THE EFFECT OF SILODOSIN AND SODIUM DICLOFENAC TO REDUCE PAIN AFTER DJ STENT REMOVAL IN SOETOMO HOSPITAL: DOUBLE-BLINDED RANDOMIZED-CONTROLLED TRIAL

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ABSTRACT

Objective: *To analyze, measure, compare, prove, and evaluate effectiveness of silodosin, diclofenac sodium, and the combination of both drugs in pain management after stent removal.* ***Materials & Methods:*** *Thirty-three patients were divided into three groups. Group I was given diclofenac Sodium 50 mg, group II was given silodosin 8 mg and group III was given the combination of diclofenac sodium 50 mg and silodosin 8 mg. The Wong Baker Pain Scale (WBPS) was assessed serially: two hours before the DJ stent removal, during DJ stent removal, and after the DJ stent removal (2 hours and 24 hours after). The data was analyzed by ANOVA and Kruskal-Wallis test.* ***Results:*** *In this study, 33 patients who underwent DJ stent removal were obtained. Wong Baker was presented in median (min-max) form. The WBPS study in each group did not differ statistically significant. Lowest WBPS during DJ stent removal was found in group III. Group III was better and statistically significant in reducing pain compared to group I and group II ($p<0.05$). WBPS two hours after removal in each group decreased and group III was better and statistically significant in reducing pain compared to group II, whereas group III compared to group I had an equivalent effectiveness. While the WBPS 24 hours after removal had the same value and did not differ significantly. No side effects or adverse events were found in the use of diclofenac sodium, silodosin, and their combinations.* ***Conclusion:*** *Single oral dose of diclofenac sodium combined with silodosin is effective to reduce pain after DJ stent removal.*

Keywords: *Silodosin, diclofenac sodium, pain, DJ stent removal, Wong Baker Pain Scale.*

ABSTRAK

Tujuan: *Untuk menganalisa, mengukur, membandingkan, membuktikan dan menilai efektifitas antara silodosin, natrium diklofenak, dan kombinasi antara silodosin dan natrium diklofenak terhadap nyeri paska pelepasan Double J (DJ) stent.* ***Bahan & Cara:*** *Sebanyak 33 pasien dibagi menjadi tiga kelompok. Kelompok I (natrium diklofenak 50 mg), kelompok II (silodosin 8 mg) dan kelompok III (kombinasi natrium diklofenak 50 mg dan silodosin 8 mg). Wong Baker Pain Scale (WBPS) dinilai secara serial, sebelum tindakan aff DJ stent (2 jam), durante lepas DJ stent dan setelah aff DJ stent (2 jam & 24 jam). Analisa data dengan uji ANOVA dan Kruskal-Wallis.* ***Hasil:****Wong Baker disajikan dalam bentuk median (min-max). WBPS pada tiap kelompok tidak berbeda signifikan secara statistik (WBPS) terendah durante op didapatkan pada kelompok III. Kelompok III lebih baik dan signifikan secara statistik dalam menurunkan nyeri dibandingkan dengan kelompok I dan kelompok II ($p<0.05$). WBPS 2 jam post op pada tiap kelompok menurun dan terlihat kelompok kombinasi lebih baik juga secara statistik dalam mengurangi nyeri dibandingkan dengan kelompok II, sedangkan kelompok kombinasi dan kelompok I memiliki efektifitas yang sama. WBPS 24 jam post op memiliki nilai yang sama dan tidak berbeda secara signifikan. Tidak ditemukan adanya efek samping dan adverse event pada penggunaan natrium diklofenak, silodosin dan kombinasinya.* ***Simpulan:*** *Penggunaan dosis tunggal obat oral kombinasi natrium diklofenak dan silodosin, efektif dalam mengurangi nyeri setelah pelepasan DJ stent.*

Kata kunci: *Silodosin, natrium diklofenak, nyeri, pelepasan DJ stent, skala nyeri wong baker.*

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INTRODUCTION

Ureteral stent recently being used in urological practice nowadays. The usage of ureteral stent in treating upper urinary tract obstruction has been proved beneficial.[1]The aim of (double-J) DJ Stent insertion is to treat ureteral obstruction that requires urinary drainage.[2]

