

## Functional bladder capacity by ultrasound in patients with monosymptomatic primary enuresis

### Capacidad vesical funcional mediante ultrasonido en pacientes con enuresis primaria monosintomática

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Received: 18-01-2017; Accepted: 15-05-2017

#### Abstract

**Introduction:** Nocturnal enuresis is a common clinical problem affecting 5% to 10% of school-age children. Etiology is not known but a diminished functional bladder capacity it has been proposed as a predisposing factor. There exist only a few studies evaluating it by ultrasound. **Objective:** To identify if there is a difference of the functional bladder capacity measured by ultrasound between nocturnal enuresis group and healthy children. **Patients and Method:** A cross-sectional study from February 2014 to May 2015 including two groups, nocturnal enuresis and a control group of 40 patients each, 5 to 15 years old. A single blinded operator measured the functional bladder capacity by ultrasound with an Acuson S2000 Siemens<sup>TM</sup> 3.5 and 5 MHz transducer. Analytics and descriptive statistics were performed using IBM SPSS 20<sup>TM</sup> software. **Results:** Patients with enuresis showed a decreased functional bladder capacity vs. controls (171.7 ml vs 225.5 ml;  $p = 0.025$ ). A history of first-degree relative with enuresis increased the risk of having enuresis OR = 2.81 (95% CI: 1.06-7.42), a second-degree relative presented OR = 4.0 (95% CI: 1.48-10.78). Functional bladder capacity presented a weak correlation with the bladder capacity estimated by Kaefer's formula. **Conclusion:** The functional bladder capacity is lower in the patients with nocturnal enuresis when compared to control group. There is little correlation between functional bladder capacity and Kaefer's formula to determine the normal bladder capacity. We reaffirmed that the family history with enuresis strongly increases the risk of developing nocturnal enuresis.

#### Keywords:

Monosymptomatic primary enuresis. Bladder Capacity. Bladder ultrasonography. Postvoid residual urine volume

## Introduction

Monosymptomatic primary enuresis (MPE) is a common clinical problem, with a prevalence of 5 to 10% in children up to 7 year old, and can reach 0.5 to 2% in teenagers and adults, with or without treatment. The exact etiology has not been defined yet, however, it has been established that the MPE is a heterogeneous condition of many types of bladder dysfunction. The diminished functional bladder capacity (FBC), voiding dysfunction and detrusor overactivity are causes of a failed treatment and refractory symptoms<sup>1,2</sup>.

There are 3 physiopathological mechanisms explaining enuresis: nocturnal polyuria, nocturnal detrusor overactivity and a high excitability threshold, the last 2 can be connected to a diminished bladder capacity<sup>3,4</sup>.

There exist studies that have demonstrated that children with enuresis have a bladder capacity diminished up to a 50%, however, these studies are inconsistent and they rely on inter-individual variations of each patient.

Performing a bladder ultrasound, at the time the patient has a maximum voiding urgency, to measure the FBC and the bladder wall thickness can help with the diagnosis and treatment of the MPE. If so, it is possible to avoid urodynamic studies, although being the gold standard, it is an invasive method and has a risk of morbidity<sup>5</sup>.

There are a few tests to evaluate the FBC by ultrasound, some authors use bladder diaries to identify it, however, this method does not evaluate the residual urine or the bladder wall thickness, parameters highly important to differentiate the MPE from the non-monosymptomatic. Our goal was to determine if the FBC in the MPE is diminished in comparison with healthy pediatric patients through bladder ultrasound.

## Patients and Method

Analytic cross-sectional study, with non-probabilistic sample of consecutive cases, performed at the Hospital Civil de Guadalajara "Dr. Juan I. Menchaca" between February 2014, and May 2015. Patients 5 to 15 years were included, out-patients of both genders, making two groups; one of 40 patients with MPE and one of 40 without MPE. Patients with secondary enuresis, that stayed dry at night for more than 6 months, or polysymptomatic, e.g. urinary urgency, urinary incontinence, dysuria, such as encopresis or urinary tract anomalies.

### Sample size determination

A formula for 2 samples was used, where the FBC was the variable of interest, using the 2.5% prevalence as  $p^1$  in healthy controls, reported by Hagstroem 2006,

and the 34% prevalence as  $p^2$  in cases with enuresis with a diminished FBC, reported by Jun-Mo 2014. The estimated sampling size was 22 individuals per group, taking into account that 40 individuals per group integrate this study.

### Variables

The FBC was determined, the amount of urine that a child can hold before expressing an urgent need to void<sup>8</sup>.

