Original Article

Role of Tolterodine in the Management of Postoperative Catheter-Related Bladder Discomfort: Findings in a Nigerian Teaching Hospital

KH Tijani, NO Akanmu[1], JO Olatosi[1], RW Ojewola

Department of Surgery, [1]Department of Anaesthesia, College of Medicine, University of Lagos/Lagos University Teaching Hospital, Lagos, Nigeria

Abstract

Background: Patient discomfort secondary to an indwelling urethral catheter in the post operative period can be very distressing. These symptoms resemble the overactive bladder (OAB) syndrome. Muscarinic receptor blockers have been successful in the management of OAB. However, information on the use of these drugs in the management of the postoperative catheter-related bladder discomfort (CRBD) in sub-Saharan Africa is still relatively sparse. **Objective:** To assess the efficacy of preoperative oral tolterodine in the management of CRBD in surgical patients in the immediate postoperative period. **Methods:** This was a double-blind placebo-controlled study consisting of 56 patients in each arm who underwent general anesthesia. Each patient was given oral tolterodine or placebo 1 hour before the induction of anesthesia. The patient was later assessed at the recovery room at intervals after recovery from anesthesia. The presence of CRBD was noted and graded. **Results:** The overall incidence of CRBD in both the tolterodine group and the control were 85.7% and 91.1%, respectively. Overall, tolterodine prophylaxis (TP) was associated with an absolute risk reduction (ARR) of 5.4%, relative risk reduction (RRR) of 5.8%, and a number needed to treat (NNT) of 19. The incidence of moderate-to-severe CRBD in the tolterodine and control groups were 10.7% and 78%, respectively, with an ARR of 74.5% with TP. **Conclusion:** TP does not significantly reduce the incidence of CRBD in the immediate postoperative period but appears to be efficient in the reduction of the severity of postoperative CRBD.

Keywords: *Catheter-related bladder discomfort, indwelling urethral catheter, tolterodine, postoperative*

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Introduction

Patient discomfort secondary to an indwelling urethral catheter can be very distressing. Many of these patients often complain of severe bladder discomfort or strong urge to pass urine.

There are many indications for indwelling urethral catheterization. It could be for the simple monitoring of the urinary output in the perioperative periods or in critically ill patients. Therapeutic indications include the management of patients with incontinence and patients with urinary retention and in the prevention of fistula after a urethral, prostatic, or bladder surgery.

Even though the worldwide incidence and severity of bladder discomfort secondary to an indwelling catheter has not been reported, many clinicians would agree that these troublesome adverse effects are not uncommon. It is not unusual to see semiconscious patients making attempt to forcibly remove their indwelling catheters while patients with recurrent episodes of acute urinary retention are known to demand the premature removal of their indwelling catheter despite being aware of the risk of another episode of painful retention.

Patients with catheter-related bladder discomfort (CRBD), defined as the presence of suprapubic discomfort and or strong urge to pass urine in the presence of a patent indwelling urethral catheter,[1] present with symptoms that resemble those of an overactive bladder (OAB)

Address for correspondence: Dr. Kehinde Habeeb Tijani, Department of Surgery, College of Medicine, University of Lagos, Lagos, Nigeria.
E-mail: habeeb_tijani@yahoo.com or khtijani@cmul.edu.ng

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syndrome.[1,2] These symptoms are caused by the involuntary contractions of the detrusor mediated by muscarinic receptors.[1-3] CRBD is known to exacerbate postoperative pain and can be resistant to conventional analgesics.[4] Although many drugs have been used successfully to treat OAB,[3] a recent local survey indicated that most clinicians tended to manage CRBD by reassurance, prescribing ineffective analgesics, whereas others prescribed antibiotics under the false notion that irritative bladder symptoms were always due to infections. Drugs used in the management of OAB include the anticholinergic-oxybutinin, tolterodine, and gabapentin.[3,5] Although there are numerous reports on OAB, the literature on CRBD is very sparse. In view of the frequency of urethral catheterization in our environment, a study on the incidence and prevention of CRBD in the immediate postoperative period is long over-due.

Objective

The aim of the study was to determine the incidence of CRBD in surgical patients and to assess the efficacy of oral tolterodine in the management of CRBD in surgical patients in the immediate postoperative period.

Methods

This was a prospective double-blind study. The study was approved by the hospital ethics committee and informed consent taken from the patients.

Sample Size Estimation

Assuming a 95% confidence level and power of 80% with a 55% incidence of CRBD without tolterodine and 36% incidence with tolterodine, the estimated sample size for each arm was 53.[6,7] As a result, 56 patients were recruited into each arm.

Inclusion Criteria

The inclusion criteria included all adult patients with physical status I or II as per American Society of Anaesthesiologists, who underwent general anesthesia for mastectomy and open or laparoscopic abdominal procedures.

