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USE OF TRANYLCYPROMINE IN SEVERE RESISTANT DEPRESSION : A CASE REPORT

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ABSTRACT

This case report describes the improvement obtained by using tranylcypromine in a patient of severe treatment resistant depression. The adverse effects faced and steps taken to overcome them have also been discussed.

Key words: Treatment resistant depression, monoamine oxidase inhibitor (MAOI), tranylcypromine

The first MAOI, iproniazid, was identified as an antidepressant in 1952 (Himmelhoch, 1995). Other types of MAOI were gradually developed and their use as antidepressants continued till 1962. Around that time concern regarding hypertensive crises and hepatotoxicity increased. A case report of death on consumption of cheese was reported and over a few years MAOI went out of use. It's only in the mid 1980's that MAOI again began to be used when it was found that fears regarding their side effects were not as serious as to limit their use completely for valid indications. Now MAOI as antidepressants are well accepted and described in pharmacological texts (Hollister, 1995).

Pare et al. (1962) thought patients responding to MAOI had a different genetic specification in comparison to those responding to imipramine. Quitkin et al. (1979) has shown the use of phenelzine in atypical depression and tranylcypromine was also seen to show promise. Atypical depression especially those with anergia and vegetative symptoms have been found to respond better to tranylcypromine (Himmelhoch, 1995). Tranylcypromine has also been shown to be useful in anergic bipolar depression (Himmelhoch et al.,1991) Murphy et al. (1984) has reviewed its use even in endogenous depression.

Use of MAOI in treatment resistant depression has been outlined by Trivedi et al. (1993), Amsterdam & Hornig-Rohan (1996), Hornig-Rohan et al. (1996) and Sharan & Saxena (1998).

However in India, there has been no reported use of MAOI in psychiatric literature in the recent years.

The present case is being reported to describe our experience with tranylcypromine in a patient with resistant depression.

CASE REPORT

Mr. P. S., a 42 year old, married, sanitary inspector presented with a 5 year continuous illness of insidious onset and fluctuating course. The initial symptoms were of anxiety, giddiness and sadness. He was investigated for cardiological problem by a specialist and no anomaly was evident on ECG, cardiac angiogram and TMT. Gradually over 1 year the symptoms worsened. He preferred to remain alone and didn't feel like interacting with other family members or guests. He also used to express sadness of mood and irritability. At times he suspected that someone had done some sorcery (jadu tona) on him which had caused the illness. The symptoms waxed and waned but

showed no particular exacerbating or remitting factor. Within 2 years of onset of illness he started to have, reduced interest in work and lethargy. He stopped going to his job. He did not find any pleasure in any activity and had pessimism, death wishes, reduced personal care, reduced appetite, weight loss and inability to sleep throughout the night. He had no history of hearing voices, thought insertion, thought withdrawal, thought broadcast, suspiciousness of being followed or poisoned or selfmuttering. He had never shown any features of increased happiness or elation or grandiosity. No history suggestive of altered conciousness, loss of memory or intellectual decline was present.

Past history showed alcohol use which had stopped since his illness started however no features suggestive of dependence were present. No other history suggestive of psychiatric illness was present. Family history did not reveal any psychiatric illness. There were no history of continuing stress in the personal life and premorbidly he seemed well adjusted.

Till his first admission at our centre he had been treated with various combinations of medicines which included lorazepam (upto 2 mg/day), alprazolam (upto 1.5 mg/day), diazepam (upto 35 mg/day), propranol (upto 40 mg/day), imipramine (upto 150 mg/day), fluoxetine (upto 20 mg/day). Medications were never given for adequate time intervals or in adequate doses.

At the time of admission his physical examination and preliminary investigations including thyroid function showed no abnormality. Mental status examination showed an average built man with normal psychomotor activity but with depressed affect, ideas of persecution, hopelessness, worthlessness, death wishes. No perceptual abnormality was detected. Other cognitive functions were normal and insight was present.

A diagnosis of severe depressive episode without psychotic features as per ICD-10 was made and the patient was initially started on nortryptiline upto 200 mg/day along with benzodiazepine. Lithium augmentation upto 900 mg/day was started after 3 weeks when no improvement occurred. Even after 6 weeks of nortryptiline of which 3 weeks were with lithium augmentation the patient showed no improvement. Modified ECT were then started and 2 ECTs per week were given for 5 weeks and then stopped when the patient started to show mild memory impairment. By now the improvement shown by the patient was only 30%. At that point lithium and nortryptiline was also stopped and imipramine upto 225 mg/day was given for 4 weeks. Beyond that the patient showed postural hypotension. Fluoxetine 20 mg/day was added after that and at discharge, after a total stay of three and half months, he was on imipramine (200 mg/day), fluoxetine (20 mg/day) and alprazolam (1 mg/day). This continued for 6 weeks with no further improvement above the 30% improvement shown before. On follow-up he was taken off all these medications and put on buspirone (30mg/day) chlordiazepoxide (60 mg/day) and flurazepam (15mg/day). The patient took these medications for 3 weeks, did not find any improvement, and dropped out of follow-up. His condition continued to worsen till he again followed up with us after 7 months during which he had been often taking alprazolam upto 1 mg for sedation.