To determine the estimated bladder capacity (EBC), Kaefer's formula was implemented ( $\text{age}/2+6$ ) x 30 to convert it into milliliters<sup>9</sup>, determining an increased bladder capacity when the individual showed more than 130% of the EBC, through the formula  $\text{FBC}/\text{EBC} \times 100$ . A normal bladder capacity when the individual showed between 70% and 130% of the EBC and a diminished bladder capacity when the patient obtained less than 70% of the EBC<sup>10</sup>.

After a complete medical history, a somatometry was performed in each patient. It included weight, size, and body mass index (BMI).

### Method

Two ultrasound studies were performed in each individual, the first one renal and vesicular during the maximum need to void and the second one post-voiding with a Siemens ultrasound, model Acuson S2000TM with convex sectorial transducers (frequency 3.5 and 5 MHz). Every ultrasound was performed in the same place and schedule by one blind pediatric radiologist. The vesicle volume was determined in milliliters by a hemiellipsoid formula ( $\text{longitudinal diameter} \times \text{transversal} \times \text{anteroposterior}$ ) (0.5). The post-urination residual urine and the vesicle wall thickness in milliliters were also recorded.

### Statistical analysis

The qualitative variables were reported by frequencies and simple percentages, such as Chi-square and Odds ratio (OR) with a confidence interval (CI) of 95%. An exploratory analysis was performed on the datum obtained by the Shapiro-Wilk normality test from the qualitative variables. A Student's t-test was used in independent samples when the variables showed a normal distribution or the U Mann Whitney test, where there was a non-normal distribution. A correlation of variables by a Pearson (r) linear correlation and a Spearman's rho for non-parametric was performed. The analyses were carried out in the statistical package IBM SPSS v20. It was considered significant, in every case, a value  $p < 0.05$ .

### Ethical considerations

The study complies with the stipulated in the regulations of the General Health Law in the Field of

Research for Health in Mexico, title second chapter I, article 17, section II, a research with minimum risk and requires informed consent. Parents or tutors of the patients that decided to participate in this study were required to sign an informed consent. This project has the approval of the Ethics Committee at the Hospital Civil de Guadalajara “Dr. Juan I. Menchaca”.

**Table 1. Characteristics of the study population**

| Variables       | Enuresis<br>n = 40     | Control<br>n = 40      | P-value  | (CI=95%)      |
|-----------------|------------------------|------------------------|----------|---------------|
| Gender          | Male                   | Male                   | 0.058*   | (0.346-2.29)  |
|                 | 27 (67.5%)             | 28 (70%)               |          |               |
|                 | Female                 | Female                 |          |               |
|                 | 13 (32.5%)             | 12 (30%)               |          |               |
| Age (years)     | 9<br>(5-13)            | 10<br>(5-15)           | 0.075**  |               |
| Weight (kg)     | 29<br>(13.7-101)       | 33.7<br>(17-88)        | 0.264**  |               |
| Height (cm)     | 130.4<br>DE $\pm$ 12.5 | 136.7<br>DE $\pm$ 15.9 | 0.052*** | (-0.064-12.7) |
| BMI             | 16.5<br>(12.2-43.1)    | 18.4<br>(14.4-27.5)    | 0.118**  |               |
| Paternal<br>age | 37.4<br>DE $\pm$ 6.7   | 39.5<br>DE $\pm$ 7.0   | 0.173*** | (-0.974-5.3)  |
| Maternal<br>age | 35.4<br>DE $\pm$ 6.8   | 36.2<br>DE $\pm$ 6.9   | 0.605*** | (-2.2-3.8)    |

Statistical significance;  $p < 0.05$  (bilateral). CI = Confidence Interval. SD = Standard deviation. \*Chi square Test. \*\*U-Mann Whitney Test. \*\*\*Students-t test

**Table 2. Bladder Ultrasound Results**

| Variables               | Enuresis<br>n = 40     | Controles<br>n = 40     | P-value  | (CI = 95%)      |
|-------------------------|------------------------|-------------------------|----------|-----------------|
| Bladder<br>volume (ml)  | 171.7<br>DE $\pm$ 88.2 | 225.5<br>DE $\pm$ 120.1 | 0.025*** | (6.8-100)       |
| Bladder<br>wall (mm)    | 3.0<br>DE $\pm$ 1.3    | 2.7<br>DE $\pm$ 1.1     | 0.326*** | (-0.857-0.0288) |
| Residual<br>urine (ml*) | 10<br>0-80             | 14<br>1-164             | 0.309**  |                 |

Statistical significance  $p < 0.05$ . SD= Standard deviation. \*Residual urine (median). \*\*U-Mann Whitney. \*\*\*Students-t-test.

