

Effectiveness of Oral Desmopressin Therapy in Posterior Urethral Valve Patients with Polyuria and Detection of Factors Affecting the Therapy

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Abstract

Objectives: The present study aims to evaluate the effect of desmopressin treatment on urine output, density and glomerular filtration rate (GFR) in patients with posterior urethral valve (PUV) and the factors affecting the response to this treatment.

Methods: A total of 68 PUV patients who were followed-up after valve ablation were examined with the fluid intake, urine output and GFR. Sixteen patients who were polyuric (a urine output more than 30 ml/kg/day) and had hypoosmolar urine (urinary density of 1015 or lower) included in the study. Blood chemistry and serum ADH level were studied. Following 5 days of observation, patients were given DDAVP perorally with a dosage of 0.4 mg/day, two equal doses per day. After 7 days and after a 3 month period of treatment, voiding characteristics, day-time and night-time urine densities and also GFR have been re-evaluated.

Results: The mean age was 6.8 years (range 2 to 11 years). The mean age at valve ablation was 20.7 months (range 5 months to 6 years). The mean daily urine output during first week and at the third month of the treatment had decreased significantly ($p = 0.004$ and $p = 0.006$). There was increase in night-time and day-time urine density in 10 patients (62%) and in 13 patients (81%) respectively at the third month evaluation. Increments in urine density were statistically significant for the third month evaluation. Nine (56%) patients had ADH levels within normal (<7 pcg/ml) levels and 7 patients had higher levels. There was no statistically significant difference between pretreatment and posttreatment micturation characteristics. However patients with voiding dysfunction responded better to DDAVP treatment.

Conclusions: Desmopressin treatment improves polyuria in PUV patients. The responses are better particularly in PUV patients with significant bladder dysfunction. This supports the harmful role of polyuria on bladder dysfunction. The DDAVP treatment improves the day-time and night-time in PUV patients. Combination of DDAVP treatment with overnight catheterization may be a good alternative that needs to be evaluated by further prospective randomized studies.

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1. Introduction

Posterior urethral valve (PUV) is the most common cause of obstructive uropathy in male newborns and

neonates [1]. The initial treatment option is often the ablation of PUV. Despite the successful ablation, progressive decrease in glomerular filtration rate (GFR), polyuria and bladder dysfunction may endure. Polyuria and deterioration in urine concentration is thought to be secondary to the antidiuretic hormone

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(ADH) insensitivity developed following the renal tubular damage in the embryological period [2].

The end stage renal disease and delay in continence is reported in PUV patients with bladder dysfunction [3]. The urodynamic studies performed many years after valve ablation revealed bladder dysfunction in 75% of patients [3]. The long lasting polyuria probably plays a significant role in smooth muscle dysfunction of the bladder and ureter [4]. Polyuria in PUV disease is considered to be secondary to the renal tubular damage caused by obstruction and therefore should be defined as a form of nephrogenic diabetes insipidus (DI). Although correction of polyuria by introduction of antidiuretic hormone analogues is less likely to happen in such condition and physiology, this has not really been clinically tested in a prospective trial. Theoretically one would expect to see some response in less severe cases and in fact the response rate may also give information as regard to the severity of the obstructive uropathy. Desmopressin (1-Desamino 8-D Arginine Vasopressin–DDAVP) is a potent synthetic analogue of vasopressin used intranasally, intramuscularly or intravenously as an antidiuretic in pituitary DI. The duration of effect is five times longer than the original molecule and can last up to 10 hours. Mizuno et al. reported that DDAVP in combination with thiazide was efficient in the treatment of partial nephrogenic DI [5]. Therefore, DDAVP may actually be successful in some PUV patients with polyuria. At least, there is no alternative medical treatment available other than DDAVP. Moreover, response to DDAVP treatment may prove to be a sign of partial defect. The present study aims to evaluate the effect of desmopressin treatment on urine output, density and GFR in patients with PUV and the factors affecting the response to desmopressin.

2. Materials and methods

A total of 68 PUV patients who were followed-up after valve ablation were examined with the fluid intake, urine output and GFR. Patients underwent a detailed genitourinary system examination. Then, ultrasonography, urine analysis, urine culture, uroflowmetry and postvoiding residual urine volume have been assessed. Patients with additional urinary system abnormalities, urinary tract infection and infravesical obstruction have been excluded from the study. Sixteen patients who were polyuric and had hypoosmolar urine were included in the study. Older children have also been assessed for their micturition characteristics. A questionnaire which has been previously validated (Voiding Disturbances Symptom Score-VDSS) was used to evaluate micturition characteristics [6].

Patients were hydrated according to their body weights. The daily urine output, the urine densities at 8 am (night-time urine) and 10 pm

(day-time urine) have been recorded. Patients who have a urine output more than 30 ml/kg/day have been accepted as polyuric and the cases that have urinary density of 1015 or lower at both measurements have been accepted as hypoosmolar [7]. Patients who had both polyuria and hypoosmolar urine have been included into the study.

The fluid intake which was controlled and measured by number of glasses of fluid and urine output of the patients have been recorded during a five-day period. The GFR has been calculated by the formula, (daily urine volume \times daily urine creatinine)/(1440 \times serum creatinine) \times (1.7/body surface area). Blood chemistry (BUN, Cr, Na, Cl, K, Ca) and serum ADH level have been studied of the venous blood sample obtained at 8 am. All the patients underwent urodynamic study in order to evaluate the bladder dynamics. During the urodynamic study, contractions causing an intravesical pressure more than 15 cm H₂O prior to estimated bladder capacity (EBC) have been considered as uninhibited contractions and progressive increase in bladder pressure and increment of pressure more than 10 cm H₂O during the filling phase has been considered as hypocompliance.

Following five days of observation, patients were given DDAVP per oral with a dosage of 0.4 mg/day, two equal doses per day. After 7 days of treatment daily urine outputs, voiding characteristics, day-time and night-time urine densities and also GFR have been evaluated. The tests have been repeated after a 3 month period of treatment. Prior to all these tests, the fluid intake was controlled as at the beginning of the study.

The decrease in daily urine output, increase in urine density and decrease in symptom scores have been considered as the success of treatment.

Statistical analyses were done by using the software programme SPSS 10.0 for Windows. One way Anova Post Hoc multiple comparison tests were applied to compare the means of variables before and after treatment since the patient group had a homogenous distribution. However, the subgroup comparison of means were done by using Mann Whitney-*U* for independent or Wilcoxon test for dependent variables since the numbers of patients were small in subgroups. $p < 0.05$ was used to determine significance.

3. Results

The mean age of 16 patients was 6.8 years (range 2 to 11 years). The mean age at valve ablation was 20.7 months (range 5 months to 6 years). Valve ablation and vesicostomy closure was performed in a 2 years old patient who had previously undergone vesicostomy at the third month of his life. Table 1 demonstrates the patients' age at operation time, degree of hydronephrosis, findings of renal scintigraphies and urodynamic studies, state of reflux, creatinine clearances (GFR), serum ADH levels and VDSS prior to the DDAVP treatment.

During the period between the valve ablation/vesicostomy and the DDAVP treatment, 3 (19%) patients had undergone nephrectomy because of nonfunctioning kidneys. Ureteral augmentation was performed in the same session in one of these patients. All these patients had normal creatinine clearances and ADH levels.

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