Several studies have been done by researchers to reduce the pain and discomfort related to stent with medication like alpha blocker, anticholinergic, phosphodiesterase inhibitor, and stent material.[3,4] Most of the literature available are focused at morbidity related to stent when the stent was inside the ureter. But for Urologist, it is common if the patient experience renal colic after releasing the stent, therefore more analgesic are needed depend on pain severity. The results of the study by Tadros et al., suggested the efficacy of rofecoxib in reducing pain after stent release in the Randomized Control Trial (RCT) study, found that a large number of patients complained of severe pain after stent release in the group given placebo and no pain complaints in the group given NSAIDs.Rofecoxib, a selective cyclooxygenase (COX) inhibitor is effective in reducing pain after stent release, rofecoxib also acts as an analgesic, anti-inflammatory and relaxes smooth muscle.[5] The result study by Gangkak et al., found that use of single oral dose of diclofenac, combination and silodosin was very effective to relieve pain after stent removal.[6] Alpha-1 blocker can inhibit basal tone and peristaltic frequency, dilating ureteral lumen and reduce Lower Urinary Tract Symptoms (LUTS). Silodosin shows higher improvement in treating voiding symptom and retrograde ejaculation. It shows that silodosin is an effective and tolerable medication for voiding and storage symptom in patient. Sodium diclofenac is one of NSAID that has longer duration of action and faster onset of action. Urologist should also concern how to reduce pain after stent removal.

Gangkak et al., proved that silodosin or diclofenac is very effective in relieving pain after stent removal and the combination is not found to be more effective than the single agent. They recommend use of oral diclofenac or silodosin before stent removal to prevent pain after stent removal.[6]

Due to the absence of this study in Indonesia, this prompted us to conduct this study, that evaluates effectiveness of silodosin, sodium diclofenac and combination of both drugs in reducing pain after stent removal.

OBJECTIVE

The aim of this study was to analyze, measure, compare, prove, and evaluate effectiveness of silodosin, sodium diclofenac, and the combination of both drugs in pain management after stent removal.

MATERIAL & METHODS

An experimental double blind RCT study which was divided into three groups, which each group consumed oral drugs in single dose. Group I (diclofenac sodium 50 mg), group II (silodosin 8 mg) and group III (combination of diclofenac sodium 50 mg & silodosin 8 mg). The Wong Baker Pain Scale (WBPS) was assessed serially, before the DJ stent removal (2 hours), during DJ stent removal and after the DJ stent removal (2 hours and 24 hours). During March until July 2018, the research was carried out including 33 patients completed inclusion criteria and exclusion criteria, disposed undergo releasing DJ stent. The patient will undergo with anamnesis about the chief complain, physical examination, urologic status examination and laboratory examination (Figure 1).

Radiologic examination, and pain scale before - after releasing DJ stent on the patient before the treatment started. The inclusion criteria were: patients with history of indwelling DJ stent for 1 to 3 months that will be undergoing release DJ stents procedure, no abnormalities in kidney and heart function, able to fill out and sign a statement of willingness to take part in the research. The exclusion criteria were: patients who have a history of allergy to non-steroidal anti-inflammatory drugs (NSAIDs) and alpha-blockers, history of suffering from peptic ulcer, based on history in the form of pain or burning sensation in the epigastrium, nausea, vomiting, and/or bloating, patient having an alpha-blocker therapy or COX-2 inhibitors in the past 2 weeks, patient having an anticoagulant drug therapy in the past 2 weeks, patients diagnosed with coronary heart disease, chronic renal failure, residual stones and urinary tract infection (UTI), pregnancy, and patients with complications of using DJ stents and during stent removal, prolonged homeostasis function. The WBPS used to be the standard score.

The patient undergo operation releasing DJ stent with local anastesia which used Cathejell® (lidocaine jelly 2%) and clamped for 3-5 minutes, then undergo cystoscopy using telescope 0'.30' with sheath 20 Fr and pick out the DJ stent with forcep stent, which the operator did not know the information of grouping releasing stent. The WBPS rated serially: two hours before releasing DJ stent, during the release of DJ stent and after releasing DJ stent (2 hours and 24 hours after). The serial outpatient care after releasing DJ stent needed approval for all patients at IIU ward and finished

