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FACTORS PREDICTING SUCCESS OF MEDICAL THERAPY IN THE MANAGEMENT OF CLINICAL BENIGN PROSTATIC HYPERPLASIA: ROLE OF POSITION-RELATED CHANGES IN URINE FLOW RATES

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ABSTRACT

Introduction:
We examined the role of voiding position-specific flow rates in predicting success of the medical therapy for clinical benign prostatic hyperplasia (BPH).

Material and methods:
Treatment naïve men older than 50 years with bothersome lower urinary tract symptoms (LUTS) defined as IPSS score >7 and global quality of life (QOL) score >2 were enrolled. Men with diseases other than BPH affecting LUT-function were excluded. Participants were asked to void in digital uroflowmeter three times, all on separate occasions, once in each of the standing, sitting and squatting positions. Post-void residue (PVR) was measured using ultrasound. The study was repeated in the same manner 12weeks after starting medical management for BPH (tamsulosin with/without dutasteride), whose success was defined as IPSS ≤ 7 or QOL ≤ 2.

Results:
Thirty men with mean age 65.4±7.0y, IPSS 23±8, QOL 4±1 & prostate volume 38.8±14.8cc completed the protocol. Volume-corrected maximum flow rates (cQmax) were highest in standing position in 11, sitting in 5 and squatting in 14 patients. A significant improvement was observed in flow-rates and PVR with treatment (p<0.05). Baseline prostate size <30 (p=0.016), maximum cQmax in squatting position (p=0.009) and QOL (p=0.017) predicted success in terms of QOL. The former also predicted the success in terms of IPSS (p=0.008).

Conclusion:
Men with symptomatic BPH tend to have highest flow rates in squatting position, irrespective of preferred voiding position. The outcome of medical therapy for BPH can be predicted by baseline QOL, prostate size <30gm and finding of highest cQmax in squatting position.

KEYWORDS : Micturition position, uraflowmetry, BPH

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the commonest cause of lower urinary tract symptoms (LUTS) in men over 50 years of age and constitutes a major factor impacting the health of men worldwide (Madsen & Bruskewitz, 1995). Such LUTS occur due to bladder outlet obstruction as well as bladder dysfunction. Uroflowmetry is a pivotal screening urodynamic investigation for evaluation of men with LUTS, and helps in follow up as well. Voiding position may have a significant impact on urinary flow rate (Choudhury et al., 2010; Gupta, Kumar, & Kumar, 2008; Uluocak et al., 2008). The preferred voiding position in men is affected by several factors including social, cultural and medical. Increased severity of symptoms in patients with BPH may make them urinate in sitting or crouching positions, because these positions are thought to contribute to a full relaxation of pelvic floor muscles and let the patients with hesitancy wait enough without exhaustion (Aghamir, Mohseni, & Arasteh, 2009; Amjadi, Madaen, & Pour-Moazen, 2009).

The effect of voiding position on flow rates in men with symptomatic BPH is scarcely studied (Aghamir et al., 2009; Amjadi et al., 2009; Ünsal & Cimentepe, 2004) and remains controversial. The effect of medical therapy on these position related changes is unknown. We planned this study to examine the effect of medical therapy for BPH on uroflow parameters in various voiding positions. As a secondary aim, value of demographic and uroflowmetry factors in various voiding positions was also examined in predicting the outcome of medical therapy.

MATERIALS AND METHODS

Clinically symptomatic patients with BPH of age ≥50 years with international prostatic symptom score (IPSS) ≥7 and global quality of life score (QOL) ≥2 who would qualify for medical treatment were enrolled. The study protocol was approved by the institutional ethics committee and informed consent was taken from each participant before enrolment in the study. Men with diseases / procedures affecting lower urinary tract (LUT) e.g. urethral stricture, bladder stone and bladder / prostate cancer, abdomino-perineal resection of rectal cancer, urinary tract infection within last 4 weeks, neurological disorders affecting lower urinary tract function (e.g. cerebrovascular accidents, parkinsonism, seizure disorder, spinal trauma and other spinal diseases, diabetes mellitus etc.), patients on medication affecting lower urinary tract function (e.g. anticholinergics, alpha blockers, alpha agonists, 5 α-reductase inhibitors, etc.) and men with inability to perform uroflowmetry in all three positions (standing, sitting and squatting), were excluded.

