PJSS Vol. 66, No. 2, April-June, 2011

PJSS PHILIPPINE JOURNAL OF SURGICAL SPECIALTIES

Bethanechol Chloride for the Prevention of Postoperative Urinary Retention After Anal Surgery Under Spinal Anesthesia

Billy James G. Uy, M.D.; Blas Anthony M. Yu, M.D.; Maila Rose L. Torillo, M.D. and Don Arlie S. Romero, M.D.

Background: Postoperative urinary retention is a commonly encountered problem after anal surgery particularly under spinal anesthesia. Bethanechol chloride, a muscarinic cholinergic receptor agonist was used to determine whether it could prevent this problem.
Methods: One hundred six patients with mean age of 37 ± 9 who underwent anal surgery under spinal anesthesia from January to August 2007 were included in this nonblinded randomized prospective experimental study. Forty-six patients were given bethanechol chloride 25mg/tab 1 hour post-op then another dose after 4-6 hours. Intravenous fluid was limited to ≤750ml perioperatively and patients were asked to void within 6-8 hours post-op. Those with the urge to void but unable to do so within the hour or had hypogastric pain (VAS ≥ 8) were immediately catheterized and the amount drained recorded.
Results: The study showed that the number of patients catheterized in the bethanechol group was significantly lower (6.52% vs 23.33%, P=0.038) and the mean amount of urine drained was less than the control (<400cc, P=0.001). Using Z test, the proportion of patients catheterized in the bethanechol group was significantly lower than the control (P=0.0097). No significant relationship was noted between the patient's age (<50 or ≥50) and gender with regards to urinary retention (P=0.254 and P=0.187, respectively). The number needed to treat (NNT) showed that six patients treated with bethanechol are needed to prevent one patient from experiencing urinary retention.
Conclusion: Although bethanechol chloride did not completely prevent the development of postoperative urinary retention, its use was associated with reduced need for catheterization.

Key words: Bethanechol chloride, postoperative urinary retention, spinal anesthesia

Urinary retention is a common postoperative problem encountered in patients especially in the geriatric population. The occurrence of postoperative urinary bladder distention and retention is associated with risks of overdistention and permanent detrusor damage which might even lead to atony of the bladder.[1] Prevalence of urinary retention ranges from 7% to more than 50%. The risk factors for urinary retention include age (≥50 or 60 years), spinal anesthesia, duration of surgery (>2 hours), and amount of intraoperative fluids used (≥750 ml).[1,2] Current management of urinary retention includes insertion of either an indwelling or straight catheter to allow painless drainage of urine postoperatively allowing time for the return of normal bladder function and preventing urinary retention. These procedures although not so invasive are without accompanying complications (i.e. traumatic insertion, urinary tract infection[3], and pain.) Medications to stimulate bladder contraction may also be used.

Bethanechol chloride, a cholinergic agent, is a synthetic ester that is structurally similar to acetylcholine. This is used by urologists for treatment of acute postoperative or postpartum non-obstructive (functional) urinary retention and for neurogenic atony of the bladder with retention. This drug works by neurologically stimulating "muscarinic cholinergic receptors" in the autonomic nervous system. It increases the tone of the detrusor muscle, usually producing a contraction sufficiently strong to initiate micturition and emptying of the bladder. In micturition, the bladder's detrusor muscle contracts (squeezing the bladder empty) while the lower sphincter relaxes simultaneously. The coordination of these two muscles is disrupted by certain types of spinal injuries and also by spinal anesthesia. The resulting sacral blockade in spinal anesthesia inhibit voiding through loss of the parasympathetic activity of

the pelvic nerves (S2-S4) leading to loss of sensation of bladder distention.

This study was performed to determine whether the use of bethanechol chloride can prevent the development of postoperative urinary retention.

This study aimed to determine if there is a significant relationship between the patient's age or gender and the occurrence of urinary retention. It also aimed to determine if the number needed to treat is significant for application in general surgical practice to prevent or reduce urinary retention.

Methods

The study is a non-blinded randomized prospective experimental study done at a single institution within an 8-month period starting from January 2007 up to August 2007. The study population consists of patients who underwent anal surgeries (i.e. hemorrhoidectomy and/or fistulectomy/fistulotomy) under spinal anesthesia within the duration of the study period. Patients with history of renal or urinary tract disorders, neurological disorders, previous bowel resection or anastomosis, intraoperative catheterization, or those that underwent multiple interventional procedures/ operations on the same day were excluded. Procedures which lasted for >2 hours were also excluded. Informed consents for use of the drug were obtained from the patients through their attending physicians. There was no ethical principle for medical research involving human subjects violated in accordance with the World Medical Association Declaration of Helsinki.

