Utilization of Ketorolac for Pain Control During Nephrostomy and Nephroureteral Stent Exchange: A Quality Improvement Study

Wendy Rash, MSN, AGPCNP-C, Doctoral Candidate[1,2]

Michael Miller, Jr, MD[2]

Diane Caruso, DNP, FNP-BC[2]

Elaine Harwood, DNP, FNP-BC[2]

Ann Jessup, PhD, FNP-BC[2]

[1]School of Nursing, Lenoir Rhyne University

[2]Interventional Radiology, Wake Forest Baptist Health

Author Note

Wendy Rash, MSN, AGPCNP-C https://orcid.org/0000-002-2646-5178

Michael J Miller, MD

Diane Caruso, DNP, FNP-BC https://orcid.org/0000-0001-5645-8537

Ann Jessup, PhD, FNP-BC https://orcid.org/0000-0002-9792-6576

Abstract

Patients with nephrostomy/nephroureteral stents undergo exchange procedures every six to eight weeks to maintain patency. This procedure is commonly performed with moderate sedation using opioid medications. These medications are not without risks relating to maintenance of airway and rate of breathing. A quality improvement study was conducted to evaluate the effectiveness of adding ketorolac to a reduced amount of opioid administration during this procedure to examine pain scores. Pain scores were measured by the Visual Analogue Scale during the pre procedure, during procedure and post procedure periods.

Ketorolac has shown to be effective in other areas of pain management but there was a gap in research related to this procedure. Six of the ten patients required half of the previous total of opioids. Four of the ten patients received the full dose of opioids. There were no significant differences between these groups in pre procedure pain score or the post procedure pain score. The patients receiving half the dose of opioids were able to achieve similar pain control compared to those patients receiving the full dose.

Keywords: Opioid, pain, nephrostomy, nephroureteral, sedation, ketorolac

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Death rates from opioid use have increased dramatically since the 1990s due to increased prescription medication misuse (National Institute on Drug Abuse [NIDAa], 2020). The use of prescription opioids has increased over the last two decades (Dart et al., 2015), and overdose deaths were more than four times higher in 2018 than they were in 1999 (Centers for Disease Control and Prevention [CDC], 2020). Opioid dependence can be influenced by family history and prior substance use, including cigarettes and alcohol (NIDAb, 2020). Dependence or abuse may begin from short-term opioid use (Mayo Clinic, 2018). Early and short-term opioid prescribing patterns are associated with long-term use depending on the patient's characteristics as well as the clinician's prescribing behaviors (Deyo et al., 2017).

The cumulative effects of opioid use can lead to addiction. The mortality rate of opioid addicts is about six to 20 times greater than that of the general population (Hser et al., 2015). The opioid-naïve patient presents a scenario that requires cautious prescribing (Koo et al., 2020). This is further exacerbated by patients with chronic diseases. Opioid use in chronic situations can be both beneficial and harmful (Vowles et al., 2015). For example, a patient who requires a nephroureteral stent must undergo exchanges every six weeks to maintain patency. This equates to the need for moderate sedation roughly every eight weeks. The impact on healthcare is significant given the rate of opioid influenced death and psychological disabilities related to the nature of use. Physicians and advanced care providers can change the process of pain management by identifying medications that carry less potential for abuse/addiction (Deyo et al., 2017).

Theoretical Framework

Developed over three decades of research, the Praxis Theory of Suffering was created by Morse. The initial goal of this theory was to develop illness experience and evaluate various dimensions of suffering (Butts and Rich, 2018). Over the following years, this theory was expanded to identify the role of suffering in comforting suffering behaviors and their patterns, and the theory can be employed to evaluate the concept of comfort and comforting. This theory was studied within a wide range of patient and caregiver populations such as family presence in trauma care, cardiac patients, and the impact of chemotherapy in patients/families (Butts and Rich, 2018).

Review of Literature

Nephroureteral stents are catheters that permit urine flow from the kidneys to the bladder via the ureter. They must be exchanged every six to eight weeks to maintain patency of the stent and facilitate urinary drainage. This procedure is painful and is commonly managed by combined narcotic (fentanyl) and benzodiazepine (midazolam) administration. One potential complication of nephroureteral stents is spasms. Because the stent is exchanged through manipulation of the ureter, spasms can occur and can mimic renal colic, which is characterized by severe pain in the lumbar region (Montiel-Jarquín et al., 2017). Sedation for analgesia allows patients to better tolerate diagnostic imaging and image-guided procedures by relieving anxiety, discomfort, and/or pain (Johnson, 2010). It facilitates and may optimize diagnostic imaging, image-guided interventions, and radiation oncology procedures that require patient cooperation (American College of Radiology, 2020).

