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The effect of methylphenidate for giggle incontinence in children

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Abstract

Introduction: Giggle incontinence (GI) is a rare form of urinary incontinence that occurs during or immediately after laughing due to involuntary and complete bladder emptying. Few studies in the literature report that methylphenidate can be effective in treatment of this condition.

Objective: The aim of this study is to characterize children with GI and evaluate their response to methylphenidate, as well as describe treatment duration, dosage of methylphenidate, relapse rates after discontinuation of medication, and side effects.

Methods: Medical records and 48-h frequency-volume charts from children treated with methylphenidate for GI in the period January 2011–July 2021 were retrospectively analyzed.

Results: Eighteen children were diagnosed with GI and fulfilled inclusion criteria. Fifteen patients were included in analysis, as 3 out of 18 children decided not to take the methylphenidate that was prescribed. In total, 14 out of the 15 GI patients treated with methylphenidate experienced clinical effect. All patients included in the study had methylphenidate prescribed in a dose range of 5–20 mg daily. Treatment duration ranged from 30 to 1001 days, with a median of 152 days (IQR 114, 243.5). Ten children experienced complete response and two of those reported symptom relapse after discontinuation of the methylphenidate. Only mild and short-lasting side effects were reported by two patients.

Discussion: Our study demonstrates that methylphenidate is an effective treatment in children diagnosed with GI. Side effects are mild and uncommon.

KEYWORDS

enuresis risoria, giggle incontinence, methylphenidate, urinary incontinence

Abbreviations: EBC, expected bladder capacity; GI, giggle incontinence; ICCS, International Children's Continence Society; MVV, maximum voided volume.

1 | INTRODUCTION

Giggle incontinence (GI) or enuresis risoria is a rare form of urinary incontinence defined by the International Children's Continence Society (ICCS) as a condition in which involuntary and complete bladder emptying occurs during or immediately after laughing, with normal bladder function when there is no laughter.[1] However, GI can in seldom cases coexist with overactive bladder complicating diagnostics and definitions. The condition is most frequently seen among prepubertal females[2–5] and may be associated with a positive family history.[6]

Although GI is considered benign, these episodes of incontinence may constitute a significant psychological burden for the patients resulting in decreased self-esteem and withdrawal from social activities.[7,8]

The pathophysiology of GI has not yet been fully understood and reflecting our lack of knowledge, the appropriate treatment is also debated.

Two theories on the pathophysiology are presented in the literature. The first suggested by Sher and Reinberg[5] hypothesizes that the condition may have its origin in the central nervous system. Thus, the phenomenon may be a type of cataplexy where laughter causes loss of muscle tone resulting in urinary incontinence. The authors were among the first to successfully treat GI with central stimulants.[5] The second theory highlights bladder and pelvic floor dysfunction as an essential part of the pathophysiology.[9] Bladder retraining improving sphincter contraction through pelvic floor muscle exercise and muscle recruitment by use of biofeedback techniques have been found to have modest success.[10] It is suggested that biofeedback therapy may have a role in GI patients before or in combination with pharmacotherapy.[4]

At present, it is widely accepted that methylphenidate is a viable option for symptom management in GI.[2,11] However, the mechanism of action by which methylphenidate improves continence remains unclear. Moreover, only few case series studies have been conducted, documenting a high rate of treatment success.[2,4,5,11]

In some clinical settings, methylphenidate is offered to patients with GI as first line treatment, even though only small sample size studies have been conducted to evaluate the effect. Further knowledge of the efficacy and treatment duration of methylphenidate in GI is needed. Moreover, studies addressing prognosis after drug discontinuation are warranted.

The aim of this study is to characterize children with GI and evaluate their response to methylphenidate as well as describe treatment duration, dosage of methylphenidate, relapse rate after discontinuation of medication, and side effects. We hypothesize that GI is a centrally mediated disorder, which can be treated effectively by methylphenidate.

2 | MATERIALS AND METHODS

We retrospectively reviewed medical records of children, who presented with symptoms of GI referred to three pediatric outpatient incontinence clinics in Denmark, at Gødstrup Hospital, Aarhus University Hospital, and Aalborg University Hospital, from January 2011 to July 2022.

The medical record registries in Denmark are based on ICD-10 codes (International Classification of Diseases 10th revision code), however, there is no specific ICD-10 code for GI. Therefore, a search for a prescription of methylphenidate to patients from the three outpatient clinics was made. This was done because GI is the only diagnosis for which methylphenidate is prescribed at the three included pediatric outpatient incontinence clinics. The medical records of all the identified patients were systematic reviewed to ensure, that included patients fulfilled the in- and exclusion criteria.