The patients were asked to void before being brought to surgery and they were not catheterized preoperatively. Only crystalloid IV fluids were used for volume loading and were limited to ≤750ml perioperatively.[1] Spinal anesthesia was performed by the anesthesiologist and the operation was subsequently started. IV fluids were limited to 40-80cc per hour postoperatively. A single dose of IV analgesia was given immediately post-op followed by round-the-clock oral analgesics for maintenance.

The study group was given bethanechol chloride (Uriflow, Ying Yuan Chemical, Taiwan) 25mg/tab 1 tablet one hour post-op then another dose after 4-6 hours while the control group received no other medications. Patients were assessed for hypogastric fullness or pain based on Visual Analog Scale (Figure 1) or the inability to void once the urge to urinate is present. Both groups were expected to void within approximately 6 hours to a maximum of 8 hours postoperatively. Patients were encouraged to void within the hour once there is the urge to void. If the patient was unable to urinate voluntarily, the need for catheterization was assessed (with hypogastric fullness or patient's discomfort due to pain VAS ≥8). When indicated, catheterization was done and the amount of urine drained was recorded. Patients with hypogastric fullness but did not void within 8 hours postoperatively, those with no urge to void; and those with the urge but unable to urinate were also catheterized and the amount drained recorded. Any adverse reactions to bethanechol were duly noted. Postoperative urinary retention was determined by the inability to void urine for 6 to 8 hours after the surgical procedure[4], and a residual urine volume of 400ml measured after catheterization.

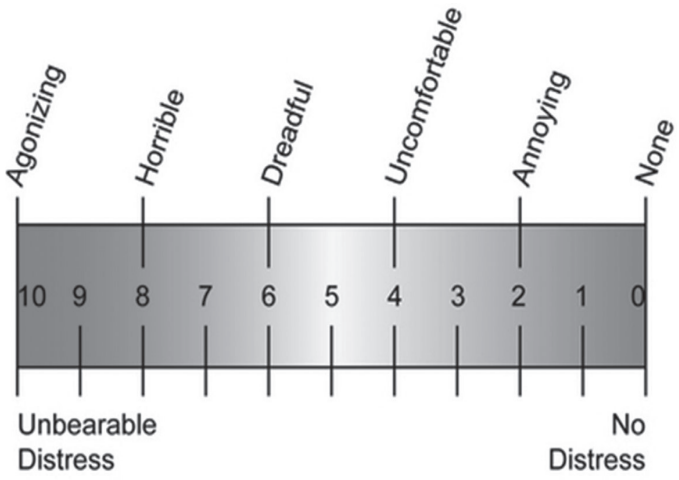

Figure 1. Visual analog scale (VAS)

For the purpose of statistical analysis, patients in the experimental and control group were subclassified according to age (below 50 or ≥ 50 years), gender, and the need for catheterization indicated. Patient characteristics were compared between groups using

Pearson chi-square test for independence. Development of need for catheterization was also compared between groups and against the patient's age and gender to check for any relationship. A *P*-value of <0.05 was considered as statistically significant.

Results

One hundred and six patients (79 males, 27 females) were included in the study. (Table 1) The mean age of the patients was 37 ± 9 with ages ranging from 20 to 60. Forty-six patients were assigned to the bethanechol group and 60 to the control group by fishbowl sampling.

Table 1. Gender distribution of the treatment group.

Gender	Treatment Group		Total
	None	Bethanechol	
Male	44	35	79
Female	16	11	27
Total	60	46	106

Demographic characteristics were compared between the experimental and the control groups. There was no significant difference between the two groups in terms of the gender of the patient with a P-value = 0.922 (Table 2). Likewise, there was no significant difference between the patient's age and the treatment group that he/she was assigned to with a P-value of 0.201. (Tables 3 & 4)

Table 2. Chi-square test for independence according to gender.

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.104(b)	1	.747
Continuity Correction(a)	.010	1	.922
No of Valid Cases	106		

Table 3. Age distribution of the treatment group.

Age Group	Treatment Group		Total
	None	Bethanechol	
< 50	50	43	93
≥ 50	10	3	13
Total	60	46	106

Table 4. Chi-square test for independence according to age.

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.490(b)	1	.115
Continuity Correction(a)	1.637	1	.201
No of Valid Cases	106		

The chi-square test was used to determine whether there exists a significant relationship between the need for catheterization and the age or gender of a patient that might affect the study. The incidence of urinary retention based on age showed that 13 out of 93 patients <50 years developed urinary retention compared to 4 out of 13 for patients ≥50 years old (Table 5). Urinary retention occurred in 10 out of 79 male patients compared to 7 out of 27 female patients. (Table 6). There was no significant relationship between the age of the patient; whether or not he/she is above 50 years of age; and the incidence of urinary retention with a P-value of 0.254 (Table 7). Likewise, there was no significant relationship between the patient's gender and occurrence of urinary retention with a P-value of 0.187 (Table 8).

