

Is Response to Enuresis Treatment with Desmopressin Influenced by Family History, Associated Comorbidities or Obesity?

Matjaž Kopač, MD, DSc

Matjaž Kopač, Division of Pediatrics, Department of Nephrology, University Medical Centre Ljubljana, Bohoričeva 20, 1000 Ljubljana, Slovenia, EU

Conflict-of-interest statement: The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Corresponding Author: Matjaž Kopač, Division of Pediatrics, Department of Nephrology, University Medical Centre Ljubljana, Bohoričeva 20, 1000 Ljubljana, Slovenia, EU.

Email: matjaz.kopac@kclj.si

Telephone: +386-1-522-9626

Received: December 18, 2018

Revised: January 19, 2019

Accepted: January 21, 2019

Published online: March 20, 2019

ABSTRACT

AIM: To evaluate the role of family history of enuresis, associated comorbidities and body mass index in predicting response to enuresis treatment with desmopressin in children.

MATERIALS AND METHODS: 100 patients with monosymptomatic enuresis were evaluated in this retrospective study. The associations between family history of enuresis, associated comorbidities, body mass index and response to enuresis treatment with desmopressin were analysed with χ^2 statistical test.

RESULTS: Family history of enuresis was positive in 58.8% of patients who responded to desmopressin treatment and in 54.5% of non-responders. Among patients who responded to desmopressin treatment, obesity was present in 14.3% and overweight in 19% of

patients. Among non-responders, obesity was present in 13.2% and overweight in 7.9% of patients. Among patients who responded to desmopressin treatment, comorbidity was present in 40.5% of patients. Among 38 non-responders, comorbidity was present in 21.1% of patients. The difference was not statistically significant in either of compared groups.

CONCLUSION: The study did not prove statistically significant association between family history of enuresis, associated comorbidities or body mass index, and response to treatment with desmopressin.

Keywords: Monosymptomatic enuresis; Desmopressin; Attention deficit hyperactivity disorder; Body mass index; Family history

© 2019 The Author(s). Published by ACT Publishing Group Ltd. All rights reserved.

Kopač M. Is Response to Enuresis Treatment with Desmopressin Influenced by Family History, Associated Comorbidities or Obesity? *Journal of Nephrology Research* 2019; **5(1)**: 159-161 Available from: URL: <http://www.ghrnet.org/index.php/jnr/article/view/2482>

INTRODUCTION

Enuresis is common in school age children. The occurrence of primary nocturnal enuresis was found to be 8.7% in the population of Slovenian 5-year olds which is comparable with data from other countries^[1]. Monosymptomatic nocturnal enuresis is defined by the absence of any daytime voiding symptoms. Desmopressin is a vasopressin analogue and is the most widely used drug for treatment of monosymptomatic nocturnal enuresis with proven efficacy. It is considered as the first-line treatment, especially for children with enuresis in families who are not motivated enough to use the alarm therapy, who have recently unsuccessfully used the alarm or in those who are unlikely to use it correctly^[2]. Several factors have been proposed to negatively influence clinical response to desmopressin treatment. One of them is constipation and it must be addressed before treatment^[3,4]. The formulation of desmopressin also appears to influence the response to treatment: desmopressin melt (oral lyophilizate formulation of desmopressin) has better response,

compared with tablet, in children with primary monosymptomatic nocturnal enuresis, mainly due to increased compliance^[5,6].

METHODS

100 patients with monosymptomatic enuresis were evaluated in this retrospective study. Body mass index (BMI) was calculated in all of them. Children were defined as normal if their BMI was below 85th percentile (p), overweight if between 85th and 95th p and obese if their BMI was above 95th p. Family history data was available in 84 patients. All children, treated with desmopressin, received desmopressin melt oral formulation. The associations between response to enuresis treatment with desmopressin and family history of enuresis, body mass index and associated comorbidities (such as attention deficit hyperactivity disorder, mental disability, history of head trauma, difficult socioeconomic situation, language disorders and allergies) were analysed with χ^2 (chi-square) statistical test, using computer programme Microsoft Excel statistical tests.

