservative. For minor side effects ATT should be continued along with symptomatic measure such as antacids, antiemetics, antihistamines or analgesic as appropriate, in case of major side effect the regimen or the culprit drug if identified must be stopped. Further management depends on the nature of side effects and may have to be under direct patient's care.^[14] Majority of the symptoms associated with ATT induced Adverse Drug Event (ADE) are mild such as abdominal pain, nausea, drowsiness. Whereas the patients who are presented with symptoms due to ADE of ATT that requires treatment are categorized as the severe symptoms. There was a marked association between alcohol consumption and smoking with the increase incidence of ADR within the age group of 21-30 years especially in males. There was no marked sign of hepatotoxicity in this patient who was taking ATT since last 3 months. But the patient was presented to tertiary care hospital with the complaints of abdominal pain associated with vomiting indicating the presence of ATT

induced gastritis. Patient intervention and knowledge regarding the management of this ATT induced ADR may have a significant impact on patient compliance to ATT strategy ultimately providing beneficial outcome in treatment of TB.

Family or companion support will also play an important role in combating which is significant in better patient care. Ajwain is most frequently used home remedy in the management of GI symptoms. A fine and comprehensive balance has to be established between ATT and ADR related to it, along with the measure that are taken in management of such ADE to have a better outcome in patients with active TB who are on ATT.

CONCLUSION

By considering this case report of ATT induced Gastritis. We as a Clinical pharmacist suggest to monitor the liver parameters and to perform endoscopic studies in order to evaluate the effects of ATT.

Tuberculosis patients who are under ATT should be under proper vigilance. Management of TB with ATT can pose a challenge with its wide spectrum of ADR that can lead to patients compliance and exacerbate patients condition, Proper diagnosis of ADE and adequate knowledge regarding the pharmacological aspects of drug inducing ADR, and appropriate studies in this regard may reduce economic and psychological burden on each individual patient in near future and can help in improve patient's compliance and quality of life

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