Table 5. Crosstabulation of age group vs. urinary retention.

Age Group	Retention		Total
	No	Yes	
< 50	80	13	93
≥ 50	9	4	13
Total	89	17	106

Table 6. Crosstabulation of gender vs. urinary retention.

Gender	Retention		Total
	No	Yes	
Male	69	10	79
Female	20	7	27
Total	89	17	106

Table 7.Chi-square test for independence (Age vs Urinary Retention).

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.388(b)	1	.122
Continuity Correction(a)	1.304	1	.254
No of Valid Cases	106		

Table 8. Chi-square test for independence (Gender vs Urinary Retention).

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.631(b)	1	.105
Continuity Correction(a)	1.738	1	.187
No of Valid Cases	106		

Data on the need to catheterize patients were obtained. Only 3 out of the 46 patients who were given bethanechol chloride were catheterized while 14 out of 60 patients of the control group needed catheterization. There is a significant difference between the bethanechol and control groups in terms of the patient's need for catheterization with a P-value of 0.038 (Table 10). Using the Z test, the proportion of patients who needed catheterization in the bethanechol group is significantly lower than that of the control group with a P-value of 0.0097 (Table 11). The mean amount drained from the patients who needed catheterization in the group that was not given bethanechol chloride is significantly greater than 400 cc (P=0.001). Since the mean amount drained from the patients that were given bethanechol chloride was less than 400cc, there was no reason to test if the mean amount is greater than 400cc. No adverse reactions associated with bethanechol chloride were noted in the experimental group.

Table 10. Chi-square test for independence (Treatment vs. Urinary Retention).

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.465(b)	1	.019
Continuity Correction(a)	4.288	1	.038
Likelihood Ratio	5.970	1	.015
No of Valid Cases	106		

Table 11. Z-test for proportions.

Treatment Group	Prop	Value	Asymp. Sig.
Control	0.233	5.8218	0.0097
Bethanechol	0.065		

The number needed to treat (NNT) to prevent urinary retention was computed using the formula 1/ARR where Absolute Risk Reduction (ARR) is equal to the difference of control and experimental groups' rates of retention. Since the control group rate of retention was 23.33% and the experimental group rate of retention was 6.52%, the NNT for this study was 6.

Discussion

Postoperative urinary retention (POUR) is reported in the literature with incidences ranging between 7% and 52%.[1] Some newer studies have used ultrasound to accurately measure the bladder volume to determine the need for immediate urinary bladder catheterization in patients who developed POUR.[1,2,6] The authors opted to gauge the need for catheterization based on the inability to void after 6-8 hours, physical examination of hypogastric fullness or pain, and patients' urge to urinate instead of ultrasound since this is the standard practice for determining POUR in the institution where the study was done.

Lamonerie, et al. concluded that the inability to void occurs more frequently among patients who had spinal anesthesia.[2] The parasympathetic innervations of the bladder occur through the S2-S4 pelvic nerves which stimulate detrusor contraction and bladder neck relaxation. The pudendal nerves (S2-S4) also innervate the external sphincter of the bladder. Sympathetic innervation of the bladder which originates from the T10 to L2 spinal nerves has an inhibitory effect on detrusor activity and excitatory effect on the bladder neck. The stretching of the sensory receptors located in the bladder wall activates the parasympathetic pathway and inhibits sympathetic pathways to promote micturition. After spinal anesthesia, a long-lasting sensory block may affect the voiding capability and requires regression of the sensory block to at least a dermatomal level of S3 in order to obtain normal detrusor function.

Normal bladder capacity ranges between 400 and 600ml. Healthy subjects would usually experience the first need to void at a bladder volume of 150ml and the urgency to void at 300ml. In a previous prospective study done by Mulroy and colleagues, they found out

that urinary retention occurred at bladder volumes exceeding 400ml[7] while others considered 600ml as the bladder volume threshold[8]. We adopted 400ml as the threshold to be considered as significant amount of urinary retention in this study.

