COMPARING THE EFFECTIVITY OF INTRAVENOUS ANALGETIC TRAMADOL AND INTRAVENOUS PARACETAMOL FOR ACUTE POST-PERCUTANEOUS NEPHROLITHOTOMY

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ABSTRACT

There are many management strategies and interventions both preoperative, intraoperative, and postoperative that can be carried out in dealing with postoperative pain. Guidelines for pain management have been prepared by the American Pain Society (APS) with recommendations from the American Society of Anesthesiologists (ASA) where there are many recommendations in postoperative pain management in adults or children by promoting the provision of preoperative education, the use of various modalities both pharmacological and non-pharmacological to the establishment of pain management procedures or policies in each institution. For this reason, the author was interested in examining the comparison of the effectiveness of analgesia between intravenous tramadol and intravenous Paracetamol in minimally invasive Percutaneous Nephrolithotomy (PCNL) postoperative patients at RSUP Dr. M. Djamil Padang. The research was a prospective study with a single-blind randomised controlled trial design. The data used were sourced from clinical trials conducted on post-PCNL patients divided into two subgroups given intravenous tramadol analgetics and others given Paracetamol tablets. In this study, the incidence of Nephrolithiasis was obtained, which was dominated by the male sex, compared to women and suffered a lot at the age of 41-60 years. There was a significant difference in VAS effectiveness between the use of Paracetamol IV and Tramadol IV in post-PCNL patients. The use of Paracetamol may be considered to replace tramadol in the disappearance of acute pain after PCNL postoperative patients in those patients who are allergic to tramadol.

INTRODUCTION

Postoperative pain management is the main task of a clinician (Brennan et al., 2007). Many patients experience a fairly high level of pain postoperatively. In a 2016 cross-sectional study, it was found that in 15,000 patients undergoing surgery in the UK, 11% reported experiencing severe pain and 37% reported the incidence of moderate pain in the first 24 hours postoperatively (Walker et al., 2016). An annual report from the Perioperative Quality Improvement Programme (PQIP) for 2017-2018, which included data from 79 hospitals in the United Kingdom, found that 48% reported moderate pain and 19% experienced severe pain at the site of surgery within 24 hours postoperatively (NIAA, 2018). Similar data were also found in PQIP’s annual 2018-2019 report (NIAA, 2019). A cohort study in Germany found 47.2% of the study's 50,523 patients experienced severe pain (pain score of at least 8) in surgical wounds in the first 24 hours. The variation in scores found depends on the type of operation performed (Gerbershagen et al., 2013). Research evidence suggests that less than half of cases have adequate pain management (Apfelbaum et al., 2003). In
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

fact, uncontrolled postoperative pain management can influence the tendency to chronic or persistent pain (Glare et al., 2019; Kehlet et al., 2006) and affect the quality of life, the process of restoring organ function and the increased risk of postoperative complications (Kehlet et al., 2006).

There are many management strategies and interventions both preoperative, intraoperative, and postoperative that can be carried out in dealing with postoperative pain. Guidelines for pain management have been prepared by the American Pain Society (APS) with recommendations from the American Society of Anesthesiologists (ASA) where there are many recommendations in postoperative pain management in adults or children by promoting the provision of preoperative education, the use of various modalities both pharmacological and non-pharmacological to the establishment of pain management procedures or policies in each institution. The pharmacological modalities often referred to in the management guidelines are the use of opioids, Paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) in postoperative pain management adjusted to the pathophysiology of tissue damage during surgery and the level of pain felt by patients (Chou et al., 2016).

There are many medications of analgesia that are commonly used in treating postoperative pain. Opioids are the most commonly chosen class of painkillers for moderate to severe postoperative pain, but their long-term use is associated with side effects that can prolong the duration of treatment (White, 2008). Tramadol is a synthetic drug of the aminocyclohexanol group that acts centrally with weak agonist opioid properties (Ahmad et al., 2010). Tramadol was chosen because of its less severe side effects compared to other opioid groups, namely the rare incidence of respiratory depression, as well as a lower incidence of dizziness and drowsiness (Scott & Perry, 2000). Meanwhile, Paracetamol is the drug of choice when NSAIDs have a bad effect on patients. Paracetamol is known to have analgesia and anti-pyretic properties for both adults and children with very rare incidence of side effects, namely <1: 10,000 cases (Duggan & Scott, 2009).

