

Tranlycypromine (MAOI) in Attention Deficit Hyperactivity Disorder in Children

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Tranlycypromine (MAOI) was administered to twenty seven children (mean age 7.4 years $\pm$ 3.2) with DSM-III-R Attention Deficit Hyperactivity Disorder (ADHD). Comparison of pre-and post-medication behavioral assessments using the Conners Abbreviated Hyperactivity Rating Scale showed a statistically significant difference ($P < 0.001$) which suggests that tranlycypromine could be an effective antihyperactivity drug.

(Egypt.J. Psychiat.,1992,15:66-70).

Introduction

It is generally accepted that attention deficit hyperactivity disorder (ADHD) is a heterogenous disorder. The comorbidity of attention deficit hyperactivity disorder (ADHD) occurs in combination with other psychiatric disorders of childhood including conduct disorders, mental retardation, pervasive developmental disorders, anxiety disorders and epilepsy. Children with ADHD respond to a variety of drugs including neuroleptics, antidepressants, and anticonvulsants (Biederman et al., 1989, Evans et al., 1987, Ornitz, 1985). Antidepressants and neuroleptics when used in the treatment of ADHD are not without deleterious side effects (Biederman, 1991; Perry et al., 1985).

Psychostimulant intervention remains the most common treatment for Attention Deficit Hyperactivity Disorder in children (Rapport et al., 1986, Solanto and Wender, 1989 Strayhorn et al., 1988; Birmaher et. al., 1988) . Zimetkin et al., (1985) have shown that monoamine oxidase inhibitors (MAOIs) have immediate, clinically significant benefits and were clinically indistinguishable from dextroamphetamine.

Previous studies of MAOI in childhood psychiatric disorders suggested its effectiveness in depressed and phobic children (Kelly et al., 1970 and, Frommer, 1967).

Psychostimulants are not well recognized as the drug of choice in the treatment of ADHD in Egyptian children because these agents are controlled drugs and their prescription is extremely restricted and even prohibited. Because psychostimulants (dextroamphetamine and methylphenidate) are not available in Egypt, this study was designed as an open clinical drug trial to evaluate the efficacy of tranlycypromine in Egyptian children with hyperactivity (ADHD).

Subjects and Method

Twenty seven children (23 boys and 4 girls) aged 4-12 years (mean 7.4 ± 3.2 years), with moderate to severe hyperactivity diagnosed according to the DSM-III-R criteria of ADHD, were behaviourally assessed regardless of concomitant diagnoses. All of the children went through a 1-month period of assessment during which diagnostic evaluation and laboratory studies were completed. The initial evaluation included a complete medical pediatric examination and psychiatric, psychological, neurological, speech, and hearing evaluation. Labora-

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tory test included complete blood count, metabolic screening, chromosomal study, routine urine analysis, and electroencephalogram. All children were at least 2-week drug free before initiating treatment. Thereafter the patients underwent 1-week baseline observation, a period of dose adjustment and at least 2 weeks of treatment with clinical effective doses of tranlycypromine.

All children were rated by parents using the Conners Abbreviated Rating Scale, a 10-item scale measuring the degree and severity of hyperactivity for two weeks, medication-free period. (Conners, 1969). Children co-diagnoses included (1) Mental Retardation, N=6; (2) Nocturnal Enuresis, N=5; (3) Conduct Disorder, N=5, (4) Infantile Autism; N=2; (5) Epilepsy N=1; and (6) Oppositional Disorder, N=1. Dosage ranged from 5 mg to 30 mg /day given in divided doses. Parents were given a list of tyramine containing food to avoid and were asked not to give children cold medications.

Ratings were obtained once per week during baseline and subsequent periods of the trial.

Children were behaviourally assessed every week using the Conners Scale and parents were asked for side effects. A side effects checklist for stimulant medications and MAOIs was used to track tranlycypromine side effects. Pulse, blood pressure and weight were measured and recorded regularly. Children's weight and vital measures did not change significantly from baseline to latest follow up.

The duration of treatment ranged from two weeks to more than 15 months. Comparison of pre- and post-behavioral assessments used the mean means of the total scores of two or more behavioral ratings.

Two tailed paired t test was carried out.

Results

Comparison of the pre (mean 22.9 $\pm$ 3.1) and post (mean 14.9 $\pm$ 4.5) total scores of Conners Rating Scale revealed a statistically significant difference ($p < 0.001$) (Figure 1). It was observed that the drug reduces hyperactivity with short onset and offset of action in most children. Therefore, doses had to be adjusted and administered twice per day (in the morning and at noon time).

Children with nocturnal enuresis were almost completely dry during tranlycypromine treatment. In only three children, tranlycypromine was discontinued. In the first, a 5-year old girl developed hyper-irritability, volubility and insomnia with tachycardia.

In the other two children, headache and loss of appetite were the reason for discontinuation.

Side effects within first week of treatment included loss of appetite (81.4%), anorexia (51.8%), insomnia (51.8%), decreased weight (48.1%), headache (25.9%), drowsiness (18.5%), depressed mood (11.1%), dullness (11.1%), abdominal pain (11.1%), agitation (7.4%) and rebound hyperactivity (11.1%). However, most of these undesirable effect disappeared within 2-3 weeks of drug administration.

