How common is attention deficit hyperactivity disorder in a cohort of children with functional constipation, and does ADHD treatment improve functional constipation?

Type
Research paper

Keywords
children, attention deficit hyperactivity disorder, constipation

Abstract
Introduction
Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders in children. Functional constipation is common in children and has a significant impact on the quality of their life, affecting both physical and emotional well-being. The aim of this study was to evaluate the frequency of ADHD in functional constipation patients and its treatment effect on constipation.

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In this clinical trial study, 80 children with simultaneous ADHD and functional constipation were allocated to two equal groups by block randomization method. One group was treated only with ADHD drugs and the second group was treated for ADHD and functional constipation. Subsequently, the treatment outcome was evaluated in both groups.

Results
The frequency of ADHD in functional constipation patients was 13.87%. The frequency of functional constipation recovery in the first and second group was respectively 2 (5%) and 39 (97.5%) (p <0.001). ADHD treatment has no significant effect on the recovery of constipation. There was no statistically significant relationship between the response to treatment with age, sex and duration of having ADHD and constipation.

Conclusions
In patients with simultaneous ADHD and functional constipation, ADHD treatment alone did not influence on the recovery of functional constipation and vice versa.
How common is attention deficit hyperactivity disorder in a cohort of children with functional constipation, and does ADHD treatment improves functional constipation?

Short title: Attention deficit hyperactivity disorder in children with constipation.

Abstract:

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Keywords: Attention deficit hyperactivity disorder, Constipation, Children
**Introduction:** prevalence of constipation in the worldwide general population is very variable. It is estimated that between 0.7% and 29.6% of children suffer from constipation[1]. Functional constipation is constipation with no specific anatomical, medical or pharmaceutical causes that is more common in children[2]. Functional constipation in children is multifactorial and two factors inadequate fiber intake in dietary and delayed bowel movements often lead to progression of constipation[3]. Much effort is being made till now to standardize the terminology of children's constipation and several international guidelines have been accepted for its definition, including NASPGHAN[4], PACCT [5], ROME III[6], but none of them have been widely used in clinical practice or research work. ADHD is one of the common behavioral problem in children[7, 8]. ADHD defines as sustained pattern of low attention or low attention with hyperactivity and impulsive behavior that is more than expected due to the age and level of development of the child [9]. The reported incidence of this disorder in school age children is between 3% and 8% [7, 10, 11]. It is more common in male than female (3 in 1 to 5 in 1) and the symptoms of the disease usually present by 3 years old[7]. Children with ADHD are at increased risk of other problems such as antisocial behavior, anxiety disorders, mood disorders, learning disorders, drug abuse and communication problems [12, 13,14].

Experts have experimentally found that in children's constipation, the importance of managing constipation-related behaviors is not less than dietary or therapy regime[15]. Considering the higher prevalence of constipation and fecal incontinence among children with ADHD and the hypotheses explaining this relationship including behavioral problems, neurobiological disorders, defects between the nervous system of the digestive system and the central nervous system, and the delay in maturation of the gastrointestinal tract[16], the aim of this study was to determine the frequency of ADHD in children with functional constipation and the effect of ADHD treatment on their constipation.
Materials and methods: In this study, 2,090 children aged 4 to 12 years old with constipation referred to pediatric gastroenterology clinic of Besat Hospital in Hamadan City, Iran, during the years 2016 and 2017, after confirming the diagnosis of functional constipation by pediatric gastroenterologist (based on the criteria of 2006 ROME III[6]), were evaluated to determine simultaneous existence of ADHD using the Conners Questionnaire. If the patient had total score of 34 points he/she was referred to a psychiatrist, and if ADHD was approved by psychiatrist, he was entered into the study. Patients with organic causes of constipation including Hirschsprung's disease, hypothyroidism, spina bifida occulta, anorectal abnormalities, non-retentive fecal incontinency, chronic intestinal pseudo obstruction, history of anorectal/colon surgery, and taking medications which could modify bowel habit, were excluded from the study. All parents gave a written informed consent and the parents took the oral assent of the children.