A study by Kaur (2021) with a trial on 100 postoperative patients given intravenous tramadol and Paracetamol intravenously, it was found that the group of patients who got Paracetamol had a higher Visual Analogue Scale (VAS) value than patients in the tramadol group at 1 hour, 4 hours, 8 hours, 12 hours and 24 hours postoperatively. This suggests that patients receiving Paracetamol intravenously have not received adequate pain management. Another literature concludes that the effectiveness of these two drugs has the same degree as more side effects arising in those patients given tramadol. The study by Kela et al, which compared pain reduction in cardiothoracic postoperative patients found that the effectiveness of tramadol and Paracetamol was the same (Akcali et al., 2010; Kela et al., 2011). However, there are several studies that state that intravenous administration of Paracetamol is more effective than tramadol as in studies conducted by Mohammad et al and Sinatra et al in postoperative orthopedic patients. The study also found that morphine consumption was significantly reduced in the first 24 hours in patients given Paracetamol intravenously. Similar results were also shown in the Singh B et al study in elective postoperative patients (Shahid et al., 2015; Sinatra et al., 2005; Singh et al., 2015).

One minimally invasive method of dealing with urolithiasis is percutaneous nephrolithotomy (PCNL). International guidelines recommend PCNL as a first-line therapy in
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

cases of kidney stones larger than 20 mm in size. At the beginning of its development, the procedure resulted in a serious problem due to bleeding, infection and other complications. But now, the effectiveness and safety of PCNL has grown considerably even though it still has some risk of complications. PCNL surgery is mainly performed in general anesthesia or intrathecal anesthesia. However, there have been some reports of the implementation of PCNL in infiltration local anesthesia (PCNL-LIA). Local anesthesia is safe and easy to perform and does not affect the physiological status and behavior of the patient as much as general anesthesia so that after the procedure is performed the patient can recover quickly and consciously during the procedure. The postoperative pain experienced by PCNL patients is mostly with a VAS value of <7 (Wang et al., 2019).

In the pain management guidelines compiled by APS with recommendations from ASA, there is one recommendation point that states that the administration of NSID analgesia is preferred over Opioid because of the minimal side effects of NSID. This is due to many studies that have found no superiority of intravenous administration of opioids over intravenous NSID in postoperative patients (Chou et al., 2016). For this reason, the author is interested in examining the comparison of the effectiveness of analgesia between intravenous tramadol and intravenous Paracetamol in minimally invasive Percutaneous Nephrolithotomy (PCNL) postoperative patients at RSUP Dr. M. Djamil Padang. This research can be used as a basis for management for evaluation, input and consideration in understanding the effectiveness of intravenous tramadol and Paracetamol intravenous analgesics in patients undergoing PCNL procedures at RSUP Dr. M. Djamil Padang.

METHOD

This research is a prospective study with a single-blind randomised controlled trial design. The data used were sourced from clinical trials conducted on post-PCNL patients divided into two subgroups given intravenous tramadol analgetics and others given Paracetamol tablets. The study was conducted in November-December 2022. The research was conducted at RSUP Dr. M. Djamil Padang. The study used primary data, where data collection was carried out through VAS examination in post-PCNL patients after being given intravenous Paracetamol analgesics or intravenous tramadol at Dr. M. Djamil Padang Hospital, then the data was tidied up.

The study population was all patients after undergoing the PCNL procedure at RSUP Dr. M. Djamil Padang in the study time span. The sampling technique of this study was Slovin modification and obtained a minimum number of samples of 36 samples. The inclusion criteria for determining the subject of the study are patients after the PCNL procedure is carried out for the first time. Meanwhile, the exclusion criteria are post-PCNL patients with diabetes mellitus, post-PCNL patients with preoperative infections, and post-PCNL patients with a history of surgery on the abdomen before.
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

RESULT AND DISCUSSION

Patient Characteristics

Table 1. Characteristics of PCNL Postoperative Patients with the use of Analgesics at RSUP M. Djamil Padang (N: 36)

<table>
<thead>
<tr>
<th>Sociodemographic characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36-45</td>
<td>2</td>
<td>5.5</td>
</tr>
<tr>
<td>46-55</td>
<td>11</td>
<td>30.5</td>
</tr>
<tr>
<td>56-65</td>
<td>18</td>
<td>50</td>
</tr>
<tr>
<td>66-75</td>
<td>3</td>
<td>8.3</td>
</tr>
<tr>
<td>76-85</td>
<td>2</td>
<td>5.5</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>19</td>
<td>52.8</td>
</tr>
<tr>
<td>Woman</td>
<td>17</td>
<td>47.2</td>
</tr>
</tbody>
</table>

In Table 1, it can be seen that patients with kidney stones with the age of 36-45 years as many as 2 people (5.5%), 46-55 years as many as 11 people (30.5%), 56-65 people as many as 18 people (50%), aged 66-75 years as many as 3 people (8.3%) and aged 76-85 years as many as 2 people (5.5%). From data on the male sex as many as 19 people (52.8%) and the female sex 17 people (47.2%). Meanwhile, 18 people (50%) received Paracetamol analgesics, and 18 patients (50%).

