Effect of Cyclooxygenase-2 Inhibitors in Double J Stent Removal under Local Anesthesia

Rulianov Rulianov[1], *Jumadi Santoso*[2], *Aryo Teguh Abriansyah*[2], *Safendra Siregar*[1]

[1]Department of Urology, Faculty of Medicine Universitas PaDJaDJaran, Hasan Sadikin Academic Medical Center, Indonesia

[2]Department of Urology, Faculty of Medicine, Universitas PaDJaDJaran, SoekarDJo Hospital, Tasikmalaya, Indonesia.

Correspondence to: Dr. Rulianov Rulianov; email: rulianov@gmail.com

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Abstract

Background: Celecoxib is a selective cyclooxygenase-2(COX-2) inhibitor that can reduce the inflammatory process during double J (DJ) stent removal procedure. This study aimed to determine the differences in pain levels in patients undergoing DJ stent removal under local anesthesia by oral administration of celecoxib before the procedure. Materials and methods: A total of 46 male patients who underwent removal of DJ stent under local anesthesia from December 2019 to February 2020 were included. Patients were divided into two groups according to oral administration of celecoxib 3 hours before the procedure. The visual analog scale (VAS) and side effects were compared between the two groups. Results: The mean patient age was 50.26 ±14.92 years in the group without celecoxib and 50.35 ±15.61 years in the group with celecoxib. The mean intra-operative VAS score was significantly higher in the group without celecoxib (6.87 ± 1.51) than that in the group with celecoxib (3.74 ± 1.65) (p=0.04). The VAS scores on the first day after the procedure were 2.08 ±0.79 and 1.34 ± 0.98 in the groups without and with celecoxib, respectively (p=0.53). Only 1 patient had nausea as side effect of celecoxib. **Conclusion:** Celecoxib can reduce pain during DJ stent removal.

Keywords: Cyclooxygenase-2 inhibitor, double J stent removal, local anesthesia

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Introduction

Ureter stent placement is commonly performed in urological surgery both in open surgery and endourology(1,2). Its indications for use have continued to grow in the last 10 years(2). In general, temporary placement of ureteric stents in the ureter to help drain the urinary tract, thus preventing ureteral stenosis and giving the wound suture time to heal(1,3,4). Among various ureteric stents available in the market, the double J (DJ) stent is often used(4). This stent was first introduced by Finney in 1978, and both of its ends are shaped like a letter J in order to prevent displacement after placement in the ureter(2). However, the DJ stent has several complications(1,2), such as stent encrustation, migration, and fragmentation (1). Research shows that, to avoid such complications, the optimal duration to use a DJ stent is 6 to 8 weeks(1,2). Therefore, ureteral stent removal is a crucial step in patient management. In patients with stent related

complications, 64% had symptoms after stent removal (pain, hematuria, frequency, urgency, or fever), and among those with symptoms, 60% experienced pain or discomfort(1,5).

A variety of techniques are used in ureteral stent removal, starting from the use of a cystoscope, direct pulling on the thread in the DJ stent, using a catheter that is knotted at the end, and using a DJ stent that is specially designed to have a magnet at the tip(4).

Among these techniques, the use of a rigid cystoscope retrograde through the urethra under general anesthesia is the technique often used when removing ureteral stents(3).The end of the DJ stent is clamped using a special clamp that is inserted into the cystoscope and then pulled out. Even though this procedure only takes a short time, it still requires surgical personnel, anesthetic team, in-room care, sterilization of equipment, operating rooms, anesthesia equipment, and so on; all of which contribute to its high costs(4).To reduce these costs, DJ stent release can be switched from general anesthesia to using local anesthetic(6).

The local anesthetic used in this procedure is a lubricating jelly containing lidocaine that is inserted into the urethra(7). A flexible cystoscope with a smaller diameter is a better alternative to a rigid cystoscope. However, this tool is not available worldwide. A common complication of the DJ stent release in post-procedure patients is pain, which is believed to originate from the production of prostaglandins in the tissue due to trauma caused by the entry of rigid cystoscopy into the urethra(3,7).

The cyclooxygenase (COX) enzyme has the role of converting unsaturated arachidonic acid fats into prostaglandins. COX has two isozymes, namely COX-1 and COX-2, and 60% of their amino acid sequences are the same, but they have different gene encoding, location, and receptors for non-steroidal anti-inflammatory drugs (NSAIDs). COX-1 is found in almost all tissues that produce prostaglandins in small amounts for physiological functions. Meanwhile, COX-2 is produced in response to growth and inflammatory factors(8,9).

Trauma due to surgical processes triggers the production of the COX enzyme leading to the production of prostaglandins. Prostaglandins increase the sensitivity of nociceptors (pain receptors) in the periphery, causing hyperalgesia(8,9).This hyperalgesia also occurs in healthy tissue around the trauma

with a history of allergy to COX-2 inhibitors, and those with a history of bleeding disorders and gastro intestinal site(8,10).This process also increases the expression of c-Fos protein in sensory nerves in the spine by activating N-methyl-d-aspartate (NMDA) and neurokinin receptors, which further increase nociceptor sensitivity(8).

Pre-operative NSAID administration before tissue trauma can prevent hyperalgesia. NSAIDs inhibit COX action, thus inhibiting prostaglandin formation.

NSAIDs also inhibit pain impulses, increase pain thresholds, block NMDA receptors, and suppress local inflammatory processes(8).

Celecoxib is an NSAID that is selective against COX-2. Administration of this drug can reduce the inflammatory process due to DJ stent removal, thus reducing pain(8).With celecoxib's selective nature against COX-2, platelet aggregation is not inhibited, thereby reducing the risk of intra- and post-operative bleeding and side effects on the gastrointestinal (GI) tract(11-13). In addition, research from Sciarra and colleagues demonstrated the protective effect of COX- 2 inhibitors in preventing urethral stricture after surgery as a side effect of the inflammatory process(10,14-16).