Inclusion criteria were age 5–18 years, confirmed diagnosis of GI according to ICCS standard[1] and prescription of methylphenidate. Exclusion criteria included urge incontinence and/or enuresis, as well as known genitourinary structural abnormalities or neurological problems.

Each patient had been monitored with regular consultations and was individually adjusted in administration form and dosage according to treatment response. Patients had received information on the duration of action of each form of methylphenidate.

Demographic data were extracted from the medical records along with data on voiding habits, clinical presentation, medical history, and effect of methylphenidate.

Treatment outcome was characterized as follows: nonresponse (<50% decrease in number of incontinence episodes), partial response (50%–99% decrease), and complete response (100% decrease) as defined by the ICCS.[1]

Data on maximum voided volume (MVV), fluid intake, and micturition frequency were obtained from a 48-h frequency-volume chart filled out by the patients at the time of GI diagnosis and before treatment with methylphenidate. Expected bladder capacity (EBC) was calculated by the formula: $EBC\ (mL) = (age(years) \times 30) + 30$.

Distribution of data were examined using histograms and QQ-plots. Nonparametric data were reported as median with interquartile range (IQR) for nonnormal distributed data and as mean ± standard deviation (SD)

for normally distributed data. Categorical data were presented as number (%). Data were analyzed using statistical software package R version 3.3.1.[12]

3 | RESULTS

Twenty-four patients were diagnosed with GI and received a prescription of methylphenidate at the three outpatient incontinence clinics during the study period. By going through the medical records, it became evident that six of these patients merely suffered from ongoing daytime urinary urge incontinence treated with anticholinergic medication. Therefore, these six patients were excluded from the analysis.

In total, 18 patients were diagnosed with GI and fulfilled the inclusion criteria (Figure 1).

Demographic data are summarized in Table 1. Most of the patients were female ($n = 13$, 72%) with a mean age of 12.7 years (SD 2.3). Three patients had a known family history of GI ($n = 3$, 17%). Incontinence frequency was daily to once weekly. Mean number of weekly incontinence incidents were 5.2 (SD 2.7).

Two female patients were diagnosed with attention deficit disorder, respectively 6 months and 3 years after the GI diagnosis. The GI symptoms were treated with methylphenidate before the psychiatric diagnosis. When the attention deficit disorder diagnosis was established, the methylphenidate prescribed by the pediatrician was replaced by an extended-release tablet (Concerta® [methylphenidate HCl]) and the dose was increased. The GI symptoms responded equally to the initially lower dose of methylphenidate before the replacement; therefore, the initially lower dose is noted below.

Ten out of the 18 patients ($n = 10$, 55.5%) had filled out a 48-h flow-volume chart before starting methylphenidate treatment (Table 2). These patients had a mean fluid intake of 1114.4 (SD 353.2) mL/day and a mean voiding frequency of 6.2 times (SD 1.4) per day. While their mean value of MVV/EBC was 0.8 (SD 0.2). None of the included patients reported daytime symptoms other than GI.

Fifteen patients were included in analysis (Table 3), as 3 out of 18 patients decided not to start on the medication.

In total, 14 out of the 15 GI patients treated with methylphenidate experienced significant effect of the treatment. Ten (66.7%) patients presented with complete response. Four (26.7%) experienced partial response. Only one patient (6.7%) had no-response.

Of the 15 patients, both gender experienced effect of the treatment. Three out of 4 males and 7 out of 11 females had complete response. One male and three females had partial reduction in incidents of GI. One female presented with no-response.

Treatment duration ranged from 30 to 1001 days, with a median of 152 days (IQR 114, 243.5). Treatment duration for complete responders ranged from 91 to 368 days, with a median of 159 (IQR 150.3, 205.8).

All patients included in the study had had methylphenidate prescribed in short (4-h duration) and/or intermediate (8-h duration) acting forms in a range of

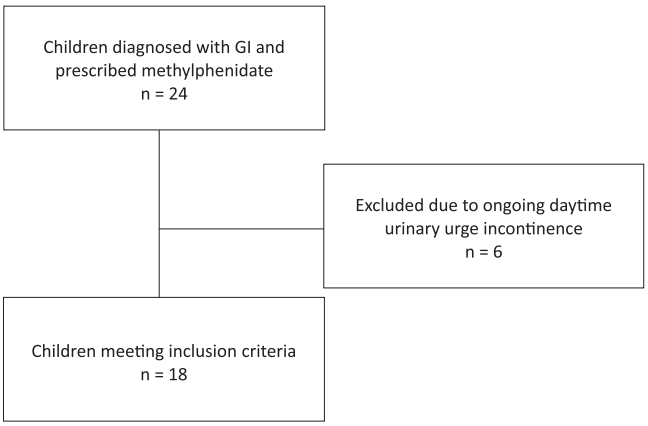

FIGURE 1 Illustration outlining the inclusion and exclusion of patients. GI, giggle incontinence.

