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# The Effect of Maximum Voided Volume on Response to Desmopressin Therapy in Children with Enuresis

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## Abstract

**Purpose:** This study was aimed to determine the effect of maximum voided volume (MVV) on the efficacy of desmopressin, which is commonly used to treat primary monosymptomatic nocturnal enuresis (PMNE) in children and adolescents.

**Materials and Methods:** Bladder capacity was measured with different methods in 52 patients with PMNE, and the effect of bladder capacity on desmopressin therapy was investigated.

**Results:** Patients with PMNE in whom MVV was 70% or less of estimated bladder capacity were found to be unresponsive to desmopressin therapy.

**Conclusion:** The MVV can be measured before desmopressin therapy in patients with PMNE as a marker to predict treatment success. Our results suggest that desmopressin should not be used in patients with low MVV.

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**Key words:** enuresis nocturna, desmopressin, maximum voided volume, children

## Introduction

Enuresis is defined as bedwetting or voiding of urine during sleep[1]. There are no lower urinary tract symptoms in children with primary monosymptomatic nocturnal enuresis (PMNE)[1]. PMNE is a common but serious problem in childhood and adolescence. It occurs three times more often in boys than in girls[2]. There are many treatment approaches for PMNE, including behavioral motivation, alarm therapy, and medications[3]. Desmopressin, which is a synthetic analogue of antidiuretic hormone, reduces the production of urine by increasing renal water reabsorption[4]. Treatment with desmopressin is most effective in children 8 years or older who have monosymptomatic enuresis with nocturnal polyuria, normal bladder capacity, and less frequent bedwetting[5]. In this study, we evaluated the efficacy of desmopressin therapy and whether the maximum voided volume (MVV) has an effect on the therapy.

## Material and Methods

Fifty-two children with PMNE referred to our pediatric outpatient clinic from January 2008 through December 2009 were prospectively

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evaluated. Patients who were older than 5 years and had a history of 2 or more bed-wetting incidents per week were included in the study, whereas patients with pollakiuria, urgency, urinary system abnormalities, or neurological problems were excluded. A detailed medical history was obtained, and physical examination was performed in all cases. The study was approved by the local ethics committee. The parents of all patients were informed that the patients were not treated with any drugs other than desmopressin.

A voiding diary was kept by each patient. The maximum amount of urine voided at one time, except the first morning void, was accepted as the MVV. Additionally, uroflowmetry and ultrasonography (USG) were performed when the child had a strong urge to urinate, the volume of the full bladder was measured with USG before voiding, and maximum urine volume was measured with uroflowmetry. A small number of patients with statistically significant differences among bladder capacities measured with these methods were excluded from the study. Age-specific estimated bladder capacity (EBC) and corrected bladder capacity (CBC) were calculated with the following formulas: EBC = [age (years) + 2 (mL)] × 30 and CBC = MVV/EBC × 100[6].

Patients were divided into 3 groups according to their response to therapy: responsive to conservative therapy (group I), unresponsive to conservative therapy but responsive to desmopressin (group II), and unresponsive to both conservative and desmopressin therapies (group III).

All patients were initially treated with a simple, conservative approach including removal of caffeine from the diet (tea, cola drinks, etc.), a fluid intake program with low intake in the evening with no restriction of daily total fluid intake, and micturition just before sleeping. The parents and the child were first provided with information about PMNE, as this is a common disorder with no harm to general health. The interviews were aimed at counseling the child to become a participant of the program with some simple rewards given for each night without enuresis.

After 3 months of conservative therapy, a decrease in bedwetting frequency of 90% or more was defined as a complete response, a decrease of 50% to 90% as a partial response, and a decrease of less than 50% as an inadequate response. Patients with a partial or inadequate response to conservative therapy were treated with desmopressin for 1 month and then revaluated. No side effects of desmopressin were seen.

Bladder capacity values of all patients obtained with the 3 different methods were compared with age-specific ideal EBCs.

The software program IBM SPSS Statistics 11.5 for Windows (IBM Corp., Armonk, NY, USA) was used for data analysis. Data are presented as means and standard deviations (SD). The independent t-test and one-way analysis of variance were used to compare groups. A p value $< 0.05$ was accepted as indicating significance for all statistical tests.

## Results

A total of 52 patients aged 5 to 16 years (mean age, 9.8 ± 2.6 years) were enrolled in this study. The ratio of boys (n = 36) to girls (n = 16) was 2.25 : 1. Initially 19.2% of the patients responded to conservative therapy. The responses to conservative therapy and desmopressin therapy in patients with PMNE are shown in **Table 1**. The effectiveness rate of desmopressin therapy was found to be 64.2%, and the relapse rate was 48.1%. In each of the 3 patient group based on treatment responses, there were differences in MVV values determined with the voiding diary and with bladder capacity measured with USG and uroflowmetry, but these differences were not significant (**Table 2**). The MVV and bladder capacities determined with USG and uroflowmetry were significantly lower than EBC in all 3 groups. The mean MVV and the CBC were significantly higher in patients responsive to desmopressin therapy than in patients unresponsive to desmopressin therapy. Patients with a mean CBC of 70% or greater showed a good response to desmopressin therapy (**Table 3**).