With a stent, access to the kidneys is achieved via an antegrade approach. The stent terminates in the urinary bladder. To secure its placement, retention loops are created in the renal

collecting system and distally in the urinary bladder. An antegrade nephrostogram, contrast injection through the existing stent to determine its location and patency is performed (Makramalla & Zuckerman, 2011). While the patient is lying prone on the table, the skin is prepped and draped in a sterile fashion. The exchange is conducted over a stiff wire, such as an Amplatz. The catheter is injected with dilute contrast media to visualize the renal pelvis and bladder. The wire is advanced under fluoroscopic guidance and coiled within the bladder. The catheter is then exchanged over the wire for a new one. If the old catheter has additional side holes, similar holes are created in the new stent. The catheter is then sutured in place with a nonabsorbable suture such as Prolene (Makramalla & Zuckerman, 2011).

Medications Used

Midazolam

A commonly used benzodiazepine for sedation during procedures, midazolam is an opioid and controlled narcotic. It has been associated with respiratory depression and cardiac arrest in elderly patients (Nordt & Clark, 1997). It does have a reversal agent, flumazenil, but this agent can cause seizures (Penninga et al., 2015).

Fentanyl

Commonly used for intraoperative analgesia, fentanyl has been used for many years to control “breakthrough” pain. It has minimal cardiac effects but can cause severe respiratory depression (Stanley, 2016). It has a reversal agent, naloxone, that can be given intravenously or nasally.

Ketorolac

In addition to opiates, non-steroidal anti-inflammatory drugs (NSAIDs) are first-line therapies for analgesia (Patti & Leslie, 2020). NSAIDs work in two ways in renal colic. First,

NSAIDs decrease the production of arachidonic acid metabolites, which mediate pain receptors, alleviating pain caused by distension of the renal capsule (Patti & Leslie, 2020). Additionally, they cause contraction of the efferent arterioles to the glomerulus, reducing glomerular filtration and hydrostatic pressure across the glomerulus.

Renal colic pain emerges from the obstruction of the urinary flow by a kidney stone, increased pressure on the urinary tract wall, smooth muscle spasms of the ureter, edema and inflammation near the stone, an increase in peristalsis, and pressure of the proximal stone (Golzari et al., 2014). The NSAID, ketorolac has been found to significantly decrease opioid requirements and the incidence of vomiting and increase gastrointestinal motility. It has been found to be effective in pain management when there is concern about the patient developing opioid dependence (Mahmoodi & Kim, 2020).

Patients receiving NSAIDS achieve greater reductions in pain scores and are less likely to require additional analgesia in the short term than those receiving opioids (Holdgate & Pollock, 2004). In addition, opioid administration may result in a greater risk of vomiting (Holdgate & Pollock, 2004). Holdgate and Pollock (2004) conducted a meta-analysis that compared the safety and efficacy of NSAIDS with opioids and acetaminophen for the management of renal colic. They concluded that NSAIDS were equivalent to opioids or acetaminophen producing less nausea and vomiting than opioids in the treatment of renal colic (Pathan et al., 2017). Balancing an analgesic with morphine and ketorolac is more effective than using morphine or ketorolac alone, as determined by lower pain scores obtained 40 minutes after injection and a decreased need for rescue analgesia (Hosseininejad et al., 2017).

Purpose

Utility of ketorolac as effective pain management in other pain management situations has been shown to be beneficial in the setting of acceptable renal function (Diblasio et al., 2004). There is a significant gap in research involving the utility of ketorolac in interventional radiology urological procedures such as nephrostomy/nephroureteral stent exchange. The purpose of this quality improvement study was to demonstrate decreased pain scores when ketorolac was used concurrently with midazolam and fentanyl for pain management in this procedural setting.

Methods

After receiving approval from the institutional IRB, the project moved from the planning phase to implementation. All patients were evaluated for procedural medication administration using the specialized skills of a nurse practitioner, physician's assistant, or physician in collaborative agreement. Patients received a complete history evaluation including labs, physical exam, and review of prior procedures. Appropriate patients presented with acceptable renal function evidenced by a glomerular filtration rate greater than 50, blood urea nitrogen less than 20, creatinine level of 1.0, age of 18–65 years, no reported peptic ulcer disease, no reported gastrointestinal hemorrhage, and no reported allergy to NSAIDS. Vulnerable populations were protected, and any patient that was unable to provide their own consent (e.g., power of attorney designees) were not considered for this study. A target of 30 to 100 patient encounters was the sample size for this study.