RESULTS

Family history was positive in 60% and negative in 44% of patients. Among 67 children, treated with desmopressin, family history of enuresis was positive in 58.8% of patients who responded to desmopressin treatment and in 54.5% of non-responders. The difference was not statistically significant ($p = 0.99$). Table 1 presents these data in more detail.

Obesity was present in 14.3%, overweight in 19% and normal weight in 66.7% of patients who responded to desmopressin treatment. Among non-responders, obesity was present in 13.2%, overweight in 7.9% and normal weight in 78.9% of patients. The difference was not statistically significant ($p = 0.90$). Table 2 presents these data in more detail.

Comorbidity was present in 40.5% of patients who responded to desmopressin treatment. Among non-responders, comorbidity was present in 21.1% of patients but the difference did not reach statistical significance ($p = 0.47$). Table 3 presents these data in more detail.

There were 72 patients with primary nocturnal enuresis and 7 with secondary nocturnal enuresis in the group of patients, treated with desmopressin. 52.7% of patients with primary nocturnal enuresis and 57.1% of patients with secondary nocturnal enuresis responded to desmopressin. The difference was not statistically significant ($p = 0.99$). Table 4 presents these data in more detail.

There were 23 children, treated with alarm. Family history of enuresis was positive in 50% of patients who responded to alarm treatment and in 50% of non-responders. Obesity was present in 12.5%, overweight in 37.5% and normal weight in 50% of patients who responded to alarm treatment. Among non-responders, obesity was present in 6.7%, overweight in 13.3% and normal weight in 80% of patients. The statistical analysis was not done in this group of children because of small sample size. Therefore, the results would not have been reliable enough.

Among 100 studied patients, 95 had normal urinalysis and 5 had mild isolated microhematuria. All patients had normal ultrasound of kidneys and urinary tract. Ultrasound examinations were not done or the results were unavailable in 4 patients.

DISCUSSION

The present study did not prove statistically significant association between family history of enuresis, associated comorbidities or body mass index, and response to enuresis treatment with desmopressin.

Table 1 The association between family history of enuresis and response to enuresis treatment with desmopressin.

	Positive family history	Negative family history	Sum
Response to treatment	20	14	34
No response to treatment	18	15	33
Sum	38	29	67

Table 2 The association between body mass index (BMI) and response to enuresis treatment with desmopressin.

	BMI > 95 p	BMI 85 - 95 p	BMI < 85 p	Sum
Response to treatment	6	8	28	42
No response to treatment	5	3	30	38
Sum	11	11	58	80

BMI: body mass index; p: percentile.

Table 3 The association between response to enuresis treatment with desmopressin and the presence of comorbidities.

	Comorbidity present	Comorbidity absent	Sum
Response to treatment	17	25	42
No response to treatment	8	30	38
Sum	25	55	80

Table 4 Primary vs. secondary nocturnal enuresis in terms of response to enuresis treatment with desmopressin.

	Primary enuresis	Secondary enuresis	Sum
Response to treatment	38	4	42
No response to treatment	34	3	37
Sum	72	7	79

The study also did not prove statistically significant difference in response to treatment with desmopressin between patients with primary and secondary nocturnal enuresis. The latter is defined as enuresis in a child that has previously been dry at night for 6 months or more after the age of 5 years^[7]. To the best of my knowledge, no previous studies have been conducted or published with the objective of determining the associations between above mentioned factors and response to enuresis treatment with desmopressin oral melt formulation in a single study. The role of family history was previously studied in terms of responsiveness to desmopressin therapy. It was found that 91% of enuretic children with a family history of enuresis showed a good response to desmopressin therapy while only 7% of enuretic children with no such history had a good response to this kind of treatment^[8]. There are some comorbidities, reported to be associated with poorer response rate, such as history of urinary tract infections, attention deficit hyperactivity disorder, psychological problems, autism spectrum disorder, mental and motor disability and sleep disturbances, manifested as snoring, waking up or restless legs^[9]. All proven or suspected organic comorbidities of the urinary tract, such as history of urinary tract infections or uropathy as well as patients with severe constipation, were excluded from this study. Therefore, only attention deficit hyperactivity disorder, psychological problems, autism spectrum disorder, mental and motor disability, sleep disturbances, history of head trauma, difficult socioeconomic situation, language disorders or allergies were considered as comorbidities. Another study investigated the correlation between body mass index and the efficacy of nocturnal enuresis and voiding dysfunction treatment in obese patients. It