Table 2. Differences in VAS in Analgesic Administration of Paracetamol and Tramadol

<table>
<thead>
<tr>
<th>Analgesics</th>
<th>'LL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol IV</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Tramadol IV</td>
<td>6</td>
<td>12</td>
</tr>
</tbody>
</table>

After obtaining analgesics patients with VAS 2 as many as 16 people (44.4%) and people with VAS 3 as many as 20 people (55.6%). It was also found that patients who used Tramadol analgesics after PCNL surgery with VAS 2 were 6 people, and with VAS 3 as many as 12 people. Meanwhile, those who used Paracetamol analgetics with VAS 2 as many as 10 people and with VAS 3 as many as 8 people, thus people with VAS 2 as many as 16 people (44.4%) and people with VAS 3 as many as 20 people (55.5%).

Average VAS Score of Patients with Paracetamol and Tramadol Analgesic Use in Post PCNL Patients

Table 3. Average VAS Score of Patients with Post PCNL Analgesic Use

<table>
<thead>
<tr>
<th>Analgesics</th>
<th>N</th>
<th>Mean±SD</th>
<th>*p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>18</td>
<td>2.67±0.48</td>
<td>0.186</td>
</tr>
</tbody>
</table>

2659 | Indonesian Journal of Multidisciplinary Science, 2(6), March, 2023
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

<table>
<thead>
<tr>
<th>Paracetamol</th>
<th>18</th>
<th>2.44±0.51</th>
</tr>
</thead>
</table>

*Mann-Whitney U test*

Based on table 3, it was found that patients who used intravenous tramadol analgesic therapy obtained an average VAS score of 2.67 with a standard deviation of 0.48 while patients with intravenous paracetamol analgetics obtained an average VAS score of 2.44 with a standard deviation of 0.51. After a normality test using Shapiro Wilk test, it showed that the data was not normally distributed, namely p<0.05. Then the data transformation was carried out and the normality test was carried out again, the distribution of data still remained abnormal. Therefore, the hypothesis test used was the Mann-Whitney U test to see the difference in VAS scores in post PCNL patients who received tramadol analgesic therapy with paracetamol. The results of the analysis showed no significant difference in the average VAS score of post-PCNL patients with tramadol analgesic therapy with patients who received Paracetamol analgesic therapy, with a p-value of >0.05, namely 0.186.

Patient Characteristics

This study used a sample of 36 people and was divided into two groups, 18 samples each. In the group given Paracetamol intravenously as much as 1 gram and the other group was given Tramadol intravenously as much as 100 mg. Analgesics are given to reduce postoperative pain in patients after undergoing elective surgery with general anesthesia. Based on the data above, it was also found that the most patients who suffered from kidney stones occurred at the age of 56-66 years as many as 18 people from the entire total sample. The same thing was also obtained in a study conducted by Abdurrisid LMK et al. where in the study the number of the largest samples was dominated by patients aged 41-60 years as many as 39 people in 2015, namely 71.8% and 50% in 2016 (Abdurrosid et al., 2016).

Age and gender are both associated with risk factors for kidney stones, the incidence of kidney stones in children is smaller than in adults and most of the incidence is due to genetic factors. The risk of kidney stone incidence increases with age and sex, especially in men aged 40-50 years and women aged 20-40 years (Dwyer et al., 2012; Edvardsson et al., 2013; Wagner, 2021). Several studies have revealed that kidney stones are often suffered by working-age adults and decrease in their incidence in the elderly (Croppi et al., 2012). The increase in the incidence of kidney stones in middle age is related to diet, occupation and lifestyle (Sorokin et al., 2017).

There are differences in the composition of stones at different ages. Calcium Oxalate Dihydrate (COD) stones are the most commonly found stones at a young age. In Europe, the composition of stones differs based on age and sex improvement where COD is found 5 times more often found at a young age than old age. At the age between 40 years and 70 years calcium oxalate monohydrate (COM) stones are the type of stone that most often causes kidney stone disease. Age over 10 years 40% of kidney stone disease is dominated by calcium phosphate stones which continue to decline at the age of 20-29 years (Knoll et al., 2011).
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

This is in accordance with the statement of Pearle and Lotan (2012) that the increase in the incidence of urinary tract stones less frequently under the age of 20 years increases at 40 years to 60 years of life. Research conducted by Christeven (2015) at RSUP H. Adam Malik Medan from 2013 to 2015, that the age of urinary tract stone patients is mostly more than 40 years and increases at the age of 60 years.