LUTS were assessed using International Prostatic Symptom Score (IPSS) and Quality of Life index (QOL). Upon successful inclusion, they were asked to report to our urodynamic lab with a comfortably full bladder (to normal desire) and uroflowmetry was performed in standardized manner (Schäfer et al., 2002) three times, all on separate occasions, one in each of the standing, sitting and squatting positions into gravimetric uroflowmeter (Digital Urodynamic Machine, Solar Silver, MMS International, The Netherlands). Adequate privacy was provided to each participant to minimize psychological inhibition. Post void residual urine (PVR) was measured using transabdominal ultrasound. The study was repeated in the same manner 12 weeks after starting treatment for BPH (tamsulosin with or without dutasteride). Success of medical therapy was defined as an IPSS score on treatment ≤7 (mild symptoms) or QOL score ≤2 (mostly satisfied).

The studies were performed and interpreted in compliance with the guidelines of the Standardization Sub-committee of the International continence society (ICS) (Schäfer et al., 2002). Maximum flow rate (Qmax), average flow rate (Qave), voided volume (VV), Flow time (TQ), Time to Qmax (TQmax), and PVR were recorded for each position and were compared. All the measurements computed by the software were cross checked manually against the flow curve and appropriate correction done, if any.

The following formulae were used –

a. Corrected Qmax = Qmax / $(VV)^{1/3}$

b. Corrected Qave = Qave / $(VV)^{1/3}$

c. Percentage PVR = PVR X 100 / bladder volume (VV+PVR)

The cubic-relation corrected flow rate was adapted from our earlier study (Agarwal, Choudhury, Mandal, Mavuduru, & Singh, 2010).

STATISTICAL ANALYSIS

Data were fed in Microsoft excel worksheet and analyzed using statistical package for social science (SPSS version 17, Chicago, IL) statistical software for windows. Normalcy of data was tested using one sample Kolmogorov–Smirnov test. Parametric tests (paired t-test, independent sample t-test, and ANOVA) were applied for normal data and non-parametric (Wilcoxon signed rank test, Mann–Whitney U test, and Kruskal–Wallis test) for non-normal data. Difference was considered to be statistically significant at P ≤ 0.05. Logistic regression analysis was performed using forward likelihood ratio chi square method for evaluation of factors predicting response to medical therapy.

RESULTS

A total of 30 patients completed the study protocol. Their mean age was 65.4±7.0 years, body mass index 23.2±4.6 kg/m 2, prostate volume 38.4±14.7ml, IPSS 23±8 & QOL 4±1. The most preferred natural voiding position was standing in 21, sitting in 2 and squatting in 7; none of the baseline parameters were significantly different among these groups. All patients were accustomed to standing and squatting position, while 6 patients were not accustomed to sitting position. Only 4 patients reported change in voiding position since development of LUTS. The uroflowmetry data is depicted in Table 1.

Table 1 Position wise baseline Uroflowmetry data

S. No.	Variable	Standing(1)	Sitting(2)	Squatting (3)	P value (1 vs. 2)	P value (2 vs. 3)	P value (1 vs. 3)
1	Qmax (mL/s)	8.2 ± 5.0	6.6 ± 2.9	9.0 ± 5.0	0.17	0.04	0.46
2	Qave (ml/s)	3.8 ± 1.6	3.4 ± 1.4	4.2 ± 1.7	0.39	0.05	0.28
3	Voided volume (ml)	214.4 ± 127.9	208.8 ± 108.8	223.4 ± 131.0	0.86	0.64	0.77
4	cQmax	1.38±0.66	1.13±0.48	1.49±0.63	0.11	0.02	0.48
5	cQave	0.66±0.28	0.59±0.25	0.70±0.23	0.31	0.09	0.48
6	PVR %	24.3 ± 19.3	30.4 ± 20.2	23.5 ± 17.2	0.21	0.16	0.88