Eighty patients of 290 patients with simultaneous ADHD and functional constipation were eligible by simple randomization and then randomly divided by random blocks, into two equal groups.

Non-treated group: They only treated under ADHD by standard method [17].

Treated group: At the same time, they treated ADHD and functional constipation including dietary regimen and PEG without electrolyte at maximum dose (0.7 g / kg / day, 13.8-40 g / daily), twice a day. For children with rectal impaction, disimpaction was initially performed with bisacodyl suppository for 3-5 days (5 mg/daily >4 years). No further treatment was allowed for constipation during the study.

Patients' data was collected by a questionnaire including name, sex, age, duration of constipation, consistency / size / frequency of stool, number of painful defecation, fecal incontinence per week, stool mass in the abdomen, or rectum.
Parents were given dose regulation training to record the number and consistency of stool, frequency of stomach incontinence, abdominal pain, and pain relief.

Patients were examined and re-visited at 1, 3, 6 and 12 months after starting treatment, and drug dosage was adjusted.

To evaluate the response to treatment of ADHD, the Conners Questionnaire was used again, which would have been considered as improvement if the patient's score was less than 34. The definition of response to constipation treatment was ≥ 3 bowel movement weekly, ≤ 2 episodes of fecal incontinence per month and absence of abdominal pain.

In this study, quantitative variables were presented by mean and standard deviation; and qualitative variables were described by percent. Chi-square test used to evaluate association between functional constipation improvement and sex/ type of treatment. Kolmogrove-Smirnove one sample test was used to normality detection. To compare disease duration between improve and non- improve patients, Mann-Whitney U test was used, because distribution of disease duration was not normal. Data were analyzed using SPSS 16 software. P value < 0.05 was considered statistically significant

Results:

Eighty children with simultaneous ADHD and functional constipation were enrolled.

Forty were in non-treated group and Forty in treated group.

The percentage of male and female in non-treated group and treated group was respectively 55%, 45%, 57.5% and 42.5% (P = .0822). With mean age 8.02 ± 1.9 and .807 ± 2.3 years(P = 0.458)

There were no significant differences regarding demographic data and duration of ADHD and constipation between the two groups (Table 1).
The frequency of constipation recovery in non-treated group was 5% (2) while it was 97.5% (39) in treated group which the difference was statistically meaningful (p<0.001).

There was no statistically significant relationship between functional constipation recovery in children with ADHD and age, sex, and duration of having functional constipation and ADHD .(Table 2).

The frequency of ADHD recovery in non-treated group and treated group was 100%.

**Discussion**: In the present study, 13.87% of children with functional constipation had ADHD. The recovery of functional constipation in patients with ADHD that simultaneously treated for constipation was higher than patients that only received ADHD treatment. This means that treatment of ADHD has no effect on the treatment of constipation. There was no significant correlation between the recovery of functional constipation in children were treated for ADHD and constipation with duration of having ADHD and functional constipation and patient' age and sex.

Also the treatment of constipation did not significantly affect the frequency of ADHD recovery.

In a study by McKeown et al in the United States between 2005 and 2007 in children aged 4 to 12 years old, the prevalence of ADHD were 4.4%, and the incidence of functional constipation in children with ADHD were 4.1%, while in non-affected children to ADHD, it was 1.5%. Based on the findings of this study, although the risk of ADHD may increase the risk of functional constipation, ADHD treatment has no significant effect on the increase or decrease of constipation[18].

In the present study, similar to McKeown colleagues' findings, treatment of ADHD did not influence on the functional constipation recovery.
In a study by Duel et al in the United States which its results published in 2003, in 28 patients with ADHD in comparison with 22 healthy persons with voiding dysfunction, measured by the Dysfunctional Voiding Symptom Survey questionnaire, The mean of total score of DVSS questionnaire in male with ADHD and control group was respectively $14.83 \pm 3.68$ and $6.6 \pm 5.74$, and in female with ADHD and control group, was respectively $19.0 \pm 5.3$ and $5.83$. The results of this study showed that in patients with ADHD, the mean score of DVSS questionnaire (symptoms of fecal dysfunction) was significantly higher than the control group in both male and female [19].

