Effects of Desmopressin on Symptoms and Sleep Quality in Children with Primary Monosymptomatic Nocturnal Enuresis

Lei Lv, Qingwei Wang, Jian Guo WenHenan
Joint International Paediatric Urodynamic Laboratory, Zhengzhou University. China

Introduction

Nocturnal enuresis (NE), commonly known as bed-wetting, a common clinical scenario. There is no uniform definition of NE in domestic and foreign. The latest domestic expert consensus recommends the definition of NE by International Classification of Diseases (ICD-10). That is, children aged 5 to 6 have at least 2 times of involuntary urine leakage symptoms during sleep at night every month, children aged ≥7 have at least 1 time of bed-wetting every month, and more than 3 consecutive months can be diagnosed as NE. Those who have enuresis at an early age and have not had a dry period of 6 months or more are called primary nocturnal enuresis (PNE). PNE with only nocturnal enuresis symptoms and no other lower urinary tract symptoms is known as primary monosymptomatic nocturnal enuresis (PMNE). According to domestic statistics, the overall prevalence of PNE in children aged 5-12 is 6.4%, and the overall prevalence of PMNE is 4.6%. NE not only affects the physical and mental health of children, but also increases the burden of the family. With the improvement of people's living, parents have become more dependent on diapers and put off toilet training. In recent 10 years, the prevalence rate of children with PMNE has increased significantly. The symptoms of most children with PMNE gradually improve with age, but about 0.5% to 2% of children may have persistent symptoms. Therefore, active treatment is required. The pathogenesis of PMNE is complicated, and the main etiology is considered to include sleep and wake disorders, excessive urine production and detrusor overactivity at night. Desmopressin (DDAVP) is the drug of choice for the treatment of PMNE recommended by the International Children's Continence Society (ICCS). However, not much research has been reported on its effect on the sleep of PMNE children, and this aspect has not been reported in China. The study of sleep during treatment of children with PMNE is expected to enhance physicians' attention to sleep during clinical treatment with DDAVP and is also conducive to an in-depth understanding of the mechanism of DDAVP in the treatment of PMNE, providing reference for better clinical application of DDAVP.

Methods

Children with PMNE who visited the department of Urology of our hospital from September 2018 to May 2021 were selected to be treated with DDAVP for 12 weeks according to the standard method recommended by ICCS and followed up.

After 12 weeks, the children were divided into improvement group and no-improvement group according to the improvement of enuresis. At the 12th week, compared with the previous week (baseline), if the number of enuresis nights decreased by ≥50%, it was the improvement group, and < 50% was the no-improvement group.

Inclusion criteria for the children were age 6 to 12 and the number of nights per week that bed-wetting occurred >2 nights. Exclusion criteria included: accompanied by daytime lower urinary tract symptoms such as frequent urination, urgency of urination, or urinary incontinence; constipation and fecal incontinence; urinary tract infection or a history of recurrent infection; current or previous treatment with DDAVP, anticholinergic drugs, or enuresis alarm; other drugs are currently being used; suffering from other neurological or mental diseases that may be secondary to enuresis.

The initial dose of DDAVP was 0.2mg orally, and no water was allowed 1 hour before and 8 hours after taking DDAVP. After 2 weeks of treatment, the dose was adjusted in outpatient clinic or telephone follow-up. Basic information was collected, and enuresis and sleep were recorded at baseline, 4, 8 and 12 weeks, respectively, to analyze the effect of DDAVP treatment on enuresis symptoms and sleep quality (children's sleep habits questionnaire scores, CSHQ scores).