**Table 3. Average functional bladder capacity**

| Patients | Capacity<br>< 70%<br>n (%) | Capacity<br>70 to 130%<br>n (%) | Capacity<br>> 130%<br>n (%) |
|----------|----------------------------|---------------------------------|-----------------------------|
| Enuresis | 30 (75%)                   | 9 (22.5%)                       | 1 (2.5%)                    |
| Controls | 25 (62.5%)                 | 14 (35%)                        | 1 (2.5%)                    |

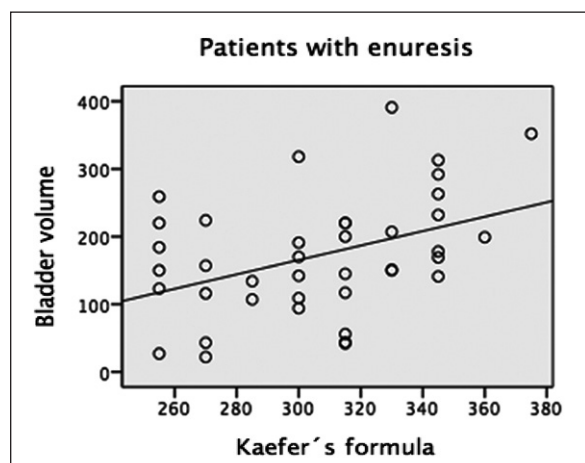
## Results

40 patients with primary enuresis and 40 patients without enuresis were analyzed. Table 1 shows characteristics of the studied subjects where males were predominant in a proportion of 3:1 with an average age of 9 years, showing datum of somatometry without finding statistical differences between both groups.

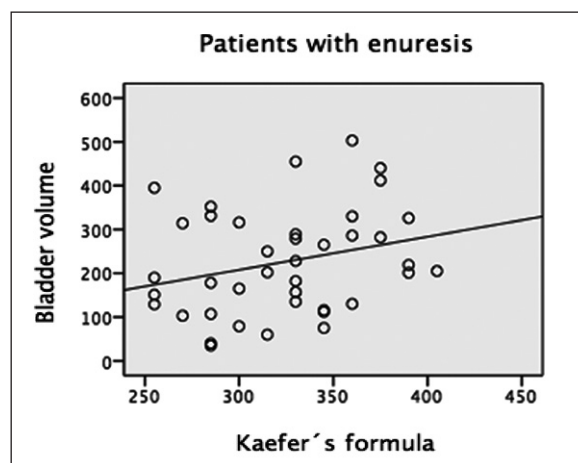
The family history of enuresis in any member of the family ended up as a risk factor to develop enuresis: a first-degree relative with enuresis OR = 2.91 (IC95%: 1.06-7.42) and a second-degree relative OR = 4.0 (IC95%: 1.48-10.78). The renal ultrasound was normal in both groups. Table 2 shows the datum obtained from the bladder ultrasound, where the FBC was lower in cases of enuresis 171.7 ml than in controls 225.5 ( $p = 0.025$ ). The wall thickness and the post-void urine did not show any difference of importance between both groups. Table 3 shows that FBC (measured with bladder ultrasound) in patients with enuresis is lower than 70% than the expected capacity (measured with Kaefer's formula) in 30 patients that corresponds to 75%, while in control visits the same datum result appeared in 25 cases (62.5%). Figure 1 shows the correlation of the datum obtained of the FBC of the group with enuresis that had the expected bladder capacity, measured with the Kaefer formula which showed a weak correlation with the Pearson test ( $r = 0.0408$  ( $p = 0.009$ )). Figure 2 shows that no correlation exists in the healthy group between the FBC and the EBC, the correlation was  $r = 0.268$  ( $p = 0.095$ ). No correlation was found between weight (kg) and the maximum bladder volume obtained by ultrasound nor with the BMI, but there was a correlation with the size with  $\rho = 0.355$  ( $p = 0.025$ ).

## Discussion

The bladder volume can be measured by an ultrasound in pediatric patients with high correlation ( $\rho = 0.96$ ) with the volume obtained by bladder catheterization as Rowe showed, et al<sup>11</sup>. In addition, there are formulas to determine the bladder capacity, such as Starfield's (1967), Kaefer's (1997) and Koff S' (1983), all of them carried out by a cystometry with catheterization and others under general anesthesia determining the bladder capacity by age<sup>8,9,12</sup>. However, the FBC is hard to define by a useful formula regarding the clinical area, since there are variation intra-individuals with differences in the volumes of urine up to a 50%<sup>7</sup>. The difference revolves around that the bladder capacity in children without anesthesia, the child is awake and participates in filling his bladder to its maximum capacity.



**Figure 1.** Scatter plot with trend line of patients with enuresis. Pearson correlation coefficient = 0.408 ( $p = 0.009$ ).