rated the WBPS. Randomized, the patients were divided into three groups. Group I underwent the treatment by 50 mg potassium diclofenac only, group II undergo treatment by 8 mg silodosin only and group III undergo a combination treatment by 50 mg potassium diclofenac and 8 mg silodosin. The patients were asked to take medicine 2 hours before the procedure. The prophylactic antibiotics were also taken by all patients according to urine culture. If the results of urine culture was sterile, patients were given empirical antibiotics, namely ciprofloxacin 500 mg orally before stent release according to our Department's protocol. Data collection was done by recording and evaluating pain for patients who had been released by DJ stent using WBPS which had been validated at IIU Soetomo Hospital. All prescription drugs used coding where patients, doctors, researchers, and pharmacists did not know the type of medication until the end of the study. The drug was packaged in capsule form by the pharmacist, so the type of drug was unknown even by the patients, doctors, researchers, and pharmacists.

The data was analyzed with parametric ANOVA test if the data was normally distributed and homogeneous data variants. If there were any differences between groups, it will be continued with Post hoc Tukey. However, if the data was not normally distributed and or the variants were not homogeneous then the data were analyzed using the Kruskal-Wallis non-parametric test. If there were any differences between groups, data will analyzed with the Mann-Whitney test. Data results were considered significant at $p<0.05$.

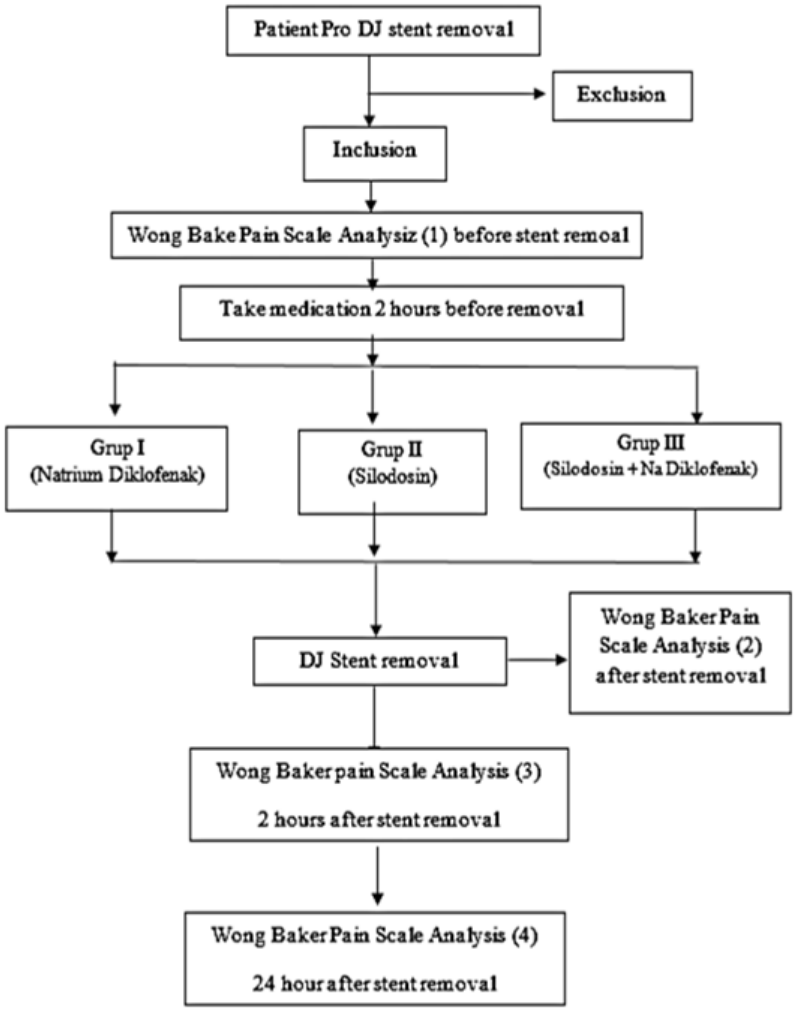

Figure 1. The flowchart showing the study design.

Table 1. Characteristics of the study sample.