Exclusion Criteria

The exclusion criteria were patients with malabsorption; patients in whom oral tablets are contraindicated; patients with known contraindications to tolterodine, diclofenac, or pentazocine usage; age less than 18 years and older than 60; patients with a body mass index greater than 30 kg/m^2; patients with known OAB, that is, nocturia more than three and frequency more than 8; patients on medical treatment for bladder outlet obstruction; and patients with bladder, prostatic, or urethral surgery or a history of chronic analgesic abuse, chronic pain, or psychiatric disease.

One hundred and twelve individuals were randomized into two groups of 56 each consisting of the tolterodine and the placebo arms. The randomization was done by the sequential opening of sealed opaque envelopes containing the random group allocation. This was generated using a block randomization method (using a block size of eight to ensure equal sample size) and a table of random numbers. The envelopes were opened in a sequence as each participant entered the study and the group subsequently allocated. The patients were premedicated with oral diazepam 5 mg at night before and 2 hours before the induction of anesthesia. Each patient was given oral 2 mg tolterodine or 200 mg vitamin C as placebo 1 hour before the induction. Induction of anesthesia was with fentanyl and propofol, whereas pancuronium was used for the muscle block. All patients were catheterized with a size 16 silicone-coated Foley catheter and the balloon inflated with 10 mL of normal saline. Anesthesia was maintained with isoflourane and air and intermittent fentanyl. All of the patients were administered intravenous 30 mg of pentazocine about 30 minutes before extubation and repeated 4 hour later along with intramuscular 75 mg diclofenac.

Bladder discomfort which was defined as the urge to pass urine or discomfort in the suprapubic region was assessed by a resident doctor who was blinded on the medication received by the patient. This was recorded at arrival at the recovery room (0 hour) and 1 hour, 2 hours, and 6 hours. Severity of CRBD was graded as mild (reported by the patient on questioning), moderate (reported by the patient without questioning and not accompanied by any behavioral response), severe (reported by the patient and accompanied by behavioral responses, for example, flailing of the limbs, strong vocal response, and attempts to remove the catheter).[7] The technique of questioning was as described by Agarwal *et al*.[8] Briefly, patients were initially engaged in casual conversation (e.g. occupation, address) and if during this period the patients complained of CRBD symptoms, it was graded appropriately in to either

Table 1: Patient characteristics and complications

	Control	Tolterodine	*P*
No. of patients	56	56	1.0
Mean age (years)	34.3	37.1	0.44
Average duration of surgery (min)	122	116	0.52
Dry mouth	2	6	0.14
Visual difficulty	1	2	0.56
Nausea and vomiting	2	2	1.0

Table 2: Incidence of bladder discomfort

Time (h)	0		1		2		6	
Groups	C	T	C	T	C	T	C	T
No discomfort %	6 (10.7)	7 (12.5)	6 (10.7)	8 (14.3)	5(8.9)	8 (14.3)	8 (14.3)	9 (16.1)
Discomfort %	50 (82.3)	45 (80.4)	50 (82.3)	48(85.7)	51 (91.1)	48 (85.7)	48 (85.7)	47(83.9)
Grading of discomfort								
Mild %	6 (10.7)	41(73.2)	7 (12.5)	42 (75)	7 (12.5)	44 (78.6)	6 (10.7)	42 (75)
Moderate %	37 (66.1)	4 (7.1)	36 (64.3)	6 (10.7)	39 (69.6)	4 (7.1)	38 (67.9)	5 (8.23)
Severe %	7 (12.5)	0(0)	7(12.5)	0 (0)	5 (8.23)	0 (0)	4 (7.1)	0 (0)

C = control, T = tolterodine group.

Table 3: Risk reduction of moderate and severe CRBD by tolterodine

Time (h)	0	1	2	6
Moderate + severe				
ARR (%)	80	78	78	74.5
RRR (%)	91.7	91.5	89.6	89.1
NNT	1.25	1.1	1.3	1.34
Severe alone				
ARR (%)	12.7	12.7	9	7.3
RRR (%)	100	100	100	100
NNT	7.9	7.9	11	13.8

ARR = absolute risk reduction, CRBD = , catheter-related bladder discomfort, RRR = relative risk reduction, NNT = number needed to treat.

moderate or severe. If they were asked whether they were comfortable, they answered ''yes'' and this was regarded as no CRBD, but if the answer was ''no'' with complaints of symptoms of CRBD, this was regarded as mild. The presence of adverse effects including nausea, vomiting, blurred vision, and dry mouth were also noted and recoded.

Comparison of the incidence of bladder discomfort was done using the *z* test, whereas severity of the discomfort was analyzed by the Fisher exact test. A *P* value <0.05 was regarded as significant.

Results

There was no statistical significant difference in the patients' characteristics including sex, age, duration of surgery, and the degree of postoperative need for analgesics. The most frequent adverse effect of tolterodine was dry mouth, which was three times more frequent than the control [Table 1]. The incidence of CRBD in both the tolterodine group and the control group were 85.7% and 91.1%, respectively [Table 2]. Overall, tolterodine prophylaxis (TP) was associated with an absolute risk reduction (ARR) of 5.4%, relative risk reduction (RRR) of 5.8%, and a number needed to treat (NNT) of 19, that is, a minimum of 19 patients need to be treated with oral tolterodine to prevent CRBD in one patient. The incidence of moderate-to-severe CRBD in the tolterodine and control groups were 10.7% and 78%, respectively, whereas at 6 hours (the least effective period of TP in this study), ARR, RRR, and NNT for moderate and severe CRBD were 74.5%, 89.1%, and 1.34, respectively [Table 3].