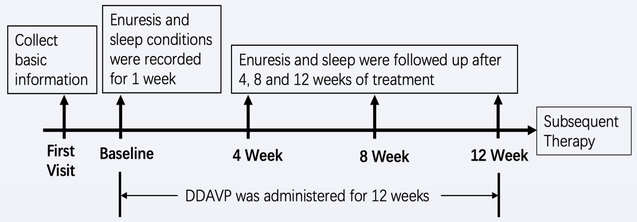

Figure 1. Flow chart of follow-up

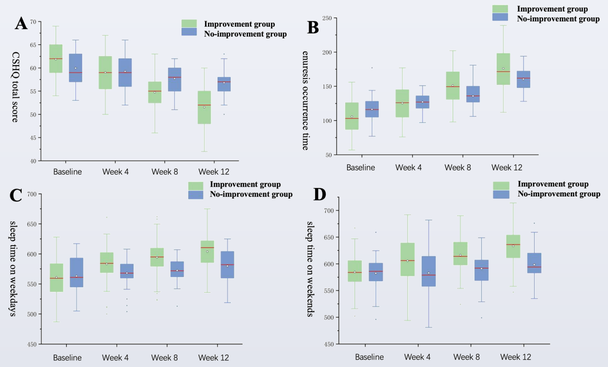

Figure 2. Changes in sleep quality before and after treatment in children with and without improvement (A: total score of CSHQ; B: Enuresis time; C: usual sleep time; D: sleep duration on weekends; * P < 0.05; ** P < 0.01)

Table 1. Changes in enuresis symptoms and sleep quality after 12 weeks of treatment

	Baseline	Week 4	Week 8	Week 12	Statistic	*P*
number of enuresis nights [$M(P_{25}$~$P_{75})$]	4.0(3.0~4.0)	3.0(3.0~4.0)	3.0(2.0~3.0)	1.0(1.0~2.5)[1)]	H=125.26	<0.001
CSHQ total score (x±s)	61.2±4.1	59.1±4.3	55.7±4.0	53.3±4.7[1)]	F=52.42	<0.001
enuresis occurrence time (x±s)/min	109.1±22.9	125.9±21.8	146.2±24.9	171.0±28.2[1)]	F=91.21	<0.001
sleep time (x±s)/min						
weekdays	561.6±31.5	578.3±30.6	587.0±28.4	595.9±30.2[1)]	F=18.09	<0.001
weekends	583.8±36.3	598.1±43.0	608.0±36.4	622.1±38.3[1)]	F=13.49	<0.001

Results

1. Follow-up conditions

A total of 85 children with PMNE were included in the study, and 77 children were included, with a male/female ratio of 43/34 and an average age of (8.8±1.9), because 8 children were not followed up completely. In the improvement group, 52 patients (67.5%) had a male/female ratio of 29/23 and an average age of (8.7±2.0). In the no-improvement group, 25 patients (32.5%) had a male/female ratio of 14/11 with an average age of (8.8±1.7). There were no significant differences between the two groups at baseline in age, sex ratio, number of enuresis nights per week, enuresis occurrence time, sleep duration on weekdays and weekends, or CSHQ total score (P>0.05).

2. Changes in enuresis symptoms and sleep quality after 12 weeks of treatment

All children with PMNE who completed 12 weeks of DDAVP treatment (n=77) were analyzed for enuresis and sleep, the number of enuresis nights and CSHQ total score decreased gradually with the duration of treatment (baseline, week 4, week 8 and week 12), while the enuresis occurrence time, and sleep time on weekdays and weekends increased gradually with statistically significant differences (P<0.01). The number of enuresis nights and CSHQ total score were significantly lower at week 12 compared with baseline [1.0(1.0-2.5) vs 4.0(3.0-4.0), P<0.01; 53.3±4.7 vs 61.2±4.1, P<0.01], whereas enuresis occurrence time, sleep time on weekdays and weekends were significantly higher (P<0.01).

The improvement group (n=52) had significantly lower number of enuresis nights and CSHQ total score after 12 weeks of treatment compared with baseline [1.0(1.0-1.8) vs 4.0(3.0-5.0), P<0.01; 51.5±4.4 vs 61.8±4.1, P<0.01], while the enuresis occurrence time and sleep time were significantly increased (P<0.01). The no-improvement group (n=25) had a decrease in the number of enuresis nights at week 12 compared with baseline [3.0(2.5-4.0) vs 4.0(3.0-4.0), P<0.05], but the decrease was <50%, and CSHQ total score decreased [56.8±3.1 vs 60.0±4.0, P<0.05], while the enuresis occurrence time and sleep time increased.