Variable	Na Diclofenac (I)	Silodosin (II)	Combination (III)	p value
Age (Mean ± SD)	51.64 ± 14.87	47.64 ± 10.67	50.82 ± 10.43	0.720
Sex n (%)				0.399
Male	7 (63.6)	6 (54.5)	5 (45.5)	
Female	4 (36.4)	5 (45.5)	6 (54.5)	
Side n (%)				
Single	10 (90.9)	8 (72.7)	8 (72.7)	
Double (D/S)	1 (9.1)	3 (27.3)	3 (27.3)	
Insertion Method n (%)				
Open	0	2 (18.2)	2 (18.2)	
Endoscopic	11 (100)	9 (81.8)	9 (81.8)	
WBPS pre op n (%)				
Mild pain (1-3)	11 (100)	11 (100)	11 (100)	
Moderate pain (4-6)	0	0	0	
Severe pain (7-10)	0	0	0	
WBPS during op n (%)				
Mild pain (1-3)	7 (63.6)	3 (27.3)	10 (90.9)	
Moderate pain (4-6)	4 (36.4)	8 (72.7)	1 (9.1)	
Severe pain (7-10)	0	0	0	
WBPS post 2 hours op n (%)				
Mild pain (1-3)	11 (100)	11 (100)	11 (100)	
Moderate pain (4-6)	0	0	0	
Severe pain (7-10)	0	0	0	
WBPS post 24 hour op n (%)				
Mild pain (1-3)	11 (100)	11 (100)	11 (100)	
Moderate pain (4-6)	0	0	0	
Severe pain (7-10)	0	0	0	
WBPS pre-op				0.695
Median	1	1	1	
Range	(0-2)	(0-2)	(0-2)	
Mean	1.36	1.36	1.18	
WBPS during op				0.000
Median	3	4	2	
Range	(3-6)	(3-6)	(0-4)	
Mean	3.55	4.09	2.18	
				(I-II) 0.103
				(I-III) 0.002
				(II-III) 0.000
WBPS 2 hours post op				0.030
Median	2	2	1	
Range	(1-3)	(1-3)	(0-3)	
Mean	1.82	2.27	1.36	
				(I-II) 0.143
				(I-III) 0.178
				(II-III) 0.011
WBPS 24 hours post op				0.218
Median	0	1	0	
Range	(0-1)	(0-1)	(0-1)	
Mean	0.36	0.55	0.18	

Table 2. Comparison of WBPS before, during, 2 hours and 24 hours post op based on sex.

Variable (Sex)	WBPS before op	WBPS during op	WBPS 2 hours after op	WBPS 24 hours after op
Male				
Median	1,5	4	2	0
Range	(0-2)	(0-6)	(0-3)	(0-1)
Mean	1.33	3.72	1.72	0.33
Female				
Median	1	3	2	0
Range	(1-2)	(2-4)	(1-3)	(0-1)
Mean	1.27	2.73	1.93	0.40
p value	0.545	0.006	0.512	0.696

RESULTS

The 33 samples were included in this study (Table 1). All of them were randomized into 3 group. Group I consisted of 11 patients, out of 7 patients (63.6%) were male and 4 patients (36.4%) were female. Mean age of group I was 51.64 ± 14.87. The number of DJ stents that removed was 10 patients (90.9%) in one side and only one person (9.1%) in two side, with an endoscopic insertion method of 11 patients (100%). All patients only experienced mild pain based on WBPS in pre-removal phase. Out of 7 patients (63.6%) experienced mild pain and 4 patients (36.4%) experienced moderate pain during DJ Stent removal. All patients only experienced mild pain in 2 hours and 24 hours post DJ stent removal. Group II consisted of 11 patients, out of 6 patients (54.5%) were male and 5 patients were female (45.5%). Mean age of group II was 47.64 ± 10.67.

The number of DJ stents that removed was 10 patients (90.9%) in one side and only one person (9.1%) in two side, with an endoscopic insertion method of 9 patients (81.8%) and open insertion method of 2 patients (18.2%). All patients only experienced mild pain based on WBPS in pre-removal phase. Out of 3 patients (27.3%) experienced mild pain and 8 patients (72.7%) experienced moderate pain during DJ stent removal. All patients only experienced mild pain in 2 hours and 24 hours post DJ stent removal.

Group III was consisted of 11 patients, out of 5 patients (45.5%) were male and 6 patients (54.5%) were female. Mean age of group III was 50.82 ± 10.43. The number of DJ stents that removed was 8 patients (72.7%) in one side and 3 patients (27.3%) in two side, with an endoscopic insertion method of 9 patients (81.8%) and open insertion 2 patients (27.3%). All patients only experienced mild pain based on WBPS in pre-removal phase. Out of 10 patients (90.9%) experienced mild pain and only 1 patient (9.1%) experienced moderate pain during DJ stent removal. All patients only experienced mild pain in 2 hours and 24 hours post DJ stent removal (table 1).