Discussion

The results here are consistent with previous reports indicating the efficacy of tranlycypromine in reducing the severity and intensity of ADHD in children (Zametkin et al., 1985).

While this study has strengths associated with the use of a reliable and valid assessment tool before and after the drug study period, the recording of drug-

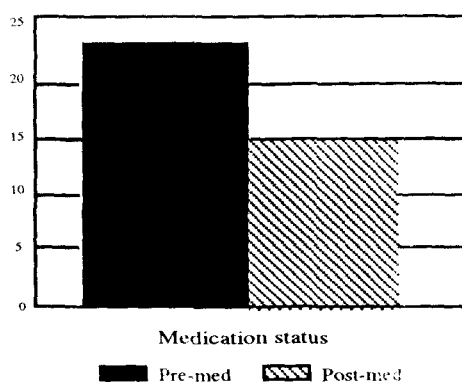
induced side effects systematically, and the trial of an available drug in the Egyptian market to treat one of the most common psychiatric disorders in children, it is nonetheless limited in several ways:

(1) parents ratings were not blind, (2) there were no controls, (3) children were a heterogenous group of diagnoses sharing hyperactivity as a common feature.

Treatment of attention deficit hyperactivity problems is very crucial because this disorder has been reported to result or be associated in academic failure and disturbed social interactions with family and peers (McGee and Share, 1988; Barkley, 1988). Treatment with stimulant has resulted in significant improvement in social and academic functioning.

The present study, although uncontrolled, demonstrates that tranlycypromine is effective in reducing hyperactivity in a heterogenous groups of ADHD children. However, in interpreting these results, certain cautions are in order, specifically the use of parents ratings as the sole source of assessment of behavioral change.

Figure 1
MAOI / ADDH in Children



Second, results could be due to type II error associated with the modest sample size.

Tranlycypromine produced significant behavioral changes which were apparent immediately and within half an hour to an hour from drug administration. However, this beneficial effect lasts from two to four hours after which the child's behavior returned to the baseline or the pretreatment threshold. In only few children, there were reports suggesting the occurrence of a rebound phenomena. This means that the child's behavior escalates slightly higher than the pretreatment level. In these cases, parents were advised to give the second dose about three hours after the first one.

Some children initially responded to tranlycypromine by sleeping, but this calming effect disappeared within few days of treatment continuation. However, in most children the reduction in the level of hyperactivity was striking in contrast to their usual hyperactivity level. In four children, the calming effect of the drug was associated with a state of fear of separation from the parent. In one child the drug has produced a clinging and attachment behaviour where the child followed his mother all over the house.

The emerged undesirable effects are in contrast of those of Zametkin et al., (1985) and suggest that caution should be considered in case selection and drug monitoring. Treatment with tranlycypromine should be preceded with a baseline evaluation and with a test dose of 5 mg or 10 mg depending on the size of the child.

The clinical effectiveness and toxicity of tranlycypromine appears to be dose related. However, since there is a wide individual variability in drug response several recommendation can be made to monitor the antihyperactivity effects of

tranylcypromine including regular check of the blood pressure, heart rate, weight, sleeping hours and level of hyperactivity.

Biochemical etiological speculations suggest that hyperkinetic disorder results from selective deficiency of dopamine in the central nervous system. It is possible that tranylcypromine functions as dopamine agonist, simply increasing CNS dopamine concentration and alleviating the clinical syndrome. However, we agree with Zametkin et al., (1985) that the effect of tranylcypromine in ADHD might be mediated through multiple neurotransmitter changes rather than a single selective alteration of a single amine.

Moreover, future studies should compare behavioral, cognitive and social effects of different dosages of tranylcypromine using multiple measures and cross - over controlled technique.

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Tranlycypromine (IMAO) dans le Trouble: Déficit de l'Attention avec Hyperactivité chez les Enfants

Un groupe de 27 enfants (moyenne d'âge 7.4 ± 3.2) ayant le diagnostic de déficit de l'attention avec hyperactivité selon le DSM III-R a été évalué avant et après l'administration d'une IMAO, tranlycypromine. Les résultats, évalués à l'aide de l'échelle abrégée de Conners, ont montré une différence statistiquement significative ($p < 0,001$) suggérant que la tranlycypromine pourrait être un traitement efficace du syndrome d'hyperactivité.

عقار الترانييل سيبرومين لعلاج اضطراب فرط النشاط وقصور الانتباه في الأطفال

في هذه الدراسة استخدم عقار الترانييل سيبرومين (مثبط أكسيداز أحادي الأمين) في علاج اضطراب فرط النشاط وقصور الانتباه لدى سبعة وعشرين طفلاً مصرياً متوسط عمرهم ٥.٧ سنة، ولقد أظهرت الدراسة أن هناك فروقاً دالة إحصائية بين تقييم مستوى النشاط الحركي قبل تعاطي العقار بالمقارنة بالتقييم الذي أجري بعد استخدام عقار الترانييل سيبرومين، واستخلصت الدراسة أن عقار الترانييل سيبرومين يظهر مفعولاً يقلل من النشاط الحركي الزائد ويفيد استخدامه في التشخيصات المختلفة التي يظهر فيها هذا النوع من الاضطراب.