Once all inclusion criteria were met and the patient gave consent to participate in the study, written consent was obtained in the procedural holding room by either the principal investigator, another provider, or the co-investigator. The patient was provided with

opportunities to opt out of participation at any time prior to administration. There was assurance that at no time will pain medications be withheld.

The patient was given 30 mg of ketorolac intravenously immediately prior to commencement of the exchange procedure, along with a half dose of previously used narcotics. The initial amount of sedation was exactly one half of their previous exchange procedure total amount. For example, if the patient received two milligrams of midazolam and 200 micrograms of fentanyl at the last exchange, the initial dose of sedation was one milligram of midazolam and 100 micrograms of fentanyl. If rescue analgesia was needed, the remaining one milligram of midazolam and 100 micrograms of fentanyl were given.

Vital signs were recorded during the procedure, and patients were monitored for any hemodynamic changes or adverse reactions, such as nausea or respiratory distress. If pain control was not achieved after two minutes, additional opioid administration was provided according to institutional policy guidelines and was equal to the total amount that the patient received during previous exchanges. At no point was a patient without pain medication.

Once the procedure was completed, patients were monitored in the recovery area for a time frame of no less than 30 minutes. The following day, telephone contact was made to collect feedback on pain control. There was no funding for this data collection. No additional resources were needed to analyze the data.

Ethical considerations included the autonomy of the patient to participate in their care. Each patient that met the inclusion criteria was given the opportunity to participate in or decline the study. Autonomy included the provider offering an alternative to previous pain management with medications that have fewer side effects and supporting the patient in the decision-making process. Fidelity adherence was demonstrated by management of pain regardless of participation

in the study. If the patient required additional pain medication, it was given immediately and without delay.

All data were collected and documented in the electronic medical record. Data were only accessible to the Principal Investigator and collaborating physician via a password-protected program (Intellectus ® USA) that adhered to all privacy and security rules in accordance with the Health Information Portability and Accountability Act of 1996 (Health and Human Services, 2013).

Measures

Procedure pain was measured by the registered nurses using the Visual Analogue Scale (Haefeli, & Elfering, 2006) and documenting the score in the electronic medical record. This scale measures pain as 0 for no pain and 10 as worst pain it could possibly be (Haefeli, & Elfering, 2006). Pain scores were measured pre, during and post procedure. Reduced opioid administration with the addition of ketorolac along with midazolam and fentanyl was evaluated by pain scores. Descriptive statistics such as age, race, and gender were collected.

Data Analysis

A Friedman test was used to see if there were differences between the pre procedure, during procedure and post procedure pain score. A Two-Tailed Wilcoxon Signed Rank test was used to show the statistical difference between the pre and post procedure pain score. The Two-Tailed Mann-Whitney *U* Test was used to see if there were differences in post-procedure pain scores between the group that received half of the previous dose and the group that received the entire previous dose.

Results

The average age of the participants was 54.9 years with a median age of 57 years. One participant was 34 years old. One participant was African-American and the remainder were Caucasian.

Friedman Rank Sum Test

The results of the Friedman test indicated there were significant differences in the median values of pre procedure pain score, during procedure pain score and post procedure pain score (p 0.05, $\chi^2(2) = 10.33$, $p = .006$). Table 1 presents the results of the Friedman rank sum test. Figure 1 presents boxplots of pre procedure pain score, during procedure pain score and post procedure pain score.

Pairwise comparisons were done to examine for differences between each combination of variables. The results of the multiple comparisons indicated significant differences in that the post procedure pain score was lower than the pre procedure pain score, ($p < 0.05$). No other differences were noted. Table 2 presents the results of the pairwise comparisons.

Two-Tailed Wilcoxon Signed Rank Test

The results of the two-tailed Wilcoxon signed rank test were significant based on an alpha value of 0.05, $V = 36.00$, $z = -2.55$, $p = .011$. This indicates that the differences between pre procedure pain score and post procedure pain score are not likely due to random variation. The median of pre procedure pain score ($Mdn = 6.50$) was significantly larger than the median of post procedure pain score ($Mdn = 0.00$). Figure 2 presents a boxplot of the ranked values of pre procedure pain score and post procedure pain score.

Two-Tailed Mann-Whitney *U* Test

The result of the two-tailed Mann-Whitney *U* test was not significant based on an alpha value of 0.05, $U = 14.5$, $z = -0.61$, $p = .542$. The mean rank for group Half was 5.92 and the mean rank for group All was 4.88. This suggests that the distribution of post procedure pain score for group Half (*Mdn* = 1.00) was not significantly different from the distribution of post procedure pain score for the All (*Mdn* = 0.00) category. Table 3 presents the result of the two-tailed Mann-Whitney *U* test. Figure 3 presents a boxplot of the ranks of post procedure pain score by Group.