3. Comparison of changes of sleep quality before and after treatment between the improvement group and the no-improvement group

At the 8th and 12th week of treatment, the CSHQ total score of the improvement group (n=52) was significantly lower than that of the no-improvement group (n=25) (54.7±4.0 vs 57.7±3.0, P<0.05; 51.5±4.4 vs 56.8±3.1, P<0.01), the enuresis occurrence time and sleep time of the improvement group were significantly longer than those of the no-improvement group (P<0.05). Comparing the changes in CSHQ scores at 8 levels, significant differences were found in Bedtime Resistance, Sleep Onset Delay, Bedtime Duration, Sleep Anxiety, Night Waking, Parasomnias, and Daytime Sleepiness in the improvement group (P<0.05), while the difference in Bedtime Duration only was statistically significant in the no-improvement group (P<0.05).

Table 2. Comparison of changes of sleep quality before and after treatment between the improvement group and the no-improvement group

	Improvement group (n=52)	No-improvement group (n=25)	Statistic	*P*
Age(x±s)/year	8.7±2.0	8.7±2.0	8.7±2.0	0.947
Male[n(%)]	29(55.8)	14(56.0)	χ^2=0.00	0.985
number of enuresis nights [$M(P_{25}$~$P_{75})$]				
Baseline	4.0(3.0~5.0)	4.0(3.0~4.0)	Z=0.92	0.360
Week 4	3.0(2.3~4.0)	3.0(3.0~4.0)	Z=0.05	0.963
Week 8	2.0(2.0~3.0)	3.0(3.0~3.0)	Z=4.18	<0.001
Week 12	1.0(1.0~1.8)[1)]	3.0(2.5~4.0)[1)]	Z=6.93	<0.001
enuresis occurrence time (x±s)/min				
Baseline	105.6±23.5	116.3±20.1	t=1.96	0.053
Week 4	125.3±24.9	127.2±13.5	t=0.36	0.721
Week 8	151.2±26.2	135.8±18.5	t=2.63	0.010
Week 12	176.1±31.0[1)]	160.5±17.2[1)]	t=2.33	0.022
sleep time on weekdays(x±s)/min				
Baseline	560.9±31.3	563.0±32.4	t=0.28	0.779
Week 4	583.2±31.5	568.1±26.4	t=2.08	0.041
Week 8	594.0±28.9	572.4±21.3	t=3.31	0.001
Week 12	603.7±28.5[1)]	579.8±27.7[1)]	t=3.47	0.001
sleep time on weekends (x±s)/min				
Baseline	584.6±37.1	582.1±35.3	t=0.29	0.775
Week 4	605.4±40.4	583.0±44.9	t=2.20	0.031
Week 8	616.2±34.8	591.0±34.3	t=2.98	0.004
Week 12	633.5±35.4[1)]	598.4±33.5[1)]	t=4.15	<0.001
CSHQ total score (x±s)				
Baseline	61.8±4.1	60.0±4.0	t=1.89	0.062
Week 4	59.0±4.6	59.2±3.8	t=0.19	0.850
Week 8	54.7±4.0	57.7±3.0	t=3.32	0.001
Week 12	51.5±4.4[1)]	56.8±3.1[1)]	t=5.32	<0.001

Conclusion

In addition to significantly improving the symptoms of enuresis, DDAVP treatment for children with PMNE can also improve their sleep quality, and children who had significant improvement in enuresis had more significant improvement in sleep quality. It suggests that we should pay attention to the sleep quality of children with PMNE when using DDAVP, and whether the sleep quality is improved can be used as a reference indicator to evaluate the effect of DDAVP in the treatment of children with PMNE.