The patient was admitted for a second time as during the past 7 months there had been 3 suicidal attempts. Mental status examination showed a depressed affect, suicidal ideas, pessimism, ideas of reference and persecution. No perceptual abnormality was present. Other cognitive functions were intact and insight was present. Hamilton anxiety and depression scores showed values of 34 and 33 respectively.

A decision to start a MAOI was taken seeing his previous poor response to other forms of treatment. A two week washout period was given prior to starting tranylcypromine. Tranylcypromine was initially started in a 10 mg OD dose with twice daily BP monitoring to look for postural hypotension. Diet monitoring was done. The dose was gradually increased by 10 mg every 2 - 3 days till 40 mg/day (10 mg/QID)

was reached. At that point the patients, Hamilton Anxiety Score (HAS) was 35 and Hamilton Depression Score (HDS) was 27. Within 2 weeks the scores were HAS-23, HDS-19. The patient also showed both objective and subjective improvement in sadness, pessimism, suicidal thoughts, ideas of reference and persecution. Weekly assessment of Hamilton Anxiety and Depression scores showed decrease of values and by 6 weeks of onset of tranylcypromine treatment the values had dropped to 16 and 12 respectively. The patient's sadness was no more sustained. Suicidal ideas, ideas of reference and persecution, pessimism, had disappeared. Mild degree of anxiety and sadness remained along with mild lethargy and insomnia. Giddiness and anxiety was also ill sustained. The patient had started socializing with other patients and relatives and the patient was sent to work from the ward. The patient continued this arrangement for 1 week with minor physical tiredness and seemed happy at being able to resume his job after 6 years of leave. The patient was discharged from the ward and during follow-ups he continued to perform satisfactorily. At 6 month follow up the patient was working, had occasional sadness and anxiety and was pleased with his condition.

During the stay in the hospital the patient had shown the following side-effects of MAOI. 1) Dizziness due to postural hypotension for which he was told to take increased amounts of fluid with added salt. At least 3 litres of water with 1 packet oral rehydration solution with added salt was used by the patient daily on which his postural drop remained within control, though dizziness to a mild degree remained. 2) Insomnia was treated initially with trazodone upto 100 mg/day but when postural hypotension worsened he was shifted to flurazepam upto 45 mg at night with which sleep improved. 3) Idiosyncratic hypertension upto 190 mg Hg systolic and 110 mg Hg diastolic occured on two occassions but these could be easily managed with sublingual nifedipine upto 10 mg period.

DISCUSSION

Ayd (1995) has defined treatment resistant depression (TRD) as unremitting depression despite treatment with at least two different antidepressants or an antidepressant and a course of electroconvulsive therapy. TRD has also been defined by others and Sharan et al. (1998) reviewed the concept of TRD and defined it as a continuum in which the degree of treatment resistance is ascertained by taking into account the number and quality of failed antidepressant trials.

In our patient we had failed with two different types of tricyclics upto the maximum tolerated dosage and for adequate duration. Lithium augmentation, electroconvulsive therapy and fluoxetine had also failed and so a diagnosis of treatment resistant depression was made and the decision to start MAOI was taken.

Our patient was taking alprazolam tablets as self medication for sedation, off and on, prior to his second admission and so a washout period was given. Tranylcypromine (Parnate), instead of phenelzine was chosen as it was available locally. The dose of tranylcypromine is generally between 20-60 mg/day but a large number of patients require higher doses (Himmelhoch,1995). The patient was then started on tranylcypromine 10 mg/day and the dose was titrated while side effects were noted and for which a 5 week inpatient stay was required. He could tolerate upto 40 mg/day when significant postural hypotension occured.

Postural hypotension and insomnia are notable side effects of MAOI and tranylcypromine has been shown to have idiosyncratic pressor reactions unrelated to food as had been seen in this patient. Different hypothesis have been forwarded by Keck et al., (1991). to explain this phenomenon but no definite reason has been found. A list of all food items to be avoided by the patient were given to him on the basis of directions given by Himmelhoch (1995) and Murphy et al. (1984). The major items among them, that are generally consumed in India are cottage cheese (paneer), chocolates, alcohol (in moderation), soyasauce, curd and some fruits. None of the above have high tyramine content and so have less chance of causing any hypertensive crises. Among alcoholic drinks only red wine is high in tyramine

content.

We could achieve significant improvement in the patient's symptoms and functioning capability within 6 weeks. Table 1 has outlined the change in score in the Hamilton Depression Scale (Marder, 1995) and Hamilton Anxiety Scale (Marder, 1995) over the 6 week period of inpatient stay and it indicates the utility of tranylcypromine in our patient who suffered from TRD.

In India, the use of MAOI for depression, has not been forthcoming probably due to its poor availability, apprehension regarding its side effects, precautions to be taken and requirement of a long inpatient stay for titration of doses. But this case shows the utility of MAOI in the treatment of TRD.

In conclusion, we suggest that MAOI can be used in clinical practice as a possible treatment for TRD, while observing all necessary precaution recommended in the literature.

TABLE 1
SCORE ON HAMILTON ANXIETY SCALE (HAS) AND HAMILTON DEPRESSION SCALE (HDS)

	Weeks	HAS max. score(56)	HDS max. score(64)
Baseline	0	34	33
The point when tranylcypromine 40 mg/day was reached	2	35	27
2 week after max. tolerated dose was reached	4	23	19
3 week after max. tolerated dose was reached	5	19	14
At discharge	6	16	12

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