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Research Article

Appetite and weight loss in children on atomoxetine therapy: an exploratory clinical study

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ABSTRACT

Background: Atomoxetine has been widely used for treating attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults. Several studies have confirmed its efficacy as assessed by parent and teacher ratings with respect to school performance and social and family functioning. Loss of appetite and weight has been its well documented side effect. In this study, we tried to assess the frequency and severity of the side effect of loss of appetite and weight loss in children diagnosed with ADHD and treated with atomoxetine.
Methods: This study was conducted at a tertiary care hospital. Children diagnosed as having ADHD were started on the minimum effective dose of Atomoxetine (0.5–1mg/kg body weight). The weight and calorie consumed by the patient per day were recorded before starting the medication. The doses were titrated over the next one month at the end of which parents were asked about any apparent change in appetite of patients. Weight and the caloric intake were noted and comparisons made with the previous record.
Results: 49 patients completed the study. 21 (42.9%) patients had a decrease in weight. However, 'clinically significant weight loss' (>5% body weight) was seen in 3 (6.1%) patients only. 17 patients (34.7%) reported a decrease in their daily calorie intake. 15 (30.6%) parents reported appetite loss, out of which 9 (18.4%) parents reported a 'major decrease' in the appetite of their children, warranting a change of dose/dosing schedule.
Conclusions: Though a significant number of patients and their parents reported loss of appetite and weight, more frequently in females, clinically significant weight loss was seen only in a minority (6.1%) of patients. Nevertheless, a regular weight monitoring is a must in daily clinical practice when maintaining a patient on atomoxetine.

Keywords: Atomoxetine, ADHD, Children and adolescents, Appetite, Weight loss

INTRODUCTION

Atomoxetine has been widely used in the management of children with ADHD. Numerous studies worldwide demonstrate its efficacy in the disorder.[1-3] Loss of appetite is one of the most commonly reported side effects with atomoxetine and is of concern in the treatment of growing children, especially when there is a substantial decrease in appetite.[4] In many patients this decreased appetite may cause a consequent weight loss.[5] Atomoxetine is associated with improved school outcome as evident by teacher ratings.[6] Social and family functioning also were improved in the atomoxetine groups compared with placebo with statistically significant improvements in measures of children's ability to meet psychosocial role expectations and parental impact as assessed by investigator and parental ratings.[7] In fact, atomoxetine treatment is associated with improvements in Health Related Quality of Life (HRQL), and the improvements are generally stable over time.[8]

Pooled data from ADHD studies in children show that the reasons for discontinuation were most often related to decreased appetite, sleep disturbances and anxiety. Adverse events that occurred statistically significantly more often than with placebo were decreased appetite, vomiting and dizziness, however amongst these, decreased appetite was reported at a consistently higher rate (about 14%).[9] This decrease if reported (peak, less than 10% at any time) would be generally at the beginning of treatment or at the time of dose escalation. Mean standardized weight declined over first 9 months of treatment, then stabilized. Again most of the weight was lost early in therapy and by the heaviest of patients.[10] Long term studies on the effects of atomoxetine over growth, in children with ADHD show that in 2 years of treatment, weight showed a decrease relative to baseline normative weight of 2.7 percentiles, corresponding to 0.87 kg, while continuous atomoxetine treatment was reported to have a minimal effect on height.[11] This side effect of atomoxetine has resulted in the use of the drug for the psychosocial management of obesity and binge eating disorder.[12,13] After an extensive literature search, we were unable to find Indian literature on this particular side effect, or no study focusing on weight loss with atomoxetine in the Indian setting had been conducted. It is well known that metabolic patterns of children in India may differ from the west.[14]

Keeping this in mind the present research was conducted with the aims of assessing the frequency and severity of loss of appetite and weight loss in children, diagnosed with ADHD and started on atomoxetine therapy.

METHODS

This prospective study was undertaken by the Department of Psychiatry in a tertiary municipal teaching hospital. The patients were recruited from children attending the child guidance clinic. 61 consecutive children over a 2 month period presenting with symptoms suggestive of ADHD were screened as per our inclusion and exclusion criteria. The study sample consists of 49 out of these 61 consecutive patients. The inclusion criteria for the study were a diagnosis of ADHD as per DSM-IV TR criteria.[15] Written informed consent was taken from the parents and assent from the children. Patients with a diagnosis of any major medical disorder, having taken any ADHD treatment in the past and past treatment with atomoxetine were excluded from the study.

