



ISSN: 0975-833X

CASE REPORT

HIGH-DOSE ISONIAZID INDUCED MANIA- A CASE REPORT CONTRIBUTORS

1,*Dr. Girish V. Gaikwad and 2Dr. Chetali V. Dhuri

¹Department and Institution, Assistant Professor, Department of Pharmacology, T.N. Medical College and BYL Nair Hospital, Mumbai Central, Mumbai, India

²Department and Institution, Consultant Psychiatrist, Group of TB hospital, Sewri, Mumbai, India

ARTICLE INFO

Article History:

Received 22nd June, 2016
Received in revised form
19th July, 2016
Accepted 17th August, 2016
Published online 30th September, 2016

Key words:

Isoniazid,
Mania,
Peripheral Neuropathy

ABSTRACT

Isoniazid (INH) has been associated with neuropsychiatric side effects commonly peripheral neuropathy and psychosis. A case of mania is rarely reported in this context. We report a case of classical mania and peripheral neuropathy in a patient diagnosed with extensively drug resistant pulmonary tuberculosis. We discuss the role of high dose of INH and pyridoxine deficiency in development of these symptoms.

Copyright©2016, Dr. Girish V. Gaikwad and Dr. Chetali V. Dhuri. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Dr. Girish V. Gaikwad and Dr. Chetali V. Dhuri. 2016. "High-dose isoniazid induced mania- a case report contributors" *International Journal of Current Research*, 8, (09), 38917-38919.

INTRODUCTION

Isoniazid (INH) induced toxic manifestation frequently reported have been those involving central nervous system, mainly peripheral neuropathy and psychiatric manifestations. Psychiatric manifestations induced by INH are well known in terms of INH induced psychosis consisting of variable symptoms like disturbed sleep, restlessness, irritability, agitation, emotional instability, agitation and abnormal behavior (Agarwala *et al.*, 1975; Bedi, 1994; Tiwari and Verma, 1997; Alao and Yolles, 1998). Jackson, in 1957 had also presented cases with symptoms of depression, euphoria, grandiose ideas, and complex paranoid delusions. [5] Subsequently, a case of classical mania is rarely reported in this context. We report a case of INH induced mania and peripheral neuropathy in a patient of extensively resistant mycobacterial tuberculosis on high dose of INH of category V regimen.

CASE REPORT

Mrs. W, 34-year-old (weight 49kg), diagnosed case of extensively drug resistant pulmonary tuberculosis was

admitted for initiation of category V regimen consisting of injection capreomycin 1 g, para amino salicylic acid granules 12 g, moxifloxacin 400mg, INH 900mg, clofazimine 200mg, linezolid 600mg, augmentin 875/125mg and pyridoxine 100mg. All these medications were given in once daily regimen. She did not suffer from any other medical illness. Her sputum was acid fast bacilli (+ve), hemoglobin - 9.00 g and chest x-ray showed bilateral diffuse opacities. Preliminary laboratory tests assessing liver, kidney and thyroid function were normal. Psychiatric evaluation prior to starting this regimen had not revealed any significant psychopathology. There was no past history suggestive of any psychiatric disorder or psychoactive substance abuse. She was described as an introvert, responsible home maker. Within 72 hours of starting this treatment, she showed abnormal behavior in form of talking incessantly with an elevated mood. Her sleep was also disturbed. These symptoms increased further on day 7 and 8. She was over familiar, singing songs and laughing inappropriately. It was difficult to interrupt when she spoke, also was irritable towards her family members. At the time of interview, she was alert and oriented. She denied suffering from any illness. She was frequently restless and tried to get out of the bed. She did not co-operative for detailed central nervous system examination. Her mood was euphoric, affect excited and speech pressured. Her thoughts were tangential and grandiose.

*Corresponding author: Dr. Chetali V. Dhuri,

Department and institution: Consultant Psychiatrist, Group of TB hospital, Sewri, Mumbai, India.

She considered herself a rich and famous movie actor, also said that her husband owned multiple jewelry shops in the city. She was paranoid towards her relatives and accused them of robbing her jewelry. Her BPRS (brief psychotic rating score) was 37 and Young's mania score was 37 (Overall and Gorham, 1962; Young *et al.*, 1978). Her repeat hematological and biochemical tests including serum electrolytes were within normal limit. Fundus examination, HIV & syphilis status was normal. Computed tomography- head was normal ruling out any neurological pathology.

As INH is known to cause psychosis, it was immediately discontinued. Due to severity of symptoms she was also started on tablet risperidone 2mg, tablet trihexyphenidyl 2mg and tablet diazepam 10 mg in divided dose. The manic symptoms resolved completely within a week of initiating antipsychotics. As her manic symptoms resolved she started complaining of paraesthesias and aches in her upper and lower extremities. CNS examination revealed mild hypotonia, power grade IV, reflexes sluggish, pin/needle sensation decreased, suggesting signs of peripheral neuropathy. Tablet pyridoxine 100 mg started prophylactically was continued. Patient was reassured that discontinuation of INH and regular intake of pyridoxine would lead to gradual decrease in parathesias. Tablet clarithromycin was substituted for high dose of INH in category V regimen. Tab risperidone, pacitane and diazepam were tapered and stopped over next 15 days. She was observed in hospital for 1month at later followed up in outpatient department on regular basis for 7 months;no reemergence of psychological symptoms was noted. Also, paraesthesias had reduced to significant extent.