Based on the ANOVA test (Table 1), there was no significant difference between each group of intervention with p value >0.05. This test showed that age was not a confounding variable in this study. Based on data analysis (Table 1) using the Kruskal Wallis test it can be seen that there was no significant difference between groups who received diclofenac sodium therapy, silodosin and a combination with p>0.05. This result showed that the length of installation of DJ Stent was not a confounding variable in this study.

Based on the ANOVA test (Table 1), there was no significant difference between each group of intervention with p value >0.05. This test showed that sex was not a confounding variable in this study. Based on data analysis (Table 1) using the Mann-Whitney test, it can be seen that there was no significant difference between the pain scale of men and women with p>0.05. This showed that male and female had the same pain scale at the time before surgery.WBPS before stent removal was similar in each group and did not statistically difference (p>0.05), with value 1 (0-2) in every group. Combination group had the lowest WBPS during stent removal with value 2 (0-4) compared with natrium diclofenac group 3 (3-6), and the silodosin group. Combination group had the best result and statistically difference compared to natrium

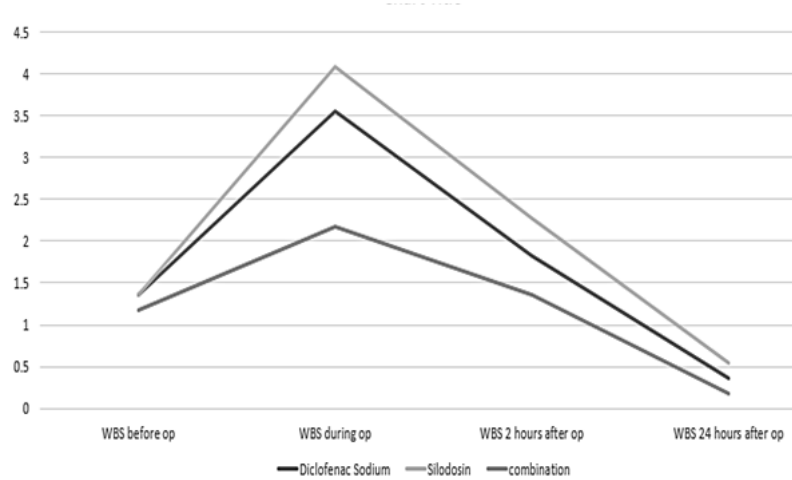

Figure 1. Mean values of WBPS before, during, & after stent removal.

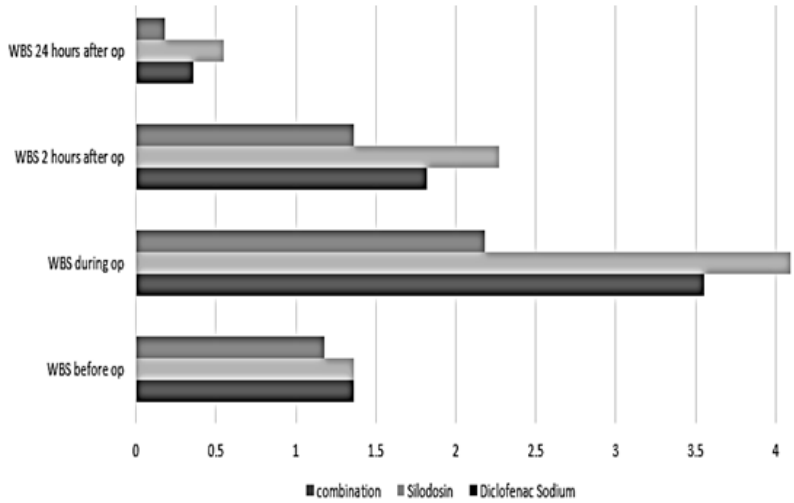

Figure 2. Changes in WBPS before, during and after stent removal.

diclofenac and silodosin group ($p<0.05$). After 2 hours of stent removal, it still showed that the combination group was better than silodosin group but had similar results compared to natrium diclofenac group. While after 24 hours of stent removal, all groups showed similar results in WBPS with value 0 (0-1), 0 (0-1) and 1 (0-1) ($p>0.05$) (Fig. 1 & 2).