**Figure 2.** Scatter plot with trend line of patients without enuresis. Pearson correlation coefficient = 0.268 ( $p = 0.095$ ).

In the comparison between both groups, there was no statistical difference of importance in the parameters that could affect the FBC, such as age, weight, size, and BMI.

Regarding the distribution of the disease by gender, the literature refers a higher chance to develop this disease in males than in females (3:2), this study shows a proportion of 3:1 with a higher number of males and an average age of 9.

The etiology of enuresis is multifactorial; however, it has been associated with heritage as an important factor. In the studied it was found group that almost half of the patients with enuresis had first-degree relatives (parents and brothers) with a history of enuresis, considering it as a factor of risk to develop the disease. Arnell et al reported in a multicenter study that 52% of the patients had first-degree relatives with the disease<sup>13</sup>.

There are three etiopathogenic mechanisms scientifically demonstrated that could explain enuresis: nocturnal polyuria, nocturnal detrusor overactivity and a high excitation threshold<sup>14</sup>.

The theory of the diminishing FBC can be the cause of primary enuresis is not new and the literature contributes with the controversial datum, some have measured it with voiding diaries (registers of the volume and frequency of urination) and a few reports exists with the measurement by ultrasound<sup>2,7,8</sup>.

The results of this study show a reduction in the FBC in the group with enuresis in comparison with the group without enuresis, however, regarding post-void residual urine where only 32.5% ( $n = 13$ ) showed a volume higher than 10% of residual urine, where there were no differences. Hagstroem et al measured the residual urine by bladder ultrasound post- involuntary urination (post-event of enuresis) showing an increase

of more than 10% of residual urine in 48% of the episodes of enuresis<sup>15</sup>.

Regarding the bladder wall thickness, which when it is increased ( $> 3$  mm), shows detrusor hypertrophy due to a probable obstruction of the urine stream or vesicle dysfunction, normal numbers were found in both groups, thus we can deduce that both groups were free of bladder dysfunction, at least with the ultrasonographic datum. Sreedhar et al reported that the bladder ultrasound parameters were well correlated with urodynamic findings, showing a high predictive value in children with monosymptomatic enuresis and in those with bladder dysfunction<sup>16</sup>.

Patients with enuresis showed less than 70% of the expected bladder capacity, 85% of them. Another important finding was when the urinary volume obtained by ultrasound and the expected urinary volume were correlated by Kaefer's formula in separated groups, a low correlation was obtained where, despite being significant in the group with enuresis, the correlation was weak ( $r = 0.408$ ) and, on the other hand, children with enuresis did not show any correlation ( $r = 0.268$ ). We are uncertain of the utility of Kaefer's formula, since, with the obtained datum and from a clinical point of view, it differs importantly from the FBC that has a higher relevance.

From the anthropometric parameters, size turned out to have a correlation of significance with the FBC  $P = 0.025$  ( $\rho = 0.355$ ), this correlation was also reported by Rodríguez et al, reporting  $r = 0.40$  with  $p < 0.05$ , and weight or BMI had no correlation with the FBC. Thus, the author suggested a regressive formula where he includes the size to measure the bladder capacity ( $1.7 \times \text{size} - 0.4$ )<sup>17</sup>.

Bladder ultrasonography findings can help to guide

the treatment for enuresis. This work is based on the measurement of the urinary volume by ultrasound. Despite having a strong correlation with the actual amount, we consider that bias that can be found in the study are the interpersonal variations of each individual, among them the maximum desire to void of the patient, where we trust that it is actually the right moment, as well as stress situations that can modify the bladder capacity and cannot be controlled, also having as a limit the lack of correlation of the findings of the urinary volume obtained by ultrasound with the maximum volumes of urination in the day (urinary diaries).

## Conclusion

The bladder ultrasound is a noninvasive method that can estimate, with precision, the urinary volume and, at any given time, the bladder capacity. It can also guide to diagnosis a probable vesicle dysfunction if the amount of residual urine is increased and if the vesicle wall thickness is also increased. An ultrasound in patients with primary enuresis can help to determine the FBC that was found statistically diminished compared to the healthy population.

It is possible to conclude that the formulas described to determine the bladder capacity, using age, carried out in patients with anesthesia or awake, but by a ureteral catheter, such as Kaefer's, are not correlated with the FBC measured at a single moment, both in patients with enuresis and in the healthy population. The hereditary antecedent must be reasserted since it

plays an important role as a risk factor to develop the disease.

## Ethical Responsibilities

**Human Beings and animals protection:** Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

**Data confidentiality:** The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

**Rights to privacy and informed consent:** The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

## Financial Disclosure

Authors state that no economic support has been associated with the present study.

## Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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