EFFICACY OF DICLOFENAC COMPARED TO PLACEBO IN PAIN RELIEF DURING REMOVAL OF URETHRAL CATHETER

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ABSTRACT

Objective: *To investigate efficacy of diclofenac compared to placebo in relieving pain on removal of indwelling urethral catheters.* ***Material & method:*** *This study was a randomized controlled trial, double blind, comparing diclofenac with placebo in relieving pain on removal of indwelling urethral catheters. Adult male patients with indwelling catheters admitted in surgical ward of RSUP Dr. Sardjito Yogyakarta who met the inclusion criteria were recruited. The independent variables were diclofenac or placebo treatment, while the dependent variables were visual analogue scale (VAS) score, and the external variables were age, education level, and duration of indwelling urethral catheter. We gave patients diclofenac or placebo in capsules 2 hours before urethral catheter removal. Immediately after removal by assistant, the patient filled VAS form. We used Chi-square test, independent T-test, and bivariate analysis with SPSS program version 11.5, with p<0,05 was set as statistically significant level.* ***Results:*** *Thirty patients met inclusion criteria. Mean VAS score of both groups was 33,467 ± 20,4577, diclofenac group was 31,567 ± 20,0934, and placebo group was 35,367 ± 21,3412. There was no statistically significant difference of VAS score between both groups (p=0,844).* ***Conclusion:*** *Efficacy of diclofenac and placebo in relieving pain when performing urethral catheter removal is not significantly different.*

Keywords: *Pain, diclofenac, placebo, urethral catheter removal.*

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INTRODUCTION

According to International Association for the Study of Pain, pain is a sensory and emotional experience related to lesion or tissue damage potential.[1] All pain may induce uncomfortable sensory sensations and create emotional experience that is different from one individual to another.[2]

Urethral catheterization was conducted to diagnose and manage urological disease. Several types and materials for producing catheter are available for urethral catheterization, and the selection of specific catheter type depends on the rationale of catheterization. Indications for urethral catheterization are varied, either for diagnosis or management. For diagnosis, urethral catheterization is performed in women to collect urine for urine culture examination in order to prevent skin bacteria contamination. If ultrasonography (USG) is not available, post-micturition urine residual volume can be determined by catheterisation. The instillation of contrast material for urethrocystography also requires the same procedure. For management, indications for urethral catheterization is to manage infravesicular obstruction, either due to prostatic enlargement, hematoma in the bladder, urethral stricture, and inflammatory process. Another indication is to monitor the amount of urine excreted from post-operative patients as well as from patients who required no surgical procedure.[3]

If the catheterization is no longer required, the urethral catheter should be removed or replaced. During the removal, the patient will suffer from pain, although only transient, due to the scraping of the catheter on the urethral luminal wall, producing intense discomfort, so that some of the patients refuse to have catheter reinsertion.[4]

Pain during the urethral catheter removal may be due to spontaneous or stimulated discomfort sensation, which is called as dysesthesia.[2] Therefore, to reduce or eliminate pain during urethral catheter, analgesics should be provided to make the patient comfortable.

Diclofenac is one of non-steroidal anti-inflammatory drugs (NSAID) with analgesic (anti-pain) as well as anti-inflammatory effects.[5] In this study the efficacy of diclofenac was compared to placebo in relieving pain during urethral catheter removal.

OBJECTIVE

To study the efficacy of diclofenac compared to placebo in relieving pain during urethral catheter removal in patients with indwelling catheter.

MATERIAL & METHOD

This study was a randomized, double blind, controlled trial, comparing diclofenac to placebo in patients with indwelling catheter. The study was performed in Surgical Ward, Dr Sardjito Hospital, Yogyakarta. Period of study was from February 2009 until the time when the planned number of samples was achieved.

Study population was adult male patients with indwelling catheter. Available population was patients hospitalized at Surgical Ward, Dr. Sardjito Hospital, Yogyakarta, from February 2009, who met the inclusion criteria. The inclusion criteria were adult males who had first catheter insertion, agreeing to join the study, and status post-operative (orthopaedic, digestive, and urological). Exclusion criteria were chronic diabetes mellitus with neuropathic complications, neurologic deficit, post-lower urinary tract surgery, malignant tumor, and pelvic fracture.