A semi-structured proforma designed for the study and having data such as DSM IV TR criteria for ADHD, socio-demographic data, clinical profile of patient, weight measurement and average daily caloric intake were answered by the patient. All weight measurements were done using a digital weighing scale and the same scale was used for the entire duration of the study. The National Institute of Nutrition (NIN), Hyderabad calorie scale for Indian foods was used as a tool for caloric calculation.[16] All parents were explained aims and nature of the study. All patients started on atomoxetine were not randomized and clinically needed atomoxetine. Those cases where the clinician felt a need to start other medication were excluded from the study. Thus unlike randomization a true clinical setting was the base for the study. Informed written consent was taken from the parents. On day 1 all children diagnosed with ADHD using the DSM IV-TR criteria were interviewed along with their parents using the specially designed proforma, while weight and average daily calorie intake were recorded before starting the medication. The patients were started on atomoxetine (0.5-1 mg/kg) and parents were asked to watch for emergence of any side-effects. Dose was titrated clinically as per response. After regular medication for a month, the patients were reassessed, weight and average daily calorie intake were re-recorded and parents were asked if they noticed any change in the appetite of their children. Their report was recorded as 'no change', 'minimal change' and 'major change' (especially those patients in whom dose had to be reduced/dose timings were changed) in appetite. The weight and other parameters were measured at the start of the study and after 4 weeks of treatment with the drug. This data was pooled, tabulated and subjected to statistical analysis. In order to ensure low drop-out rate, the patients were provided travel allowance for the study visits and this resulted in a zero drop out for the study. The statistical analysis was done using simple descriptive statistics.

RESULTS

Table 1: Patients showing a change in weight.

Change in weight	Males	Females	Overall
No change	17 (40.5%)	1 (14.3%)	18 (36.7%)
Decrease	16 (38.1%)	5 (71.4%)	21 (42.9%)
Increase	9 (21.4%)	1 (14.3%)	10 (20.4%)
Total	42 (100%)	7 (100%)	49 (100%)

Table 2: Patients showing a decrease in caloric intake.

Change in caloric intake	Males	Females	Overall
No change	28 (66.6%)	2 (28.6%)	30 (61.2%)
Decrease	12 (28.6%)	5 (71.4%)	17 (34.7%)
Increase	2 (4.8%)	0 (0%)	2 (4.1%)
Total	42 (100%)	7 (100%)	49 (100%)

The mean age of the children in the study (n=49) was 10.98 ± 3.4 years and the age range was 6-15 years. Majority of the subjects (n=42, 85.7%) were male. 57.1% children in the study (n=28) had combined type of ADHD while 34.4% (n=17) had predominantly inattentive type of ADHD. The major psychiatric comorbid disorder seen in the group was specific learning

disability (51.02%, n=25). 2 of the children had enuresis while 3 had oppositional defiant disorder. The mean dose of atomoxetine used in the study was 14.61 ± 5.58mg while the dose ranged from 5-25mg. 30.61% patients (n=15) reported loss of appetite as a side effect which is common with atomoxetine. Nausea was reported by 4 patients that subsided in the first 2 weeks itself. 38.1% (n=16) males and 71.4% (n=5) female patients showed a decrease in weight. From the total sample 42.9% patients reported weight loss after starting atomoxetine (Table 1). Clinically significant weight loss (loss of > 5% of one's body weight) was seen in only 3 (6.1%) cases.

Table 3: Appetite change as perceived by the parents.

Appetite change	Males	Females	Overall
No Change	31 (73.8%)	3 (42.9%)	34 (69.4%)
Minimal decrease	5 (11.9%)	1 (14.2%)	6 (12.2%)
Major Decrease	6 (14.3%)	3 (42.9%)	9 (18.4%)
Increase	0 (0%)	0 (0%)	0 (0%)
Total	42 (100%)	7 (100%)	49 (100%)

Reduced caloric intake was commonly reported with 12 males (28.6%) and 5 females (71.4%) reporting a decrease in appetite. Of the total sample 9 patients (18.4%) reported a major decrease in appetite (Table 2). Parents of 9 children (18.4%) reported a major decrease in appetite (Table 3).

DISCUSSION

Unlike many other drugs used in child and adolescent psychiatry, atomoxetine has been studied widely for both safety and efficacy. This is due to the weight loss and appetite reducing effect of the drug as well as the fact that it is used in children right from 6-14 years of age which is the growing phase for the child.[17] This is in keeping with the fact that there is always a worry of whether any lack of growth at this stage may be detrimental to future development of the child. Decreased appetite has been by far the most commonly reported side effect with atomoxetine with rates between 9-14% being reported across studies.[18] The rates were similar to that of studies reported abroad. It must also be kept in mind that parents and children may show discrepancy when reporting about dietary and caloric factors as parental anxiety may contribute to false reporting.[19] This study demonstrates that atomoxetine induced weight loss and reduced caloric intake as well as decreased appetite is common in the Indian population. The study is marred by the lack of a control group and being a small single centre, small duration study with just 49 cases. Larger studies would elucidate the safety of atomoxetine in a better manner. The study may have a bias that it was an open study and the focus was on side effects rather than efficacy that may have led to false reporting. Further studies in this direction using randomized controlled models are warranted.

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