TABLE 1 Demographic data.

No. of patients ($n = 18$)	
Female, *n* (%)	13 (72.2)
Age, mean (SD)	12.7 (2.3)
Known family history of giggle incontinence, *n* (%)	3 (16.7)
Psychiatric diagnosis, *n* (%)	2 (11.1)
Incidents before treatment, *n* (%)	
Weekly	3 (16.7)
Two to three times a week	3 (16.7)
Daily	12 (66.7)
Incidents weekly, mean (SD)	5.2 (2.7)

TABLE 2 Forty-eight-hour flow-volume chart.

No. of patients ($n = 10$)	
Fluid intake (mL), mean (SD)	1114.4 (353.2)
Voiding frequency per day, mean (SD)	6.2 (1.4)
MVV/EBC, mean (SD)	0.8 (0.2)

Abbreviations: EBC, expected bladder capacity; MVV, maximum voided volume.

TABLE 3 Treatment.

No. of patients ($n = 15$)	
Incidents after treatment with methylphenidate, *n* (%)	
None	10 (66.7)
Few	2 (13.3)
1–2 times a month	1 (6.7)
2–3 times a month	1 (6.7)
17 times a month	1 (6.7)
Effect of methylphenidate, *n* (%)	
No response (<50% reduction)	1 (6.7)
Partial response (50%–99% reduction)	4 (26.7)
Complete response	10 (66.7)
Days of methylphenidate treatment, median (quantiles)	152 (114, 243.5)

5–20 mg daily. The dosage was adjusted individually, but none received a daily dose beyond 20 mg. Patients with complete response of methylphenidate were treated with, respectively, 5 mg intermediate acting form ($n = 2$), 10 mg intermediate acting form ($n = 3$), 10 mg short acting form ($n = 4$), and 20 mg short acting form ($n = 1$). Patients with partial response were treated with, respectively, 5 mg intermediate acting form ($n = 1$), 10 mg short acting form ($n = 1$), and 20 mg intermediate acting form ($n = 2$). The one patient who had no effect, was treated with 10 mg intermediate acting form for only 30 days.

Methylphenidate was administered as following. The short acting form was given respectively 10 mg once a day in the morning, 5 mg twice a day morning and afternoon, 10 mg twice a day morning and afternoon. The intermediate acting form was given in the morning. Patients taking 5 mg in the afternoon were advised to take the medication before social activities.

Two of the 10 children with complete responds required up-titration/change of their methylphenidate dose to reach full effect on symptoms. One patient was treated with 5 mg × 2 short acting form in 3 months, hereafter the prescription was replaced by 10 mg × 1 short acting form. The second patient was treated with 5 mg short acting form for 2.5 months and hereafter the prescription was replaced by 5 mg intermediate acting form.

Nine of the 10 patients with complete response agreed to discontinue methylphenidate. They were followed up for minimum of 3 months after discontinuation (median 3 months, IQR 3, 4). Two patients experienced relapse of GI symptoms within the follow-up period.

Patients were instructed to pause methylphenidate after a period of at least 3 months without GI incontinence incidents. For those who stopped the medication, it was not weaned. The patients were instructed to pause the medication after a period of at least 3 months without GI incontinence incidents. Patients taking 5 mg in the afternoon were advised to take the medication before social activities.

At the latest follow-up of all 18 patients, five patients were still being treated with methylphenidate; Two patients with partial response, treated for 4 and 15 months, had tried discontinuation of the medication, but due to few wetting episodes it was decided to continue with methylphenidate as needed. One patient with complete response had been treated for 5 months and had not yet tried discontinuation of the medication at the end of study period. Two patients were treated with an extended-release tablet (Concerta®) due to concomitant psychiatric diagnosis.

Only two patients reported side effects to methylphenidate treatment. The side effects were considered mild and short-lasting but not further specified in the medical records.

4 | DISCUSSION

Our study demonstrates that methylphenidate is an efficient treatment in children diagnosed with GI. We found that 14 out of 15 patients (94%) with GI had been effectively treated with methylphenidate, and 10 out of 15 (67%) experienced complete response. The median treatment duration was 152 days (IQR 114, 243.5). The dosage was adjusted individually, but none received a daily dose beyond 20 mg, and only two patients reported mild and short-lasting side effects to methylphenidate. Two patients experienced relapse of GI symptoms after discontinuation of methylphenidate within the follow-up period.