revealed a reduced response to therapy in patients with a body mass index above the 85th percentile since patients with a normal body mass index had a lower nocturnal accident frequency than those above the 85th percentile after treatment^[10]. These findings are in contrast with the results of the present study suggesting the complex nature of enuresis pathogenesis. On the other hand, another study showed that language disorders (such as dyslexia or delayed language development) and testicular pathology could be comorbidities associated with persistence of nocturnal enuresis and treatment resistance. In addition, rate of remission in children with positive family history of enuresis was higher compared to children with negative family history but the difference was not statistically significant^[11].

Further research on other possible predictors of response to enuresis treatment would be beneficial in order to adjust treatment to individual patients and improve its efficacy.

REFERENCES

1. Semolič N, Ravnikar A, Meglič A, Japelj-Pavešič B, Kenda RB. The occurrence of primary nocturnal enuresis and associated factors in 5-year-old outpatients in Slovenia. *Acta Paediatr* 2009; **98**: 1994-1998. [PMID: 19689479]; [DOI: 10.1111/j.1651-2227.2009.01489.x]
2. Neveus T. Nocturnal enuresis - theoretic background and practical guidelines. *Pediatr Nephrol* 2011; **26**: 1207-1214. [PMID: 21267599]; [PMCID: PMC3119803]; [DOI: 10.1007/s00467-011-1762-8]
3. Lane W, Robson M. Evaluation and management of enuresis. *N Engl J Med* 2009; **360**: 1429-1436
4. Hodges SJ, Anthony EY. Occult megarectum - a commonly unrecognized cause of enuresis. *Urology* 2012; **79**: 421-424. [PMID: 22173180]; [DOI: 10.1016/j.urology.2011.10.015]
5. De Guchteneere A, Van Herzele C, Raes A, Dehoorne J, Hoebeke P, Van Laecke E, Vande Walle J. Oral lyophilizate formulation of desmopressin: superior pharmacodynamics compared to tablet due to low food interaction. *J Urol* 2011; **185**: 2308-2313. [PMID: 21511277]; [DOI: 10.1016/j.juro.2011.02.039]
6. Vinter Juul K, Van Herzele C, De Bruyne P, Goble S, Vande Walle J, Norgaard JP. Desmopressin melt improves response and compliance compared with tablet in treatment of primary monosymptomatic nocturnal enuresis. *Eur J Pediatr* 2013; **172**: 1235-1242. [PMID: 23677249]; [PMCID: PMC3742424]; [DOI: 10.1007/s00431-013-1992-9]
7. Rees L, Brogan PA, Bockenbauer D, Webb NJA. *Paediatric Nephrology*. 2nd ed. Oxford: Oxford University Press, 2012: 92-95
8. Hogg RJ, Husmann D. The role of family history in predicting response to desmopressin in nocturnal enuresis. *J Urol* 1993; **150**: 444-445. [PMID: 8326574]
9. Vande Walle J, Rittig S, Bauer S, Eggert P, Marschall-Kehrel D, Tekgul S. Practical consensus guidelines for the management of enuresis. *Eur J Pediatr* 2012; **171**: 971-983. [PMID: 22362256]; [PMCID: PMC3357467]; [DOI: 10.1007/s00431-012-1687-7]
10. Guven A, Giramonti K, Kogan BA. The effect of obesity on treatment efficacy in children with nocturnal enuresis and voiding dysfunction. *J Urol* 2007; **178**: 1458-1462. [PMID: 17706706]; [DOI: 10.1016/j.juro.2007.05.165]
11. Ferrara P, De Angelis MC, Caporale O, Malamisura M, Del Volgo V, Vena F, Gatto A, Chiaretti A. Possible impact of comorbid conditions on the persistence of nocturnal enuresis: results of a long-term follow-up study. *Urology J* 2004; Vol. 11, No 4: 1777-1781