Notes on postoperative orthopaedic, digestive, urological, tumor, and plastic surgery were found by observing the medical records. In addition, the presence of diabetic nephropathy in diabetes mellitus, neurological deficit, post-lower urinary tract operation, the presence of malignant tumor, and the presence of pelvic fracture were also found by observing the medical record of each patient.

Total sample according to hypothetical test formula on proportional difference by Lemeshow (1991) was 13 individuals for each group.[6] Level of pain was determined using visual analogue scale (VAS) score, filled by the patients after the catheter removal.

In this study, an assistant informed about the study procedures assisted the author. Patients who met the inclusion criteria were asked to sign informed consent if they agreed to join the study. The patients were informed about the procedure, drugs provided, and the effect of action of the drugs. The patients' name, age, education, number of medical record, admission date, and duration of indwelling catheter were recorded.

Diclofenac, in a dose of 50 mg, and lactose powder as placebo, were put into identical white and green capsules. All drugs were put into marked plastics bags. Only the authors knew which plastic bags contained active drugs or placebo. Study patients were given diclofenac or placebo by the assistant as determined by randomization. Post-operative patients routinely receiving analgesics, treatment was given at least 6 hours after the analgesic administration. Patients were given diclofenac or placebo, as randomized, 2 hours prior to catheter removal. Precisely two hours after the administration of either placebo or diclofenac, the catheter was removed by the assistant. The patient immediately filled in the available VAS sheet about the pain he felt.

The independent variable in this study was the administration of diclofenac or placebo, while the dependent variable was the score of visual analogue scale (VAS). Measurement scale of the variables was numeric. The external variables in this study were age, level of education, and duration of indwelling catheter.

The basic characteristics of subjects, which are numeric scale, are reported as mean and standard deviation. Difference of means for numeric data, including basic characteristics and VAS scores between both groups was tested using the independent T-test. The value of $p < 0.05$ was chosen as statistical significance. Different proportion of nominal data in both groups was tested using Chi-square test. Bivariate analysis was performed to analyze relationship of VAS scores with age, level of education, and duration catheterisation. Statistical tests in this study were performed using SPSS program version 11.5.

Ethical agreement for this study was obtained from ethical committee for human biomedical research, Faculty of Medicine, Gadjah Mada University (UGM), Yogyakarta. Patients were given clear information on the objective and the course of study. After they understood and agreed to participate, they signed the informed consent.

RESULTS

Subjects were adult male patients with indwelling urethral catheters, treated at Surgical Ward, Sardjito Hospital, Yogyakarta. Total patients meeting the inclusion criteria and agreeing to participate in this study were 30 individuals, comprising 15 individuals in diclofenac group and 15 individuals in placebo group. Mean patient age was 44,87 $\pm$ 18,955 years, with the youngest aged 18 years and the oldest 84 years.

Basic characteristics examined in this study were age, level of education, and duration of indwelling catheter (Table 1). The sex of the patients was homogeneous, male. Mean age in the placebo group was 41,930 $\pm$ 18,387 years and in diclofenac group was 47,80 $\pm$ 19,691 years. Independent t-test was used in both groups according to age. There was no statistically significant difference in age of both treatment groups (p=0,817).

Level of education was classified into elementary, secondary (SMP, SMA) and higher (university) education. In placebo group, patients with elementary education were 3 individuals, secondary education 2, and higher education 4 individuals. In diclofenac group, those with elementary education 3 individuals, secondary education 10, and higher education 2. Chi-square test analysis was performed in both groups according to the level of education. There was no statistically significant difference in level of education in both treatment groups (p=0,641).

Mean duration of catheter indwelling in both groups was 2,93 $\pm$ 2,212 days, while that in placebo group was 3,33 $\pm$ 3,039 days and in diclofenac group it was 2,53 $\pm$ 0,743 days. Independent t-test was performed on duration of indwelling catheter. There was no statistically significant difference in both groups for duration of indwelling catheter (p=0,159).

From these basic data, there was no significant difference between diclofenac and placebo groups in terms of age, level of education, and duration of indwelling catheter. It could therefore be inferred that

Table 1. Basic data characteristics of the study subjects.