Retrospective studies evaluating the effectiveness of methylphenidate in GI have found methylphenidate to have a high success rate, resulting in complete cessation of incontinence in 72%, 80%, 100%, and 100% of trial participants, among sample sizes of 21, 15, 9, and 7 patients, respectively.[2,4,5,11] The studies demonstrated a higher prevalence of complete response compared with our findings. The observed difference in prevalence of complete response may be due to the fact, that some patients may not have been treated for a sufficient time, as one patient decided to stop treatment after 30 days.

Haciislamoglu et al.[4] retrospectively studied children suffering from GI who failed to respond to behavioral urotherapy. The authors reported complete response in 72% of patients during the initial 3 months on 5 mg methylphenidate. GI relapsed in three patients after the 3 months trial, which led to only 55% being symptom free at the 12-month clinical assessment. Berry et al.[2] reported complete response in 80% during the initial 2 months period with treatment of 0.2–0.5 mg/kg daily methylphenidate. GI recurred in 9 of their 12 patients after the trial. Responders to methylphenidate remained on medication for 2 months to more than 3 years, but medication was discontinued in 6 of 12 patients. Only two patients were reported cured. Berry et al. concluded that methylphenidate is an option for GI symptom management. Chang et al.[11] reported complete cessation of wetting in all nine patients after 12 months of treatment with a daily dose of 5 mg methylphenidate. They also reported a mean symptom resolution period of 7 months (range 3–12 months), which was not elaborated. They suggested local or central efficacy of methylphenidate in urethral function increasing urethral closure pressure, as they found no changes in urodynamic parameters. Sher and Reinberg[5] reported that all seven patients were continent during treatment with 1–5 years of follow-up.

Studies had reported a treatment duration ranging from 2 months to more than 3 years.[2,4,5,11] Our study showed a median treatment duration of approximately 5 months, a median of 152 days (IQR 114, 243.5). The dosage of methylphenidate in our study ranged individually from 5 to 20 mg, in short and/or intermediate acting forms. Sher and Reinberg[5] reported treatment with an individual dosage of methylphenidate from 5 to 20 mg. In other previous studies, the dosage of methylphenidate has been reported as respectively 5 mg daily[4,11] and 0.2–0.5 mg/kg daily.[2] To our knowledge no optimal duration or dosage of methylphenidate treatment in GI has yet been established.

Relapse after end of treatment was reported by three previous studies, the time to relapse was not evaluated. Due to the retrospective design in our study, the follow-up period differed for the 10 patients who had complete effect. Nine of the 10 patients with complete response agreed to discontinue methylphenidate, and these patients were followed up minimum 3 months after discontinuation. Two patients experienced relapse of symptoms within the follow-up period. The observed difference in relapse rate between the retrospective studies may be due to a predeterminate treatment duration with a predefined dosage of methylphenidate. In our study, the dosage of methylphenidate was adjusted individually aiming complete cessation of incontinence.

In our study, only mild and short-lasting side effects were reported by just two patients. Previous retrospective studies have reported both fewer and more frequent side effects. In a study on nine children receiving methylphenidate no side effects were seen,[11] while in the study by Haciislamoglu et al., 3 out of 21 had to discontinue the medication because of side effects as irritability, agitation, and sleep disturbances.[4] Berry et al. reported side effects in three patients during a 2-month treatment period as decreased appetite and difficulty in falling asleep.[2]

An association between female gender and GI in children has been found in several previous studies.[2–5] Our study supports the hypothesis of female predominance. In our study 73% were female. Previous studies consist of a lower proportion of males, as the authors evaluated a population of 85.7%, 90%, and 100% females.[2,4,11] We found that methylphenidate had complete effect in 3 out of 4 males and 7 out of 11 females.

Our study has several limitations. This is a retrospective, observational study with a small sample size and no control group, and therefore subject to possible selection and information bias.

In our study, we did not compare different formulations of methylphenidate. Another limitation is the short follow-up period; the minimum follow-up period of 3 months might underestimate the risk of recurrence.

A strength of this study is a well-characterized patient sample with a confirmed diagnosis of GI according to ICCS standardizations.[1] Another strength is the inclusion of post discontinuation follow-up, as all patients with complete response of methylphenidate were followed up minimum 3 months after discontinuation of medication. Thus, our study provides solid data on the risk of relapse of GI.

5 | CONCLUSION

Methylphenidate is an effective treatment in the majority of children diagnosed with GI. Our study supports the value of methylphenidate in both female and male patients. The median treatment duration time was approximately 5 months. A daily methylphenidate dose with the range of 5–20 mg seems generally well tolerated. Two patients experienced relapse of GI symptoms after discontinuation of methylphenidate within the follow-up period.

These findings support the theory that GI is a centrally mediated disorder. Larger randomized-controlled trials with adequate post discontinuation follow-up are needed to draw safe conclusions on the most appropriate management of this condition.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

ETHICS STATEMENT

This research required patient consent statement.

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