Flow-rates had significant positive correlation with voided volume in all voiding positions; patient-characteristics like age, body mass index (BMI), prostate volume, IPSS score and PVR did not have any significant correlation with the flow rates.

a. Position-related effects on flow rates:
Flow rates were significantly higher in squatting than sitting at baseline; all other differences were insignificant [standing vs. sitting & standing vs. squatting]. Eleven patients had cQmax maximum in standing position, 5 in sitting and 14 in squatting. Men with maximum cQmax in squatting position had significantly lower mean cQmax of all positions considered together (p=0.038) and a trend of higher IPSS (p=0.08), compared to those with maximum cQmax in standing position (Figure 1 a, b).

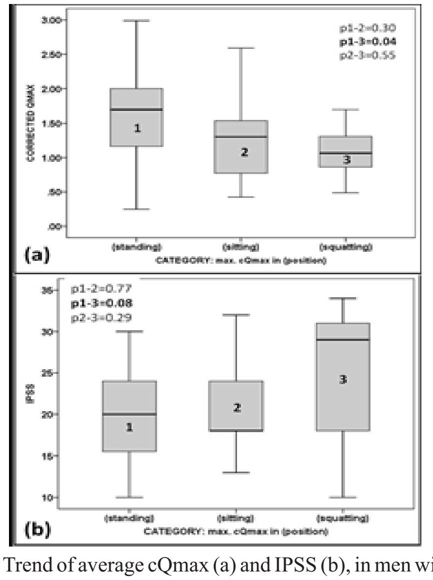

Figure 1 Trend of average cQmax (a) and IPSS (b), in men with cQmax value maximum in squatting position, compared to sitting and standing.

A significant improvement was observed in IPSS, QOL, flow rates and PVR with treatment (all p ≤0.05); except for Qmax & cQmax in squatting position (fig 2). Flow rates were significantly higher in standing & squatting compared to sitting while on treatment (p ≤0.05). Numerically, the highest degree of improvement was noted in Qmax and cQmax in standing position; however, the difference was not statistically significant (all p>0.05) [Figure 2]. Four patients changed their preferred natural voiding position; however, the degree of improvement was not different between the groups.

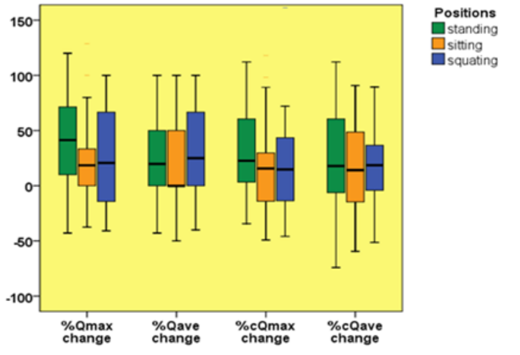

Figure 2 Boxplot diagram showing inter-positional changes in uroflowmetric parameters in different voiding positions, with medical therapy.

b. Factors predicting success of medical therapy:
Logistic regression analysis was performed to identify baseline factors predicting success of medical therapy. Factors considered were age, BMI, baseline IPSS score, QOL score, preferred voiding position, baseline flow rates (Qmax, Qave), corrected flow rates (cQmax, cQave), percentage PVR, separately in all positions as well as mean of all positions, and position associated with maximum cQmax.

I. Success in terms of IPSS:
Baseline prostate size less than 30gm was computed to be predictive of success (p=0.008) with odds ratio (OR) 12.0. Overall predictive accuracy of this model was 80% (sensitivity 85.7% and specificity 66.7%; overall p value=0.005, df=1, chi 2=7.97). However, only 33% variability could be explained on this model.

ii. Success in terms of QOL:
Baseline QOL (p=0.017), prostate size <30gm (0.016) and presence of highest cQmax in squatting position (p=0.009) were found to be predictive of the success in terms of QOL, with OR 0.028, 50.92 and 0.018, respectively. Overall predictive accuracy of this model was 90% (sensitivity 95%, specificity 80%; overall p = 0.002, df=3, chi 2=20.78). upto 69.5% variability could be explained on this model.

