

PSYCHIATRIC DISORDERS IN PATIENTS RECEIVING ANTI-TUBERCULOSIS DRUGS

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SUMMARY

Eleven in-patients of the hospital for Tuberculosis and Chest Diseases, Hyderabad, who presented with psychiatric symptoms resulting in maladjustment were examined and placed in different diagnostic groups. There were five psychotics and six neurotics. Out of the five psychotics, three were manic and two were depressive. Among the six neurotics, three were depressive and one each of anxiety, obsessive compulsive and phobic neurosis. All the patients improved on withdrawal of anti-tuberculosis drugs and there was no recurrence of symptoms on re-introduction of anti-tuberculosis drugs other than isoniazid. On re-introduction of Isoniazid, symptoms recurred. The psychiatric disorders were most likely due to Isoniazid and they were neither dose nor duration related. However, Isoniazid may be readministered in the less severe forms along with appropriate drugs to control psychiatric side-effects.

Introduction

Neuro-psychiatric complications during therapy for tuberculosis have been reported. While there have been enough studies reporting the neurological side-effects during therapy, not many studies have been carried out with regard to psychiatric side-effects. The most common anti-tuberculosis drugs with psychiatric side-effects are Isoniazid, Ethionamide and Cycloserine (Yoshikawa and Fujita 1982). The side-effects range from mild anxiety to insomnia to frank psychosis manifesting hallucinations and delusions.

The aim was to study the psychiatric disorders which occur in patients receiving anti-tuberculosis drugs and to identify the drug causing the same. Only those patients who exhibited mal-adjustment in the hospital environment were included in the study.

Material and Methods

The present study was conducted between March 1982 and March 1983 at the hospital for Tuberculosis and Chest Di-

seases, Hyderabad and included in-patients undergoing treatment already and those newly admitted during the above period. Thus in all a total of 732 in-patients were observed by the nursing staff and the ward attendants for any sign of abnormal behaviour or mal-adjustment in the hospital environment. When the nurses or hospital attendants noticed any patient exhibiting abnormal behaviour they were instructed to refer the case to the authors for detailed assessment.

Only patients who were receiving the following non-ethionamide regimens containing Isoniazid were included in the study: (i) Isoniazid and Thioacetazone regimen and (ii) Isoniazid, Rifampicin, Pyrazinamide and Ethambutol regimen.

Assessment of the patients

- a) History
- b) Mental Status Examination using Indian Psychiatric Survey Schedule. (I.P.S.S.).

Eleven patients who exhibited mal-

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adjustment in the hospital were studied in detail and their psychiatric status was classified into different clinical diagnostic entities. In all the patients no sooner the psychiatric symptoms appeared, all the anti-tuberculosis drugs were withdrawn. On withdrawal of the anti-tuberculosis drugs being given, amelioration of psychiatric symptomatology was noticed in all the patients. Later the anti-tuberculosis drugs were re-introduced after a period of ten to fifteen days in a graded fashion - firstly, drugs other than Isoniazid were re-introduced and the clinical picture was studied. Lastly, Isoniazid was re-introduced and the change in psychiatric status was assessed after a period of two to six weeks.

Results

Table-1 shows the age, sex and diagnostic distribution of the cases. Of the 11 cases reported 8 were male and 3 female. Five cases exhibited a picture of psychosis and six that of neurotic illness. Three of the psychotic cases were of manic and two were of psychotic depression. The neurotic illnesses noticed were of a wider spectrum and included cases of severe anxiety, depressive, phobic and obsessive compulsive neurosis.

Of the eleven cases reported, only two had a past history of psychiatric illness and both had past episodes of mania. In the

immediate previous episodes, both were receiving anti-tuberculosis drugs, Isoniazid and Thiacetazone at domiciliary tuberculosis chemotherapy centres and had improved on discontinuing them. The present episodes of mania were precipitated while receiving Isoniazid and Thiacetazone.