There was significant difference between the pain scale in men and women (Fig. 3 and 4) with $p<0.05$ ($p=0.006$). This indicated that male had a significant higher pain scale compared to female during surgery. Meanwhile, male and female had the same pain scale in 2 hours and 24 hours after the stent removal (Table 2).

DISCUSSION

Ureteral stent in surgery has been used since early 19th century. Insertion of ureteral stent endoscopically was done firstly by Zimskind in 1967. Ureteral stents are available in various forms and materials and divided into polymer and metal mesh. Polymer was made from silicone and poliuretan. Metal mesh was made from metal alloys, nickel-cobalt, or stainless steel. Most frequent stent design that has been used is DJ stent. Stent with double coil has (double J stent or DJ stent) the ability to preserve its position because the double coil design at proximal and distal tip have a role as anchor in upper urinary tract (renal pelvis or superior

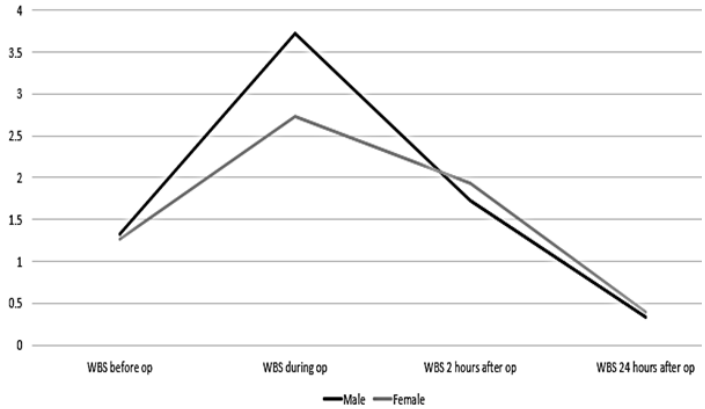

Figure 3. Mean value of WBPS before, during and after surgery based on sex.

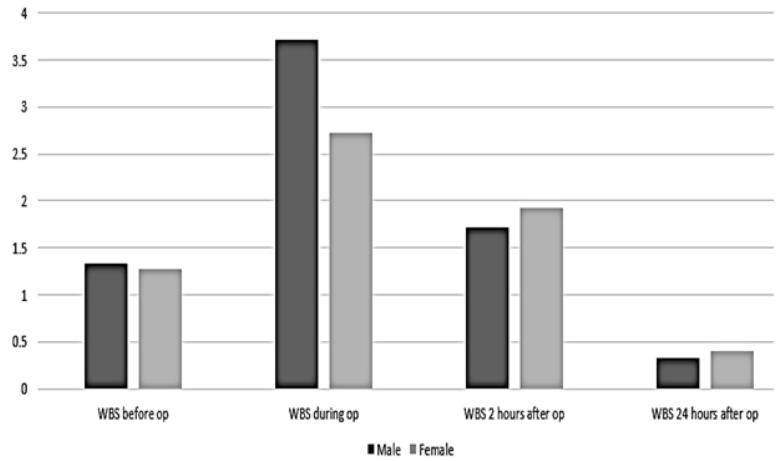

Figure 4. Value changes of WBPS before, during and after surgery based on sex.

calyces) and lower urinary tract (bladder). This mechanism prevents DJ stent migration to proximal and distal even there are urinary flow, patient movement, and ureteral peristaltic.[7]

There are two indications of DJ Stent insertion; urgent and relative. Urgent indication includes obstructive pyelonephritis and intolerable acute renal colic. Relative indication includes renal stone sized more than 2 cm that will face extracorporeal shockwave lithotripsy (ESWL) procedure, pregnancy, long impacted stone, history of urinary tract infection or sepsis, using passive DJ stent to dilate ureter and ureteral orifice, long operation duration (more than 45 minutes) and in patients that require additional procedure (i.e. second look ureteroscopy).[7]

The pain which arises during stent removal occurs due to the activation of nociceptors, friction between the stent and mucosa causing smooth muscle irritability, trigonal irritation and changes of pressure induction in the pelvic-calyceal system. Itoh et al., study showed that three types of a1-AR MRNA (a1a-, a1b-, dan a1d-) were found in human ureter, and the a1D was the most predominant.[8] Sasaki et al., recently reported that there was characterization contractile function in a1-AR subtype in human that a1-AR subtype play important role in human ureteric contraction.[9]

Several studies have been conducted to reduce pain and discomfort associated with stents using drugs such as alpha blockers, anticholinergics, phosphodiesterase inhibitor and stent materials.[3,4]

Alpha-1 receptors have been found to be widespread in the human ureter and bladder.[10] A decrease in ureteral contractions and trigonal irritation is a possible mechanism for relieving pain associated with stents with alpha blockers.