DISCUSSION

The present study showed that treatment-naïve men with clinical BPH whose cQmax were highest in squatting position had significantly lower mean cQmax compared to those with highest cQmax in standing position (fig 1a; 1.15±0.47 vs. 1.58±0.66, p=0.001). Their IPSS was higher than that of the latter, however the difference was not statistically significant (fig 1b; 25±8 vs. 20±6, p=0.08). Improvement in QOL to "mostly satisfied" with medical management was predicted by pretreatment QOL, presence of highest cQmax in squatting position and absolute cQmax in sitting position.

Uroflow is the final outcome of complex interaction between vis-a-tergo forces (detrusor pressure and abdominal pressure) and status of urethral resistance (bladder neck, prostate and pelvic floor). Various factors have been identified which affect uroflow parameters, e.g. voided volume, age, body mass index, psychological inhibition and voiding position (Barapatre et al., 2009; Choudhury et al., 2010; Gupta et al., 2008; Uluocak et al., 2008). Various studies have been conducted to study the effect of voiding position on uroflow in various age groups, from young to elderly, children, men and women. However, a consensus has not been attained. Studies conducted in pediatric age groups have found no significant difference in uroflow rates as per voiding position (Lorenzo et al., 2007; Solsnes, Hellstrom, & Sillén, 2007; Yamanishi et al., 1999). However, the situation is not as clear in adult population. Various studies in healthy adult men have found flow rates to be lower in sitting and supine position (compared to standing) (Choudhury et al., 2010; Riehmann et al., 1998; Yamanishi et al., 1999); the reasons cited were adverse gravitational vector in the latter positions and unfamiliarity with these positions (especially supine) in day to day life.

Conversely, in a population of healthy men accustomed to void in sitting position, Eryıldırım et al., (2006) found flow rates to be better in sitting and squatting positions than standing. They opined that higher intra-abdominal pressure in squatting and better relaxation of pelvic floor both the former positions would explain their findings. Furthermore, Ünsal & Çimentepe, (2004) did not find any significant difference in flow rates with respect to voiding position. Similar controversies prevail in the literature on female uroflows (Devreese et al., 2000; Gupta et al., 2008; Moore, Richmond, Sutherst, Imrie, & Hutton, 1991).

Only few studies have been conducted to evaluate the effect of voiding position in symptomatic BPH patients. Ünsal & Çimentepe, (2004) enrolled 44 patients (mean age 61.7 years) with symptomatic BPH and 44 healthy men (mean age 60.3 years) as controls. The uroflowmetric studies were performed in both standing and sitting positions. There were no significant position related differences between voiding parameters in either group. Similarly, El-Bahnasawy & Fadl, (2008) (n=200) also found that voiding position (standing vs. sitting) did not have any impact on uroflow rates in men with LUTS . However, the flowrates were higher and PVR lower in sitting than standing position in younger men (age <50 years) with Qmax >15ml/sec. Sitting was the natural voiding position of the participants of the study and they hypothesized that patients who habitually use sitting position would have their micturition reflex modified to suit that position and changing position caused psychological impact with higher cerebral inhibitory effects. The authors did not include squatting position.

Amjadi et al., (2009) (n=83) showed that micturition in crouching position improved uroflowmetry findings in patients with severe bladder outlet obstruction (Qmax < 10 mL/s) and in those with moderate obstruction (Qmax of 10 to 15 mL/s) and that the more severe the obstruction, the more significant was the improvement by position change. They opined that bladder emptying in crouching position was a simple solution for cases with bladder outlet obstruction symptoms and dysfunctional voiding. Similarly, in our study group of 30 patients, all of whom were accustomed to void in standing and squatting position, we found significant positive correlation between QOL score and percentage difference between cQmax in squatting and sitting positions (Pearson's correlation coefficient +0.522, p=0.003; data not shown in results). Conversely, in a small study of 10 participants Aghamir et al 5 found Qave to be highest in sitting position (2.5ml/sec crouching, 3.5ml/sec sitting & 3.0ml/sec standing; p=0.016); preferred voiding position was not specified.