## Discussion

A consensus is lacking regarding the pathogenesis of enuresis, although different treatments are extremely effective. Primary nocturnal enuresis is caused by a disparity between bladder capacity and nocturnal urine production: patients with PMNE have an insufficient nightly increase in vasopressin

Table 1 Responses to conservative therapy and desmopressin therapy

| | Complete response n (%) | Inadequate response n (%) | Partial response n (%) | Total n |
|---|---|---|---|---|
| Conservative therapy | 10 (19.2) | 35 (67.3) | 7 (13.5) | 52 |
| Desmopressin therapy | 27 (64.2) | 15 (35.8) | | 42 |

Table 2 Bladder capacities determined with different methods in patients groups according to treatments responses

| Patient group | MVV (mL) | USG-BC (mL) | U-BC (mL) | EBC (mL) |
|---|---|---|---|---|
| Group Ⅰ | 229.4 ± 110.6 | 202.5 ± 138.6 | 187.9 ± 181.3 | 298.8 ± 64.9 |
| Group Ⅱ | 252 ± 81.2 | 286.6 ± 172.7 | 235.1 ± 142.8 | 356.3 ± 47.4 |
| Group Ⅲ | 143 ± 67.5 | 187.7 ± 129.2 | 187.7 ± 123.1 | 341.8 ± 53.4 |

MVV, maximum voided volume; USG-BC, Bladder capacity measured with ultrasonography, U-BC, bladder capacity measured with uroflowmetry; EBC, age-specific estimated bladder capacity

Table 3 The relationship between MVV and CBC for responsiveness of desmopressin therapy

| | Patients responsive to desmopressin therapy Mean ± SD (n = 27) | Patients unresponsive to desmopressin therapy Mean ± SD (n = 15) | p value |
|---|---|---|---|
| MVV (mL) | 252 ± 81.2 | 143 ± 67.5 | 0.01 |
| CBC (%) | 70.7 ± 21 | 41.8 ± 19 | 0.012 |

MVV, maximum voided volume; CBC, corrected bladder capacity; SD, standard deviation

secretion, leading to the production of large amounts of dilute urine surpassing bladder capacity[7,8]. Despite the recovery rate of 15% per year, 0.5% of all cases remain unchanged in adulthood, with serious effects on self-esteem[9].

Conservative therapy and pharmacologic therapies may be used alone or in combination. As we found in the present study, conservative therapies have had successes rates of 21.6% and 29.5% in previous studies[10,11]. Desmopressin, which increases distal tubular water reabsorption and, consequently, reduces nightly urinary volume, has been used successfully to treat PMNE. Sixty to 70 percent of children respond to treatment, although 80 percent relapse after discontinuing therapy[7,12–14]. In the present study, desmopressin treatment was effective for 64.2% of patients, which is a rate similar to that reported in other studies, and the relapse rate was 48.1%. The lower relapse rate in the present study than in other studies may be due to our patients' higher mean age[15]. Akbal et al have suggested that relapse can be prevented by continued administration of desmopressin on alternate days after standard desmopressin therapy for 3 months[16].

It has been reported that bladder capacity measured by USG and uroflowmetry and the bladder capacity determined with urodynamic testing are correlated and accurate; thus, satisfactory evaluation of patients may be performed with USG and uroflowmetry before invasive urodynamic testing[17]. Hjalmas et al have shown that MVV can be measured with a voiding diary or uroflowmetry under favorable conditions[18]. In the present study, we found that MVV determined with a voiding diary was consistent with bladder capacities measured with USG or uroflowmetry. Therefore, our results suggest that a simple voiding diary is sufficient for predicting MVV.

The pharmacologic treatment of enuresis should be considered on the basis of nocturnal urinary volume or MVV and their response to desmopressin treatment[11]. The MVV has been demonstrated to be a reliable predictor of response to desmopressin; children with larger bladder capacities are more likely to have successful responses[11,19–22]. Rushton et al

have reported that MVV is 70% or less of EBC in 81.1% of cases unresponsive to desmopressin therapy[11]. In these studies, MVV was reported to be crucial on response to desmopressin therapy. In the present study, we found that MVV was lower than EBC and that the CBC was significantly lower in patients who were unresponsive to desmopressin therapy. Our results are compatible with previously reported findings.

Consequently, a low bladder capacity can cause enuresis. Furthermore, it can lead to a lack of response to desmopressin. The voiding diary is an effective tool for determining the MVV, as are USG and uroflowmetry, and invasive testing, such as urodynamic testing, may be unwarranted. Desmopressin will be less effective for patients with a CBC of 70% or less. Thus, MVV and CBC should be determined and can be used as markers for predicting the response to desmopressin before the start of treatment in children with enuresis.

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