Silodosin was given with 8 mg dose per day. Silodosin half-life was 13-14 hours. Silodosin had selectivity 583 higher with α1A than α1B adrenoceptor, 56 times bigger in α1A than α1D adrenoceptor.[11]

The hypotension effect was rarely found in silodosin rather than tamsulosin, prazosin, and

terazosin.[12,13]

Silodosin dosage 4 mg two times daily has been proven by Asian countries and has been used widely. On the other hand, 8 mg once daily dosage has been developed not only to improve the comfort of consumption but also improve the optimal effect in 24 hours. United States Food and Drug Administration (FDA) and European Medicines Agency (EMA) have been proved this dosage. It said that this dosage did not have differences on efficacy and side effect.[14]

Study conducted by Tsai et al., showed that patients treated with silodosin were able to reduce pain associated with stents significantly, thereby reducing the use of analgesics. Also, patients who were treated with silodosin, not only experienced pain reduced during urination, but also experienced lower back pain, perhaps because of the improved of bladder neck relaxation.[15]

Systematic review and meta-analysis studies conducted by Zhang et al., also concluded that α1 blockers were useful in reducing pain, urinary symptoms, and quality of life of the patients that have stents in their urinary tract.[16]

Ureteral colic occurs due to an increase in intra-ureteric pressure proximal to the obstruction site. a-AR antagonists block C fiber which is responsible for mediating colic ureters.[17] In the study of Jayant K et al., also showed significantly fewer pain episodes in patients that take the combination drug (tadalafil and tamsulosin) compared to tamsulosin alone. This may be due to different actions between those drugs on the ureter. tamsulosin blocking C fibers and tadalafil may reduce the frequency and amplitude of ureteric peristalsis contractions that resulted the decrease of intraureteric pressure, thereby reducing pain episodes.[18]Type of alpha adrenergic receptors found in the prostate, bladder muscle, pelvicalyceal renal system and ureteral is alpha-1 receptors (α1).[19] The α1 receptor has three subtypes, namely α1A, α1B, and α1D. In pelvicalyceal systems, there are more α1A and α1D receptors than α1B receptors. Whereas in the ureter, α1D > α1A > α1B.[20,21]Alpha-1 blockers can inhibit basal tone and peristaltic frequency, the ureteral lumen become dilated. Therefore, it can improve LUTS symptoms.

Inhibition of α1-AR antagonist in the ureter causes decreasing in ureteral peristaltic that effect on decreasing in ureteral pressure, so it can reduce pain, therefore the use of analgesic can be minimal.[22-24]

Management of transurethral postoperative pain: 4-6 hours postoperative, the patients can be given oral medications such as mild analgesics i.e. NSAIDs or paracetamol with or without stronger analgesics like codein or opioids can be given.[25] In a study conducted by Tadros et al., there was a reduction in pain immediately when the sample was given the drug refacoxib (NSAID) before the release of the stent. This suggests that the main mechanism of NSAID is to reduce pain by reducing the inflammatory process, ureteric contractility, and ureteral spasm.[26]

Several studies have shown that NSAIDs can reduce renal pain by inhibiting the synthesis of renal prostaglandins, which decreases renal blood flow and consequently decreases the pressure on the renal pelvis and ureters. Chaignat et al., investigated that in the human urothelium, there were the presence of COX-1 receptors and COX-2 receptors in the human urothelium and COX-2 inhibitors have also been shown to reduce contractility in human and pig ureters in vitro and in vivo.[10] Nakada et al., showed that selective COX-2 inhibitors reduced ureteric contractility as effective as indomethacin (COX without selective inhibitors) in both ureteral and human ureteral segments in vitro.[27]

Goto Gangkak et al., the study explained that the age of patients ranged from 19 to 55 years and all groups were comparable for age (p=0.17).[5] In our study, explained that the age of patients ranged from 21 to 72 years and all groups were comparable for age was no statistically significant difference (p=0.720).