In the sex data, it was found that the patients with the highest number of kidney stones in men were 19 people compared to women. The same thing was also obtained in the study conducted by Pearle et al. obtained distribution by sex, it was found that in 2015 the percentage of patients of the male sex (59%) was higher than the percentage of patients of the female sex (41%). Likewise, 2016 showed a higher percentage of patients of the male sex (54%) than women (46%). According to Pearle and Lotan (2012) the incidence of men suffering from urinary tract stones can reach two to three times more compared to women. Another study by Warli (2013) in one of the hospitals in Medan, there were 114 male patients and 81 female patients. In western countries, the percentage of urinary tract stone cases in men is around 8-19% and women 3-5% especially in kidney stones is also more frequent in men, while in developing countries the ratio of male and female incidence is 2.5:1 (Trinchieri, 2008).

In the administration of analgetics to the sample in equal dividing, 18 patients received Paracetamol IV analgesics and 18 other patients received Tramadol IV analgesics. Based on VAS data, 12 people with VAS 3 received Tramadol IV and 10 patients with Paracetamol IV with VAS 2 were obtained. All research samples underwent planned surgery at Dr. M. Djamil Hospital which was performed on a type of surgery with moderate postoperative pain. From the type of surgery that is not uniform but with a uniformed level of moderate postoperative pain expectation, it is expected that patients with almost the same stimulation or pain level will be obtained, so that the administration of Tramadol IV and Paracetamol IV as preemptive analgesia can be assessed in general by assessing postoperative pain using the VAS pain scale (Visual Analogue Scale).

Effectiveness of Postoperative Acute Pain Reduction from the Use of Tramadol IV and Paracetamol IV

Patients who performed surgery experienced acute pain after surgery of about 80%, pain experienced by patients 86% in the category of moderate and severe pain (Christopher & Srinivasa, 2011). The analgetic used in the inpatient surgical ward of RSUP Dr. M. Djamil Padang is tramadol injection 100mg/12 hours. Tramadol is a synthetic codeine analogue that is a weak π opioid receptor agonist. Based on literature tramadol is used for moderate to severe pain (Krueger & Martindale, 2007).

The results of the study on the effectiveness of Paracetamol for postoperative pain assessed from the Visual Analog Scale showed that the group of patients who were given Paracetamol intravenously after PCNL surgery obtained a lower VAS value compared to intravenous tramadol use, but the difference did not show significant numbers in statistical tests. This can be seen in the comparison chart of the Visual Analog Scale score listed in the previous chapter. This can also be
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

due to limited number of samples, the administration of paracetamol doses given or the subjective assessment of the Visual Analog Scale.

The same results were also obtained in a study conducted by Ulfa and Jatmiko (2014) where the results of the research he conducted found that the effectiveness of Paracetamol for postoperative pain was assessed from the Visual Analog Scale showing that the group of patients who were given Paracetamol intravenously perisurgery and continued up to 24 hours postoperatively obtained lower pain than the control group but the difference did not show significant numbers in statistical tests that viewed through VAS scores. Paracetamol can reduce postoperative pain well with much milder side effects than nonsteroidal anti-inflammatory drugs (NSAIDs) (Toms et al., 2012). Paracetamol IV 1000 mg and IV Tramadol 50 mg are both safe and effective in reducing postoperative pain, with Tramadol having an advantage over Paracetamol, in terms of average pain scores and lower need for additional analgesics, but with a higher incidence of nausea, vomiting, and drowsiness (Kaur, 2021).

The results of this study are different from the previous study conducted by hyllested m which compared two treatment groups, namely the administration of NSAIDs with a combination of giving Paracetamol and NSAIDs whose research results stated that the addition of Paracetamol was effective for reducing postoperative pain with meaningful results (Hyllested et al., 2002). There was a significant decrease in VAS scores after an initial bolus dose of tramadol IV of 2 mg/kg, however, Most patients with severe pain intensity may require an additional dose of tramadol. Intravenous tramadol is a safe and effective analgesia in trauma patients with a tendency to severe pain provided that the initial dosois and intermittent dose are administered appropriately (Ahmad et al., 2010).