Discussion

This quality improvement project was done to examine the efficacy of using a non-opioid medication to treat pain concurrently with opioids. The impact on healthcare is significant given the rate of opioid-influenced death and psychological disabilities related to the nature of use. Providers can change the process of pain management by identifying medications that carry less potential for abuse/addiction. These medications have been proven effective in pain control management in other areas of medical pain management (Diblasio et al., 2004).

The results of this quality improvement project demonstrate the utility of ketorolac given concurrently with opioids in the nephrostomy/nephroureteral stent exchange. This was demonstrated by the decrease in pain scores and total use of opioid medications to treat procedural pain. Although the sample size was small, the effect of ketorolac in pre to post procedure pain scores is clearly seen in the decrease of overall pain medication requirement and decrease in pain scores. The pain scores, overall, decreased but more importantly there were no differences in the post procedure pain scores of the group that received the entire opioid dose versus the group that received half of the previous dose.

This study carries immense implications for addressing the opioid epidemic. With a more targeted approach to pain management in this procedure, patients can receive medication with fewer side effects that can effectively manage pain. Less sedating medications decrease the possibility of airway complications that lead to significant illness (Tobias & Leder, 2011).

Even with a sample size of ten patients, it was shown that ketorolac was effective in the treatment of procedural pain. Anecdotally, verbal feedback was positive and patients expressed increased satisfaction with their procedure in terms of pain management. Two patients have since requested ketorolac as part of their medication regimen for procedural exchanges.

Limitations

A limitation of this quality improvement project included the sample size. The sample size was severely limited due to a shortage of stents available to the department. This required lengthening the time intervals between exchange procedures. It can also be considered that the decrease in pain score was a result of the full amount of opioid dose required in four of the patients.

Conclusion

The addition of ketorolac enabled administration of decreased doses of opioids in over half of the participants during previous exchange procedures. This quality improvement project demonstrates that decreased pain scores can be achieved with the addition of ketorolac concurrently with decreased opioid administration. Ketorolac has been proven beneficial in other areas of pain management such as in the post-nephrectomy setting (DiBlasio et al., 2004) and shows benefit for the patient undergoing nephrostomy/nephroureteral stent exchange procedure.

Future research could include a larger participant group and the addition of a control group comparing the addition of ketorolac to the group that does not receive ketorolac and receives opioids only.

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Table 1

Friedman Rank Sum Test

Variable	Mean Rank	χ^2	*df*	*p*
Pre_Pain_Score	2.56	10.33	2	.006
During_Pain_Score	2.11			
Post_Pain_Score	1.33			

Table 2

Pairwise Comparisons for the rank-sums of Pre_Pain_Score, During_Pain_Score, and Post_Pain_Score-

Comparison	Observed Difference	Critical Difference
Pre_Pain_Score-During_Pain_Score	4.00	10.16
Pre_Pain_Score-Post_Pain_Score	11.00	10.16
During_Pain_Score-Post_Pain_Score	7.00	10.16

Note. Observed Differences > Critical Differences indicate significance at the $p < 0.05$ level.

Table 3

Two-Tailed Mann-Whitney Test for Post_Pain_Score by Group

	Mean Rank				
Variable	Half	All	*U*	*z*	*p*
Post Pain Score	5.92	4.88	14.50	-0.61	.542