DISCUSSION

The mechanism of production of INH induced peripheral neuropathy and psychiatric disorders are not clearly known. Pyridoxine deficiency may play a role in the pathogenesis of these neuropsychiatric symptoms. INH causes deficiency of pyridoxine by causing excessive excretion of the vitamin; it also inhibits the activity of brain pyridoxal-5-phosphate (PLP) (Girling, 1984). PLP is a cofactor in the biosynthesis of serotonin, dopamine, epinephrine, norepinephrine and gamma amino butyric acid, also transaminases breakdown these neurotransmitters with PLP as a cofactor (Pallone *et al.*, 1993). PLP is also an essential component of enzymes that facilitate the biosynthesis of spingolipids. The disturbances in neuronal metabolism induced by INH account for the neuropsychiatric side effects observed.^[10] Peripheral neuropathy is known to be usually dose related, on the other hand, relation of psychosis to dosage is less observed (Jackson, 1957). Risk factors for developing these side effects include dose above 5 mg/kg, old age, slow acetylator status, diabetes, renal failure, alcoholism, malnutrition, HIV infection, chronic hepatic failure and pregnancy (Pallone *et al.*, 1993). Other predisposing factors for the occurrence of psychotic illness are family and personal history of mental illness (Goldman and Braman, 1972). The administration of pyridoxine has been advocated for the prevention and treatment of INH induced neurologic manifestations, but it has failed to achieve desired results in INH induced psychosis (Alao and Yolles, 1998).

It is known that acute psychosis induced by INH tends to resolve without specific treatment after the withdrawal of the offending drug (Alao and Yolles, 1998). This case report is distinct due to many reasons. A case of classical mania is rarely reported; and there was co-occurrence of peripheral neuropathy in our patient. She was on prophylactic pyridoxine prophylaxis, and there were no obvious risk factors to precipitate these symptoms. However, she was on high dose of INH (900mg) used in category V regimen for extensively drug resistant cases. We postulate that probably high dose of INH could have played a role in precipitation of acute onset of manic symptoms and simultaneous peripheral neuropathy. In patients receiving conventional low dose of INH therapy, symptoms do not appear until six months, but with high dose of INH symptoms may appear within three to five weeks (Goldman and Braman, 1972). Although, no obvious risk factors were evident in our patient, it could have been possible that she may be a slow acetylator. The ethnic variation in the proportion of slow acetylators is well documented; almost 60% of Indians are slow acetylators as compared to a much smaller proportion of Caucasians, Chinese and Japanese (Gangadharan *et al.*, 1961). Slow acetylators are said to have an increased risk of peripheral neuropathy particularly if it is administered at high dose (Devadutta, 1966). With regards to management, following discontinuation of INH and treatment with antipsychotics for short duration the psychiatric symptoms resolved. Also, symptoms did not recur after stopping antipsychotics. The peripheral neuropathy also gradually improved with continued oral pyridoxine and discontinuation of INH. The prevalence of drug resistant tuberculosis in India is on rise leading to increase in number of people expected to receive treatment for tuberculosis with high dose of INH. Hence, clinicians should be aware of this adverse effect of INH and that it may present with a broad clinical picture including mania as well.

REFERENCES

- Agarwala, M.C., Kansal, H.M., Gupta, R.K., Gupta, D.K., Kumar, S. 1975. Toxic psychosis due to isoniazid. *Indian J. Tuberculosis*. 3:119-20.
- Alao, A.O., Yolles, J.C. 1998. Isoniazid-induced psychosis. *Ann Pharmacother*. 32(9):889-91.
- Bedi, R.S. 1994. Isoniazid induced pyrexia and psychosis in a single individual. *Indian J. Tuberculosis*. 41:269-70.
- Devadutta, S. 1966. The optimum dosage, rhythm and duration of isoniazid therapy in pulmonary tuberculosis. *Ind. J. Tub.*, 13:158.
- Gangadharan, P.R.J., Bhatia, A.L., Radhakrishna, S., Selkon, J.B. 1961. A report on Tuberculosis. *Bull WHO*. 25:765.
- Girling, D.J. 1984. Adverse effects of antituberculosis drugs. *Bull. Int. Union Tub.*, 53:152.
- Goldman AL, Braman SS. An analysis of INH induced psychosis. *Chest*. 1972; 62:71
- Holtz, P. and Palm, D. 1964. Pharmacological aspects of vitamin B 6. *Pharmacol Rev.*, 16:113-78.
- Jackson, S.L. 1957. Psychosis due to isoniazid. *Br. Med. J.*, 28:743-5.
- Overall, J.E., Gorham, D.R. 1962. The brief psychiatric rating scale. *Psychological Reports*, 10:799-812.

- Pallone, K.A., Goldman, M.P., Fuller, M.A. 1993. Isoniazid-associated psychoses: case report and review of the literature. *Ann Pharmacother*, 27: 167-169.
- Tiwari, V.K. and Verma, S.M. 1997. Homicide by a tuberculous prisoner possibly having drug Induced acute delusional psychosis. *Indian J. Tuberculosis*. 1997; 44:95-6
- Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A.1978. "A rating scale for mania: reliability, validity and sensitivity". *Br. J. Psychiatry.*, 133(5):429-35.