Discussion

The study demonstrates a rather high incidence with CRBD in postoperative patients. Our study revealed that almost all patients (91.1%) in the control group had CRDB, almost twice the report of 52% by Agarwal *et al*.[5] The reasons for these are unclear, but sociocultural factors may play a role as they are known to influence the perception and definition of pain or discomfort.[9] Although there is no universal consensus on the grading of CRBD, the grading described by Agarwal *et al*.,[7] which was also used for this study, appears to be the most popular.[8,10] The manner of questioning of the patient for mild CRBD by the doctor may also be contributory as most cases were mild. However, the technique of questioning as described by Agarwal *et al*.[8] was used while a total of four different doctors were involved in the questioning in this study.

In this study, the incidence of CRBD in patients with tolterodine was 85.7%, whereas the ARR with tolterodine was 5.4%, the RRR was 5.8%, and NNT was 19 all indicative of poor efficacy of prophylactic tolterodine in the prevention of CRBD in our patients. This pattern was maintained across board from 0 to 6 hours. There was no statistically significant difference in overall incidence of CRBD in both the tolterodine group and the control. This is in contrast with the study by others who have reported

much better efficacy with an RRR of 19%, ARR 35–42% and an NNT of 5.[5,8,10]

When mild CRBD was excluded from the analysis the overall incidence of CRBD was 78.6% and 10.7% in control and tolterodine group, respectively. At 0 hours with TP, ARR for the development of moderate-to-severe CRBD was 71.4%, RRR of 91.7%, and NNT of 1.4, whereas at 6 hours it was 66%, 86.4%, and 1.5, respectively, all indicative of a high efficacy of preoperative 2 mg tolterodine in the prevention of moderate and severe CRBD over the first 6 hours in the postoperative period. Although some studies[7,8] have showed an almost 100% increase in the incidence of CRBD at 1 hour when compared with the 0 hour, which they attributed to the dwindling effects of the general anesthesia, in our study this did not appear to be so with only a 2% increase. The interval between oral administration and patients transfer to the recovery room may also be contributory factor to these differences as oral tolterodine is rapidly absorbed reaching peak levels after 1 to 2 hours.[8] With a half-life of up to 11 hours,[8] oral tolterodine apart from being rapidly acting also has a relatively long duration of action.

With an overall incidence of 0% and RRR of 100% for severe CRBD compared with a 13% incidence for the control group, oral tolterodine appears to be very effective in preventing severe CRBD. This is similar to the findings of others, who also found a zero incidence of severe CRBD in patients on TP.[7,8] Dry mouth, blurred vision are known adverse effects of most antimuscarinic drugs,[5] while supratherapeutic doses of 8 mg/day tolterodine have been associated with an average of 6 beats/min increase heart rate.[10] The incidence of dry mouth and blurred vision were more in patients with the tolterodine group, with dry mouth being the predominant symptom by occurring three times more frequently in the tolterodine group . In this study, we had excluded patients with bladder, prostatic, or urethral surgeries and those who had regional anesthesia to limit the variables. However, others have reported beneficial effects of tolterodine on CRBD in after prostatectomy patients, whereas a study on patients who have had regional anesthesia may also be worthwhile so as not to deny these patients the possible benefits of TP.

The different limitations of the study, however, need to be acknowledged. First, extensive literature review was difficult as only very few relevant studies on CRBD had been reported in the English literature. Secondly a triple-blind study, although ideal, was not possible. Even though randomization was done to eliminate bias, the tablets of the placebo and the tolterodine did not look exactly alike, thereby making it possible for the health care giver who administered the drugs to the patients (and possibly a well-informed patient) to be aware of the drug each patient was given. However, the anesthetist resident who recorded the symptoms in the recovery room was completely blinded on the medication given to the patients. Thirdly, even though similar doses of analgesics were given within the first 4 hours in the postoperative period the exact effect of these analgesics on the individual patient's perception of CRBD could not be determined. This study also evaluated a single uniform dose 2 mg for all patients irrespective of weight and duration of surgery as these factors may play a role in the response to tolterodine. However, despite these limitations, the study has demonstrated a possible role for TP in the management of surgical patients on indwelling urethral catheter in the immediate postoperative period.

In conclusion, even though tolterodine administration 1 hour before surgery appears to have very a limited effect in the overall incidence of CRBD, it however appears to significantly reduce the incidence of moderate and severe CRBD in the immediate postoperative period. We therefore recommend that the prophylactic use of tolterodine should be considered in the management of surgical patients who require postoperative catheterization to reduce the severity of CRBD.

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Conflicts of interest

There are no conflicts of interest.

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