Figure 1

Boxplots of Pre_Pain_Score, During_Pain_Score, and Post_Pain_Score

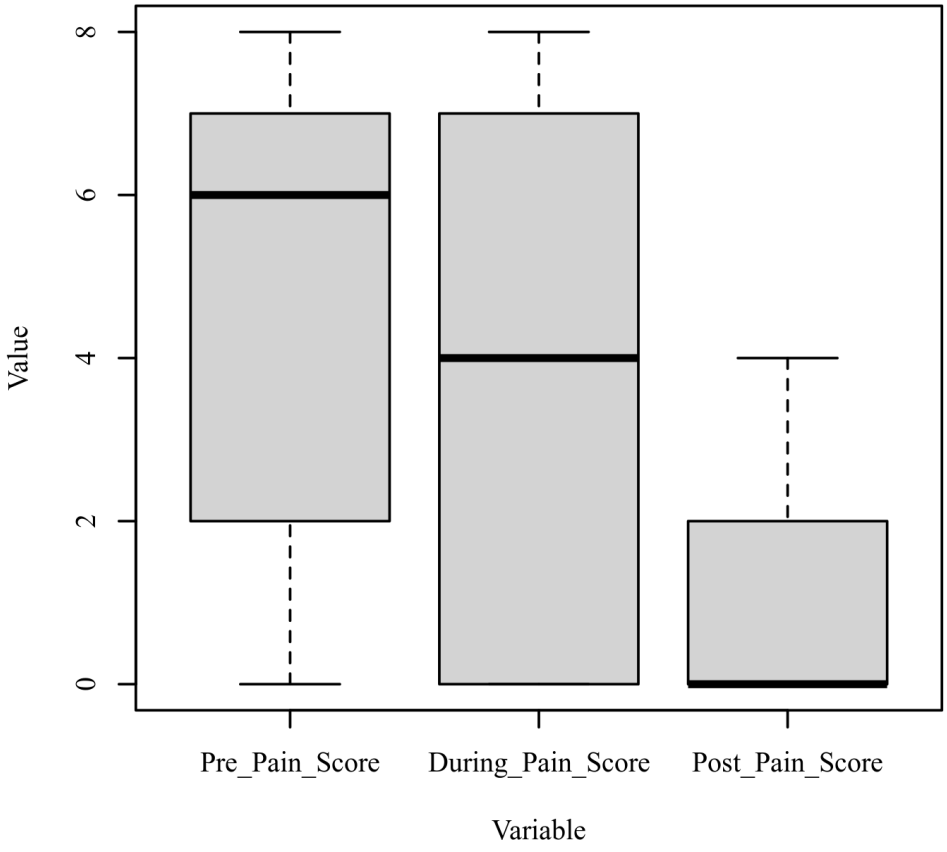

Figure 2

Ranked values of Pre_Pain_Score and Post_Pain_Score

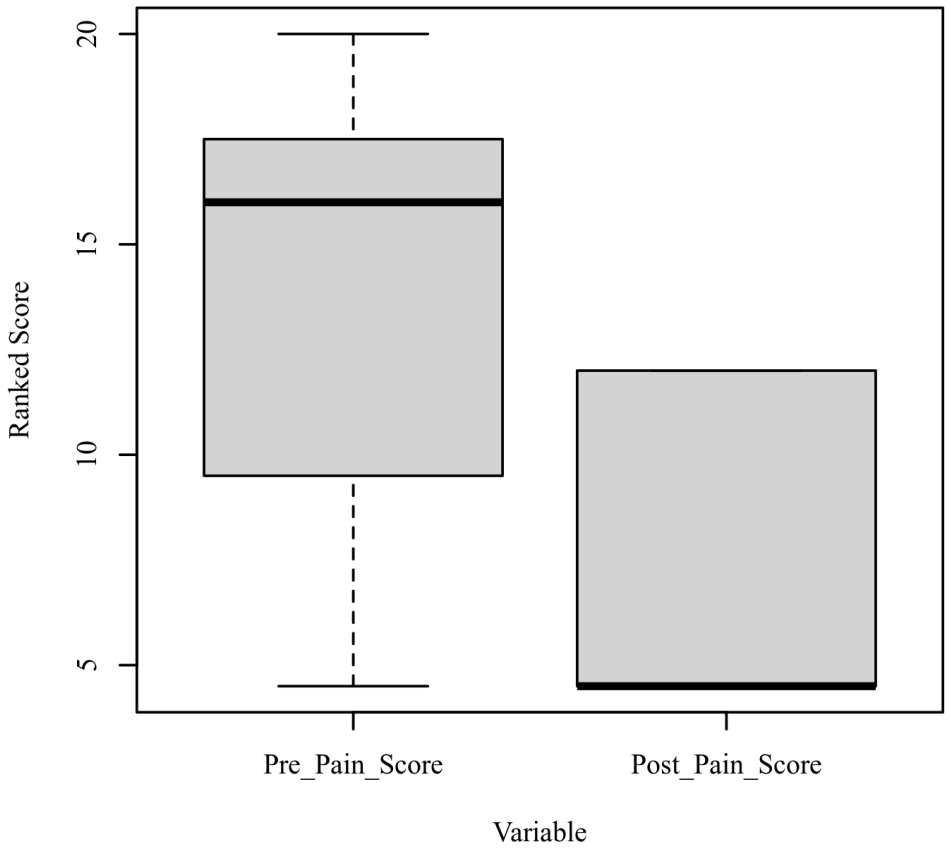

Figure 3

Ranks of Post_Pain_Score by Group