Goto Gangkak et al., study explained the number of male and female patients were not equally distributed in all the four groups, but there was no statistically significant difference (p=0.38).[5] In our study, number of male and female patients were not equally distributed in all three groups, i.e.: group I consisted of 11 patients, out of 7 patients (63.6%) were male, and 4 patients (36.4%) were female, group II consisted of 11 patients, out of 6 patients (54.5%) were male and 5 patients were female (45.5%), group III consisted of 11 patients, out of 5 patients (45.5%) were male and 6 patients (54.5%) were female. All of them did not show statistically significant difference (p=0.399).

Goto Gangkak et al., study explained that oral diclofenac was significantly able to reduce pain after stent release compared to placebo. There was a significant reduction in pain in the silodosin group compared with placebo. The average VAS score decreased significantly in diclofenac (2.9), silodosin

(3.08) and combination groups (2.85) when compared with placebo (4.20) ($p<0.001$). There was no difference in pain reduction between silodosin and diclofenac groups ($p=0.48$). There was a higher pain reduction in the sample taking the combination drug diclofenac and silodosin but not statistically significant ($p=0.9$, 0.40). The use of diclofenac and silodosin and their combinations do not produce significant side effects.[5]

Pain score in each group did not differ statistically significant, where in the combination group (silodosine and diclofenac sodium), diclofenac sodium, and silodosine with a value of 1 (0-2), 1 (0-2), and 1 (0-2) ($p>0.05$). With the lowest WBPS durante op was found in the combination group with a value of 2 (0-4), then the diclofenac sodium group 3 (3-6), and the highest in the silodosin group). The combination group was better and statistically significant in reducing pain compared to the diclofenac sodium group and silodosin group ($p<0.05$). WBPS 2 hours post op in each group was decreased, and the combination group statistically better in reducing pain compared to the silodosin group, with a value of 1 (0-3) and 2 (1-3) ($p<0.05$), while the combination group compared to the diclofenac sodium group had an equivalent effectiveness of 1 (0-3) and 2 (1-3) ($p>0.05$). While the WBPS 24 hours post op had the same value and did not differ significantly where the combination group value, diclofenac sodium, and silodosin were 0 (0-1), 0 (0-1) and 1 (0-1) ($p>0.05$).

The difference between the results of our study and Goto's gangkak et al., study lies in the assessment of pain that we did serially, while Goto's gangkak et al., study only evaluate pain 24 hours after stent removal, they did not evaluate pain scores during stent removal and 2 hours after stent removal. Because of that, we can see the effectivity of combination therapy was superior than silodosin and diclofenac sodium in reducing pain during stent removal and 2 hours after stent removal.

In this study, we found that descriptively male had a higher pain scale compared to female. Based on data analysis (Table 2) using the Mann-Whitney test it can be seen that there was a significant difference of the pain scale between men and women with $p<0.05$ ($p=0.006$). This indicates that male had a significantly higher pain scale compared to female at the time of the action. This may be due to the longer of male urethra anatomy than a woman, causing friction between the instrument and the urethra which resulted pain.

Orthostatic hypotension was reported in 1.5% (silodosin) and 2.6% (placebo) of patients.[13] Chapple examined silodosin did not affect heart rhythm and none of the orthostatic episodes of post-stimulation hypotension. According to the European Medicines Agency's Products for Human Use administration of silodosin along with other antihypertensive drugs did not increase the risk of orthostatic hypotension.[28] Undesirable side effects of diclofenac sodium can occur in about 20% of patients including gastrointestinal distress, hidden gastrointestinal bleeding, and onset of gastric ulceration.[29] In our study, no side effects or adverse events were found.

Relatively, small samples limited this research from being an evidence based for pain management after DJ stent removal. Further studies are needed with a larger sample size to obtain better data.

CONCLUSION

A single dose oral combination was effective than silodosin and diclofenac sodium in reducing pain during DJ stent removal and 2 hours after DJ stent removal. We recommend the use of a single dose of oral combination from diclofenac sodium and silodosin are taken 2 hours before removal of the stent to prevent pain during and after the release of the stent. This study is expected to be an alternative in pain management after the removal of stents without any number of side effects.

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