Variables	Placebo Group (N=15)	Diclofenac Group (n=15)	p
Age (mean $\pm$ SD)	41,930 $\pm$ 18,387	47,80 $\pm$ 19,691	0,817
Education			
- Elementary	3	3	
- Secondary	8	10	0,641
- High	4	2	
Duration of indwelling catheter (mean $\pm$ SD)	3,33 $\pm$ 3,039	2,53 $\pm$ 0,743	

SD: Standart Deviation

both groups were homogeneous. It has been known that age and education influence the perception of pain. Duration of indwelling catheter is also influential, since longer duration may lead to the emergence of crustae around the catheter, which causes pain during removal.[7] In this study, there was no significant difference between diclofenac and placebo groups in terms of the duration of indwelling catheter. In conclusion, the duration of indwelling catheter did not affect the result of the study.

VAS score evaluation was completed by the patient himself after catheter removal. The patient was asked to evaluate sensation of pain during removal catheter by the assistant. Percentage of mild pain perception in diclofenac and placebo groups were reported by 9 (60%) and 10 (66,67%) individuals, respectively, moderate pain by 6 (40%) and 4 (26,67%) individuals, while severe pain by 1 (6,66%) individual in the placebo group (Table 2).

The VAS scores were then analyzed with independent T-test to determine the significance level, with the independent variable the groups receiving diclofenac and placebo. Mean VAS score in both groups were 33,467 $\pm$ 20,4577. Mean VAS score in diclofenac group was 31,567 $\pm$ 20,0934 and that in placebo group 35,367 $\pm$ 21,3412. Pain interpretation both in diclofenac and placebo groups belonged to the criteria of mild pain (0 - 40). Mean VAS score in diclofenac group was lower than that of placebo group. However, statistically significant difference in both groups were not found in terms of VAS score (p=0,844).

Table 2. Percentage of pain perception in each group.

Pain Perception	Diclofenac		Placebo	
	N	%	N	%
Mild	9	60	10	66,67
Moderate	6	40	4	26,67
Severte	0	0	1	6,66

Table 3. Result of VAS scores for pain in each group.

Variables	Mean Score	Pain Perception	p value
Placebo group	35,367 $\pm$ 21,3412	Mild	0,844
Diclofenac group	31,567 $\pm$ 20,0934	Mild	

Bivariate analysis was performed on VAS scores in diclofenac groups according to age, and the result was -0,622 with p=0,013. This indicates that, in diclofenac group the older the patient's age the lower the VAS score. In placebo group, the p value was 0,937, indicating no significant relationship between VAS score value in placebo group according to age.

Bivariate analysis was also performed on difference of VAS score in diclofenac group according to the duration of indwelling catheter, and the result was found to be not significant (p=0,985). The same finding was also found in placebo group, where there was no significant difference between VAS score according to the duration of indwelling catheter (p=0,449).

The difference of VAS score in diclofenac groups in terms of level of education was also subjected to bivariate analysis, and there was no significant difference (p=0,198). In placebo group, there was no significant difference in VAS score in terms of level of education (p=0,911).

DISCUSSION

Sex has influence on pain perception because it is included in biological variation.[8] Subjects enrolled in this study were all male. This was intended to obtain homogeneous population in this study. In addition, males were selected as subjects in this study because the urethra is longer than that in female, 15-25 cm in male and 3-5 cm (averagely 4 cm) in female. Length of urethra may affect the induced pain during removal of catheter. Since male's urethra is longer, pain episodes during urethral catheter removal takes a longer time. It was expected that males in this study

were able to describe their pain perception during urethral catheter removal more clearly than the female patients whose urethra were shorter.[4]

Age also affects the perception of pain. In this study, mean patient age in both groups was 44,87 ± 18,955 years. Mean age in placebo group was 41,930 ± 18,387 and that in diclofenac group was 47,80 ± 19,691 years. Age variation in both groups did not show significant difference (p=0,817; IK 95%). This was consistent with the findings of Kertia & Nurdjanah (2006), that the influence of age on pain intensity was not statistically significant.[1] In that study, the mean age in experimental group was 65,94 ± 8,29 and in control group 63,95 ± 7,41, with p=0,451. A study by Maulana (2007) also showed similar findings, with mean age of placebo group 41,930 ± 18,387 years, and in diclofenac group 47,80 ± 19,691 years (p=0,817).[4]