The purpose of this study was to determine the differences in pain levels in patients undergoing DJ stent removal under local anesthesia through pre- operative administration of celecoxib.

Materials and methods

This placebo-controlled randomized controlled double blinded trial was conducted from December 2019 to February 2020 through consecutive sampling of patients undergoing DJ stent release under local anesthesia. Patients were divided into two groups: patients who were given oral celecoxib 3 hours before DJ stent release and patients who were given oral placebo.

The inclusion criteria were male patients aged 18 years and over undergoing DJ stent removal under local anesthesia. Patients who could not describe pain using

the visual analog scale (VAS), those with lower urinary tract symptoms (LUTS) before the procedure, those with prostatitis and/or urethral stricture at cystoscopy, those (GI) bleeding diseases were excluded.

Univariate analysis was performed to describe the characteristics and clinical status of the patients who are fitted with a DJ stent. This was followed by bivariate analysis to compare the characteristics of the two groups. Before the statistical test was carried out, the numerical data were assessed for normality using the Shapiro-Wilk normality test if the number was less than 50 and the Kolmogorov-Smirnov normality test if they were more than 50. The unpaired t test was used for normally distributed data, and Mann-Whitney U test was used as alternative for non-normally distributed data. A p value ≤0.05 was considered statistically significant. The data obtained were recorded in a special form and then processed through SPSS version 24.0 for Windows (IBM Corp., Armonk, NY, USA). This research has been approved by ethical committee of Hasan Sadikin Academic Medical Center in accordance with Indonesia's Ministry of Health.

Results

A total of 46 patients who underwent DJ stent removal with local anesthesia were analyzed descriptively (Table 1). Twenty-three (50%) patients were given celecoxib tablets 3 hours before the procedure, and the remaining 23 patients (50%) were given placebo. The durations of DJ stent removal procedure were 1.60 ± 0.62 and 1.87 ± 0.54 minutes in patients who were given celecoxib and placebo, respectively.

Data regarding side effects, including epigastric pain, GI bleeding, nausea, vomiting, diarrhea, headache, rash, and tinnitus/vertigo, were obtained from patients who were given celecoxib pre-operatively. Side effects were assessed until the next day after surgery. None of the 23 patients had epigastric pain, GI bleeding, vomiting, diarrhea, headache, rash, or tinnitus/vertigo, but one experienced nausea.

Discussion

In this study, we found that the use of celecoxib can reduce pain during DJ stent removal and during the first urination after the procedure.

Table 1. Subject's characteristics and results.

Variables	Without celecoxib (n = 23)	With celecoxib (n = 23)	P value
Age (years)			0.98[a]
Mean ± sd	50.26 ± 14.92	50.35 ± 15.61	
Median	49.00	48.00	
			0.58[b]
Duration of DJ stent installed (months)			
Mean ± sd	2.04 ± 0.75	2.22 ± 0.90	
Median	2.00	2.00	
			0.96[b]
Duration of DJ stent removal (minutes)			
Mean ± sd	1.60 ± 0.62	1.87 ± 0.54	
Median	2.00	2.00	
			0.04[b]*
Intra-operative vas			
Average ± sd	6.87 ± 1.51	3.74 ± 1.65	
Median	7	4	
			0.00[b]*
First void vas			
Average ± sd	5.04 ± 1.14	2.65 ± 1.02	
Median	5	3	
			0.53[b]
Post-operative day 1 vas			
Average ± sd	2.08± 0.79	1.34 ± 0.98	
Median	2	2	

[a]Unpaired t test. [b]Mann-Whitney U test. *Statistically significant.

Celecoxib works by suppressing the secretion of prostaglandins, which are the cause of inflammation and a source of pain from damage to the ureter and urethral tissues during the release of DJ stents. The results of this research showed that celecoxib can be a pain prophylaxis before releasing the DJ stent. It can significantly improve intra-and post- operative VAS scores. Recart et al.(17) reported that oral premedication with a high dose of celecoxib reduces post-operative pain. However, neither 200 mg of celecoxib was more effective than a placebo in facilitating the recovery process after outpatient surgery, as the evidenced in this study. This is similar to the findings of Karthikeyan et

al. (18) that the use of NSAIDs can reduce the post-operative pain due to DJ stent release. In other study, Mammoto et al. (19) states that administration of oral celecoxib immediately after surgical intervention, along with multimodal analgesia, could reduce VAS pain score.

Celecoxib can reduce the inflammatory process caused by DJ stent removal, thus reducing pain(8). With celecoxib's selective nature toward COX-2, platelet aggregation is not inhibited, thereby reducing the risk of intra- and post-operative bleeding and the side effects in the GI tract(11,20-22). Khan et al. (23) reported that celecoxib was associated with a reduced risk of GI bleeding compared with other NSAIDs. In another study, Shin et al. also reported that celecoxib was associated with decreased risk of GI bleeding compared with traditional NSAIDs (24). This is evidenced by the small number of patients experiencing side effects of this drug administration.

This study has some limitations. This study sample size was small. Thus, further studies with a larger patient scale are needed to determine the effect of COX-2 inhibitor drugs as an additional alternative therapy for surgical release of DJ stent under local anesthesia.

Conclusion

The use of celecoxib can significantly reduce pain during DJ stent release under local anesthesia and during the first urination after the procedure. Celecoxib has safe side effects, but aside from nausea, there were no other complaints from the patients in this study. This may be an option for aDJuvant therapy given prior to the DJ stent removal under local anesthesia.

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