According to the results of the Benninga et al study on children aged 5 to 17 years, due to problems with defecation of stool and abdomen and behavioral problems, it seems there is no relationship between colonic / anorectal function and behavioral profiles. Although, children with gastrointestinal disorders had more behavioral problems than the control group[20].

The results of Becker et al. research on neural process of excitement and fecal incontinence on 14 children with fecal incontinence and constipation showed that in children with fecal incontinence, the response process emotions and excitement was increased and could be considered as Neuro-cognitive vulnerability that it is due to the relation of Enteric Nervous System (ENS) with Central Nervous System (CNS)[16].

In a study by Niemczyk et al in children aged 7 to 17 years old with ADHD, the delayed bowel control was significantly more prevalent than children in the control group but treatment of ADHD, especially medication, can improve treatment outcome of incontinence [21], which is different with finding of the present study.

In our study, the treatment of constipation did not significantly affect the frequency of ADHD recovery. Unfortunately, no similar study was found for comparison.
Although functional constipation may be more prevalent in children with ADHD [18], or children with gastrointestinal disorders may have more behavioral disorders and neurobiological disorders, including deficiencies between nervous and central nervous system and delayed maturation of the gastrointestinal motility may have relation with functional constipation[16], but according to our research, the treatment of ADHD and constipation have no significant effect on the recovery of each other. In the other hand, each disorder requires separate treatment.

**Conclusion:** In patients with functional constipation, ADHD is a common association and treatment of ADHD is not effective on the recovery of functional constipation, also treatment of constipation has no effect on the recovery of ADHD.

**Ethical considerations:** This study was conducted with the approval of the Ethics Committee of Hamadan University of Medical Sciences. Written consent was given from parents of all participants in the study.

With the ethics code, Deputy of Research and Technology IR.UMSHA.REC.1395.535

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Conflict of interest: the results of this study are not in conflict with the interests of the authors.

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References:


Table 1: Distribution of demographic and clinical characteristic between two groups.

<table>
<thead>
<tr>
<th>variable</th>
<th>non- treated group a</th>
<th>treated group b</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>22(55)</td>
<td>23 (57.5)</td>
<td>0.822*</td>
</tr>
<tr>
<td>Number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>8.02 (1.9)</td>
<td>8.07 (2.3)</td>
<td>0.458**</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of having constipation (month)</td>
<td>11.52 (2.89)</td>
<td>11.37 (2.78)</td>
<td>0.594**</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of having ADHD (month)</td>
<td>13.47 (4.78)</td>
<td>13.14 (4.46)</td>
<td>0.624**</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Chi-square test  **. Student t test;

a Patients only treated under ADHD;  b patients treated under ADHD and constipation
Table 2: Distribution of demographic and clinical characteristic between recovered and non-recovered groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recovered</th>
<th>Not recovered</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender number</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24 (60%)</td>
<td>27 (67.5%)</td>
<td>0.485*</td>
</tr>
<tr>
<td>Female</td>
<td>16 (40%)</td>
<td>13 (32.5%)</td>
<td></td>
</tr>
<tr>
<td>Age(years) Mean (SD)</td>
<td>8.04 (2.1)</td>
<td>8.06 (2.03)</td>
<td>0.967**</td>
</tr>
<tr>
<td>Duration of having ADHD(month)</td>
<td>13.00 (4.50)</td>
<td>13.61 (4.80)</td>
<td>0.557**</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of having constipation(month) Mean (SD)</td>
<td>11.21 (2.80)</td>
<td>11.61 (2.88)</td>
<td>0.531**</td>
</tr>
</tbody>
</table>

* Chi-square test **. Student t test