In this study, bethanechol chloride was used to induce micturition by bypassing the sensory component needed to produce the stimulus for adequate detrusor muscle contraction and instead directly produce a powerful detrusor muscle contraction sufficient to cause micturition by stimulating the parasympathetic innervation of the muscle. Only 3 out of 46 patients (6.52%) given bethanechol chloride required catheterization compared to 14 out of 60 patients (23.33%) in the control group. Bethanechol chloride was not able to completely prevent the occurrence of urinary retention in patients who have undergone anal surgeries under spinal anesthesia. This may have been caused by the reflex urethral spasm caused by the pain associated with anal surgeries. However, the amount drained from the control group (518 ± 182.3) was significantly greater than those obtained from the experimental group (180 ± 72.1). This suggests that bethanechol chloride significantly reduces the amount of urinary retention postoperatively compared to no intervention at all.

Age and gender of the patients were considered to be predictive factors of postoperative urinary retention in some studies.[1,5] However, no significant relationship between POUR and the age or gender of the patient was noted in this study using Chi-square test for independence. This may have been due to the limited number of patients included in the study compared to the number compared in the other literatures. In a study done by Breebaart, et al., different local anesthetics (Lidocaine, ropivacaine and levobupivacaine) were compared as to whether the length of time of sensory and motor blockade have influence on POUR[6]. It was concluded that since Lidocaine allowed voiding after 245 minutes which was 40 minutes faster than the other two groups, the difference was not too significant considering a spinal discharge time interval of 4-5 hours postoperatively. The difference in the type of spinal anesthesia used was no longer evaluated in this study since the patients would be expected to void within the 6 to 8 hours whether long acting or short acting local spinal anesthetic was used. Not limiting the type of spinal anesthesia used would also closely mimic the actual clinical practice and increase the usefulness of this study in practice.

In this study, the NNT was 6. This means that for every 6 patients given bethanechol chloride, one (1) will benefit from the use of the drug and not develop urinary retention.

Conclusion

Although bethanechol chloride was not able to completely prevent the development of postoperative urinary retention, its use was associated with reduced need for catheterization as compared to the control group. The authors recommend duplicating this study in a larger population including other cases in addition to those that underwent anal surgery since this will help eliminate the problem of reflex urethral spasm associated with post-anal surgeries which might have influenced the outcome of this study. Also, revision of the study methodology making it a double-blinded randomized control trial would increase the credibility of the study.

References

1. Keita H, Diouf E, Tubach F, et al. Predictive factors of early postoperative urinary retention in the Post Anesthesia Care Unit. Anesth Analg 2005; 101: 592-596 [PMID: 16037182]
2. Lamonerie L, Marret E, Deleuze A, et al. Prevalence of postoperative bladder distention and urinary retention detected by ultrasound measurement. Br J Anaesth 2004; 92: 544-546 [PMID: 14977795]
3. Berkov S, Das S. Urinary tract infection and intermittent catheterization. Infections in Urology 1998; 11(6): 165-168.
4. Stallard S, Prescott S. Postoperative urinary retention in general surgery patients. Br J Surg 1988; 75: 1141-1143 [PMID: 3208051]
5. Petros JG, Bradley TM. Factors influencing postoperative urinary retention in patients undergoing surgery for benign anorectal disease. Am J Surg 1990; 159: 374-376 [PMID: 2316800]
6. Breebaart MB, Varcauteren MP, Hoffman VL and Adriaensen HA. Urinary bladder scanning after day-case arthroscopy under spinal anaesthesia: comparison between lidocaine, ropivacaine, and levobupivacaine. Br J Anaesth 2003; 90: 309-313 [PMID: 12594142]
7. Mulroy MF, Salinas FV, Larkin KL, et al. Ambulatory surgery patients may be discharged before voiding after short acting spinal epidural anesthesia. Anesthesiology 2002; 97: 315-319 [PMID: 12151918]
8. Pavlin JD, Pavlin EG, Gunn HC, et al. Voiding in patients managed with or without ultrasound monitoring of bladder volume after outpatient surgery. Anesth Analg 1999; 89: 90-97 [PMID: 10389784]

9. Tammela T, Kontturi M, Lukarinen O, et al. Postoperative urinary retention: II, Micturition problems after the first catheterization. Scand J Urol Nephrol 1986; 20: 257-260 [PMID: 3810055]
10. Rosseland LA, Stubhaug A, Breivik H. Detecting postoperative urinary retention with ultrasound scanner. Acta Anaesthesiol Scand 2002; 46: 279-282 [PMID: 11939918]
11. Kamphius ET, Lonesu TI, Kuipers PW, et al. Recovery of storage and emptying functions of the urinary bladder after spinal anesthesia with lidocaine and with bupivacaine in men. Anesthesiology 1998; 88: 310-316 [PMID: 9477049]
12. Tammela T, Kontturi M, Lukarinen O, et al. Postoperative urinary retention: I. Incidence and predisposing factors. Scand J Urol Nephrol 1986; 20: 197-201 [PMID: 3787196]