Bivariate analysis on the difference in VAS scores according to age in diclofenac group after treatment showed negative correlation (-0,622), where older patients had lower VAS scores (p=0,013). Placebo group showed no significant difference between VAS score in terms of age (p=0,937). It is plausible that in older individuals, sensory systems are less sensitive.[9] Pain is a sensation transmitted by sensory nerve through spinal cord to the brain sensory area, and the sensation will be received. Nociceptive pain occurs from the activation of free nerve endings of sensory nerve fibers and the viscera. In elderly, sensory and visceral sensation decreases, which sometimes results in general hypoesthesia.[7]

Level of education may also affect pain perception.[7] The higher the level of education, the lower the pain perception. In this study, levels of education were grouped into elementary, secondary (SMP-SMA), and high education (university). In both groups, most patients had secondary school education (18 individuals), followed with elementary education (6 individuals), and higher education (6 individuals). Chi-square analysis revealed that the proportion of the patients' level of education in both groups was not significantly different (p=0,641). Then, bivariate analysis was undertaken on the difference between VAS scores in both groups related to age, from which no significant difference was found, either in diclofenac group (p=0,198) and placebo (p=0,911). This demonstrates that patients' level of education does not affect pain perception in both treatment groups. The result was similar to Kertia and Nurdjanah (2006) and Maulana (2007).[1,4]

Mean duration of indwelling catheter in both groups was 2,93 ± 2,212 days, while that in diclofenac group was 2,53 ± 0,743 days and in placebo group 3,33 ± 3,039 days. In both groups, the shortest duration of indwelling catheter was 2 days (17 patients) and the longest 14 days (1 patient). Chi-square analysis was performed on the basic data on indwelling catheter, revealing no significant difference in the proportion of indwelling catheter in both groups (p=0,159). Using independent t-test, we analyzed the difference of VAS score in both groups according to the duration of indwelling catheter. In this study there was no significant difference in VAS score in terms of the duration of indwelling catheter, both in diclofenac (p=0,985) and placebo (p=0,449) groups. Pain is a signal of tissue irritation, a forthcoming injury or an undergoing injury. Sensory nerve fibers (nociceptor) in affected area become activated and transmit signals through peripheral nerve and spinal cord to the brain. Activated spinal reflex complex is followed by perception, cognitive and effective response, and possibly a deliberate movement. Lengthy duration of catheter may induce urethral mucosa injury and induce crustae surrounding the urethra. The removal of this catheter may induce higher pain stimulus.[7]

This study found that the mean VAS score in both groups was 36,96, while VAS score in diclofenac group was 31,567 ± 20,0934 and in placebo group was 35,367 ± 21,3412. These results showed that average patients in both groups only complained of mild pain during catheter removal, particularly in placebo group.

The difference of VAS score in both groups did not show statistical significance (p=0,844). This indicates that reduction of pain by diclofenac was not statistically significant compared to placebo.

Mild pain perceived by patients in diclofenac group may possibly be affected also by psychological

condition of the patients. Patients experienced psychosomatic pain due to the fear of catheter removal, not due to catheter irritation to the urethra. Fear, stress, anxiety, pain and other psychological factors may influence pain perception.[11] Before catheter removal, the patient should be informed that the procedure will not induce pain, because it is undertaken in a correct manner. Therefore, communication to the patient is important prior to removal of urethral catheter.

Another possible cause of pain in diclofenac group was the time of administration. In this study, treatment was given 120 minutes after diclofenac administration, and afterwards the concentration decreased fast. Diclofenac's half-life was 1-3 hours, with peak concentrations in 2 hours. However, other literature mentions a half-life of diclofenac 0,33 - 2 hours, with peak concentrations reached in 1 hour. Therefore, it was possible that during VAS score assessment, diclofenac concentration was starting to decrease.

In addition, short time of study (2,5) and small number of samples (30 individuals) also influenced lack of significance of diclofenac in reducing pain compared to placebo. Sample was determined from the assumption that patients who did not feel pain during urethral catheter removal, those with diclofenac were 70% and placebo 20%. In this study, there was no patient who did not experience pain at all by receiving diclofenac. However, in both groups there were two patients each with VAS scores less than 1. Since the mechanism of acute pain is multifactorial, psychological factor may also play a role. In addition to the provision of analgesics, good communication may also help relieve pain.

CONCLUSION

The efficacy of diclofenac is not significantly different from that of placebo in relieving pain during urethral catheter removal.

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