Voiding position affects the vis-a-tergo and urethral resistance factors in multifactorial manner. Sitting and squatting positions lead to relaxation of adductor and quadriceps muscles of thigh. This in turn helps relaxation of pelvic floor muscles and the 'inhibitory' effect on detrusor contraction is 'released'. Additionally, abdominal pressure rises in squatting position further facilitating the act of voiding. Despite these mechanisms, standing position remains the most common position for voiding in men by virtue of convenience. However, it is sometimes observed that men who develop obstructive voiding symptoms, tend to prefer sitting or squatting positions over standing for voiding.

In our study, a significant improvement was observed in flow rates and PVR with treatment (all p≤0.05); except for Qmax in squatting position. Flow rates were significantly higher in standing and squatting position compared to sitting while on treatment. Numerically, the highest degree of improvement was noted in standing position, compared to sitting or squatting; however, the difference was statistically not significant (fig 2). Nevertheless, this trend can be explained as follows – most would agree that α adrenoceptor–blocking agents exert their favorable effects on voiding dysfunction by affecting the smooth muscle of the bladder neck and proximal urethra; there is information in the literature that to some extent they may decrease striated sphincter tone as well (Andersson & Wein, 2007; Gajewski, Downie, & Awad, 1984; Reitz et al., 2004). Moreover, as discussed above, sitting and squatting positions per se provide more pelvic floor relaxation compared to standing position. Therefore, further improvement in pelvic floor relaxation component is expected to be least in these positions on medication, compared to standing. Hence, overall decrease in outlet resistance (and corresponding increase in flow rates) may be highest in standing position.

We examined the possible utility of position-related change in uroflow-parameters in predicting response to medical therapy. Factors like age, BMI, baseline IPSS, position specific flow rates / PVR did not predict response to medical therapy. Prostate size <30gm was useful in predicting favorable response in term of both IPSS and QOL. Whereas, baseline QOL and presence of cQmax highest in squatting position (compared to standing and sitting) were useful in predicting improvement in QOL. Factors predicting response to medical therapy have been studied. Lepor et al., (1998) in a multicentric trial reported lack of predictability of uroflow parameters in assessing such response. Severity of IPSS and prostate volume has been reported to be predictive of the response and risk of BPH- surgery (Hong, Ko, Kim, & Chung, 2003; Roehrborn et al., 2002). Most of these studies did not include improvement in QOL as a parameter for success. In absence of absolute indications of surgical management, it is the QOL which matters the most to the patient and has been studied by us. Moreover, role of position related changes in flow rates in predicting response to therapy has not been studied earlier; such finding from our study expands the realm of uroflowmetry and is worthy of further considerations.

Our study has limitations; firstly it is a study of small size of only thirty participants, therefore, robust statistical conclusions cannot be made. Moreover, we did not include surgically treated patients, who are expected to have more marked changes in uroflowmetric parameters, compared to medical management. Therefore, marked change could not be brought in the outlet condition to be able to optimally study the position related effects of treatment on uroflowmetry. However, the results are promising and would incite the researchers for further studies.

CONCLUSION

Treatment naïve men with symptomatic BPH who are accustomed to void both in standing and squatting position tend to have highest flow rates in squatting position. This is irrespective of preferred voiding position, which is influenced by various personal and socio- economic factors in addition to ease of voiding. Medical therapy of BPH tends to improve the flow rates more in standing position as compared to other voiding positions. The outcome of medical therapy for BPH can be predicted by baseline QOL, prostate size <30gm and finding of cQmax value highest in squatting position (compared to sitting and standing).

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