The results of the same study were also obtained from the research of Handayani et al. (2019) where obtained from 13 patients who used injectable tramadol, 1 patient with moderate pain, and 12 patients with severe pain. Of the 13 patients who had severe pain after getting the injection of tramadol turned into moderate pain, 5 patients and experienced a decrease in pain to mild by 8 patients. Intravenous use of tramadol 50 mg is safe and well tolerated in postoperative pain management. Tramadol intravenously alone or administered together with non-opioid drugs (when required) as a multimodal combination analgesia approach results in higher patient satisfaction as a pain reliever (Minkowitz et al., 2020).

Comparison of the Effectiveness of Acute Pain Reduction Post-PCNL Procedure in Patients Given Tramadol IV and Paracetamol IV

Pain is a subjective experience that is described as an unpleasant sensory and emotional experience, however, it can be assessed using VAS (Visual Analog Scale), which is a tool to measure the intensity of pain that is considered the most sensitive and accurate in assessing the perception of pain experienced by patients (Price, 2006).

Based on the results of the study (table 2) a comparison of the effectiveness of acute pain reduction after PCNL procedures in patients given Tramadol IV and Paracetamol IV obtained a p value of > 0.05 so that it can be concluded that there is no significant difference between the two
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

uses of analgesics. This is in accordance with research conducted by Muhammad et al. (2013) where it was found that there was no significant difference from the VAS results between the use of oral Paracetamol and the administration of oral tramadol after TURP surgery at the 3rd hour, 5th hour and 7th hour after spinal anesthesia. The same results were also obtained by Lee et al. (2010) also reported that the administration of Paracetamol 1 g IV has analgesic properties similar to ketorolac 30 mg IV in patients after undergoing thyroidectomy surgery so that Paracetamol is used as an alternative to replace ketorolac for mild to moderate pain in conditions where NSAIDs cannot be used (Muhammad et al., 2013). The findings of this study are consistent with studies conducted by Gulen B et al and various other studies comparing the efficacy of Paracetamol with tramadol in various pain patterns (Gulen et al., 2016; Kaur et al., 2015; Shahid et al., 2015).

The same results were also obtained in a study conducted by Dendi Karmena et al. 2015 obtained results that in the tramadol group of Paracetamol 1 gram intravenously and tramadol ketorolak 30 mg i.v where there was no statistically meaningful difference in VAS values at 6 measurement times. In the 30th minute and 24th hour NRS values were found to be meaningful at 2 measurement times, but they were still in the same range and did not affect the use of additional analgesics (Kara et al., 2010).

The results of this study are different from those reported by Kara et al. (2010), comparing the effectiveness of using non-steroidal anti-inflation drugs (NSAIDs) injecting diclofenac with Paracetamol drip. They got the average VAS value in both groups was > 3 cm in the first 30 minutes to 4 hours post-TURP. However, the next 6 hours there was a significant increase in Paracetamol compared to diclofenac (Lee et al., 2010). In this study, it can also be concluded that there is no significant difference between intravenous use of Paracetamol and intravenous use of tramadol to treat post-PCNL pain assessed from the patient's VAS, so that Paracetamol can be used for patients who are contraindicated using tramadol. The same research was also obtained by Shrestha R et al. (2020) where the results showed that there was no significant difference between the use of injectable Paracetamol and injection tramadol in acute pancreatitis patients, so the study concluded that intravenous Paracetamol could be used as an effective alternative to replace tramadol in pain management in acute pancreatitis patients. Gulen et al. (2016) compared the efficacy of the two drugs in the management of acute pancreatitis pain and found that the two were equivalent (Langley et al., 2010).

CONCLUSION

In this study, the incidence of Nephrolithiasis was obtained, which was dominated by the male sex, compared to women and suffered a lot at the age of 41-60 years. There was a significant difference in VAS effectiveness between the use of Paracetamol IV and Tramadol IV in post-PCNL patients. The use of Paracetamol may be considered to replace tramadol in the disappearance of acute pain after PCNL postoperative patients in those patients who are allergic to tramadol.

In this study, the effects of giving Paracetamol IV and Tramadol IV analgetics were not reviewed for the side effects that appeared, so it is necessary to conduct the same research to
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy

examine the side effects resulting from the administration of the two analgesics. It is necessary to conduct further research on the analgesic effects of intravenous use of Paracetamol and Tramadol in treating acute post-PCNL pain in single puncture and double puncture can be used as material for further research in assessing the effects of oral analgetic paracetamol and oral tramadol.

REFERENCE
Comparing the Effectivity of Intravenous Analgetic Tramadol and Intravenous Paracetamol for Acute Post-Percutaneous Nephrolithotomy


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