Discussion

Isoniazid is known to cause psychiatric side-effects but these side-effects rarely result in mal-adjustment to the environment. In the present study, all the eleven patients have shown mal-adjustment to their environment in the hospital. The duration of treatment ranged from three weeks to three years and the regimen included Isoniazid. None of the patients received Ethionamide and Cycloserine. Ethionamide and Cycloserine are the other anti-tuberculosis drugs known to cause psychiatric side-effects (Petersun 1980). All the patients were receiving three hundred milligrams of Isoniazid in a single daily dose and tablet B-complex. None of them was admitted to the hospital for psychiatric problems. They developed psychiatric symptoms while staying in the hospital as in-patients.

Previous studies by Jackson et al (1957) showed that psychiatric side-effects during anti-tuberculosis therapy occur when Isoniazid was given in dose ranging from 2.6 milligrams to 4.5 milligrams/kg body

Table 1
Age, Sex and Diagnostic distribution of Cases

Age	Number		Mania	Psychotic depression	OCN	Neurosis		Depression
	M	F				Anxiety	Phobic	
20 - 29	3 (2 M + 1 F)		-	2 (1 M + 1 F)	-	-	-	1 (M)
30 - 39	4 (2 M + 2 F)		-	-	1 (M)	1 (M)	-	2 (F)
40 - 49	3 (3 M)		2 (M)	-	-	-	1 (M)	-
50 - 59	1 (1 M)		1 (M)	-	-	-	-	-
Total	11		3	2	1	1	1	3

M - Male F - Females.

weight, over a period of eight to thirty six weeks.

In the above study, five cases were diagnosed as mania, hysteria, paranoid psychosis with anxiety, toxic psychosis and depressive psychosis. It was also noted that psychoses were not so much dose related as peripheral neuropathy. In our study, out of the five cases of psychoses, three had mania and two had psychotic depression. Unlike the study of Jackson et al, we did not encounter any cases of paranoid psychoses or toxic psychoses. Majority of the previous studies (Jackson 1957, Gupta 1981) have reported regarding the occurrence of psychotic reactions following chemotherapy for tuberculosis. Except for Jackson study reporting one case of hysteria, there have not been many studies reporting neurotic side-effects during treatment. In our study, we encountered six cases with neurotic symptomatology - three cases of neurotic depression and one case each of phobic neurosis and obsessive compulsive neurosis.

After diagnostic categorisation of the cases, all anti-tuberculosis drugs were withdrawn and it was noticed that there was alleviation of symptoms. However, in two cases of mania, we were constrained to use Chlorpromazine in a dose of 100 mg daily to control the manic excitement. After a period of two weeks, anti-tuberculosis drugs other than Isoniazid were re-introduced and no change in psychiatric status was noticed, i.e. the patients did not manifest psychiatric symptoms as before. Even the anti-psychotic drugs which were used to control manic excitement in two cases were withdrawn within two weeks of starting them. In these two cases manic symptoms disappeared. After a period of two weeks, Isoniazid was re-introduced in all cases and it was noticed that recurrence of psychiatric symptomatology occurred in all case within one to six weeks. To prevent recurrence, in cases of psychosis, Isoniazid

was deleted from the drug regimen. But, Isoniazid was continued in three cases of neurosis along with an anxiolytic.

Acute psychotic episodes following administration of Isoniazid have most often been reported to be seen in patients who have past history of psychiatric illnesses (Weidorn and Ervin 1954, Goldman and Braman 1972). However, in our study, except for two cases of mania who had history suggestive of manic illness in the past, all the other nine patients had no such history.

The present study highlights the following points:

1. That Isoniazid could be implicated in the causation of wide range of psychiatric symptomatology in patients receiving antituberculosis drugs.
2. That withdrawal of isoniazid results in alleviation of psychiatric symptomatology.
3. Despite the occurrence of psychiatric side effects due to isoniazid, it is not mandatory to omit isoniazid from drug regimen. Attempts should be made to continue Isoniazid along with psychiatric drugs in cases where the psychiatric symptoms are not very severe. This is especially important in view of the overwhelming beneficial effects of isoniazid.

Conclusions

It can be said that Isoniazid could be implicated in the causation of wide range of psychiatric disorders. Most of the disorders disappear on withdrawal of Isoniazid and the symptoms are non-dose related. In view of the importance of Isoniazid in the anti-tuberculosis drug regimens, it is stressed that attempt should be made to control psychiatric symptoms with appropriate drugs along with simultaneous administration of Isoniazid.

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