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Overview of Incidence, Clinical Manifestations and Treatment Approaches towards Uretric Colic in Patients with Nephrolithiasis – A Systemic Approach

Jobin Kunjumon Vilapurathu[1*], G.R Vijaya Sankar[2]
Assistant Professor, Department of Pharmacy Practice, Nirmala College of Pharmacy
Associate Professor, Department of Pharmaceutics, Vinayaka Missions College of Pharmacy
****Corresponding Author***
E-mail Id: jobinkunjumon@yahoo.com

ABSTRACT

Nephrolithiasis is a very common condition and involves formation of stone in any anatomical region of the Kidney. One of the most prominent clinical manifestations of renal calculi is sharp stabbing pain over the pelvic region. The treatment guidelines include the use of Intravenous Diclofenac sodium or Tramadol for immediate pain relief.

Keywords*: Uretric Colic, Nephrolithiasis, Intravenous Diclofenac sodium, Tramadol.*

INTRODUCTION

Nephrolithiasis or Renal stone is a condition in which there is formation of stone in any Anatomical region of the kidney due to super saturation of urine and is characterized by severe pain usually sudden in onset [1,2]. Nephrolithiasis is a highly prevalent disease worldwide with rates ranging from 7%-13% in North America, 5%-9% in Europe and 1%-5% in Asia [3]. Traditionally men have demonstrated a higher prevalence of stone disease than women but the gender gap is now narrowing. The lifetime prevalence of nephrolithiasis is 13% for men and 7% for women [4]. Ureteric Colic is a critical pain that a person feels due to upper Ureteric obstruction leading to an increase in intra pelvic pressure which leads to the tension in wall of urinary tract causing to the spasm of ureteric smooth muscle, edema and inflammation at the point of calculus further guiding to increased peristalsis and pressure proximal to the calculus [5,6].

75% of the people with urinary stone disease are having the symptom of pain. Over posterior renal angle area strapping renal pain is experiencing by the patient. During movement of the body worsen pain on anteriorly in the hypochondrium or both. It may be intensify on movement, especially on climbing stairs. Invading the stone in the ureter cause ureteric colic from loin to groin pain the patient can move but nothing comfort [7,8]. An attack of colic sparsely last more than 8 hour and not related to pyrexia. Bleeding amount is always small but sometimes haematuria become leading symptom. The majority of urinary stones less than 5 mm. in diameter will pass Extemporary through urinary tract. Whereas those exceeding 7 mm of diameter always require surgical intervention [9,10].

Acute renal stone may lead to flank pain occur during traveling of stone through urinary track. The pain chaperone by hematuria, nausea or vomiting and malaise; fever and chill may also be coexisting with renal calculi. However, stones in the renal pelvis may be asymptomatic [11].

A stone can also lead to dysuria once it has stretch out in to lower urinary tract [5]. The stone formation in women may result

into urinary tract infection. The stone may grow into larger size and fill the renal pelvis to produce a "stag horn" appearance [13]. Cysteine stone are uncommon, but case is most series of nephrolithiasis. The symptoms are variable and the diagnosis sometimes unclear until the stone is uncover on a radiograph. Some stones even infected stone cause no symptom. Pain is the supreme in 75% of the people with renal stone disease. Firm renal pain is pinpointed in renal angle [1, 14].

Ureteric colic is characterized by onset of unbearable pain due to acute urinary tract obstruction which induces intensive visceral nociception from increased tension in renal pelvic and ureteric wall, secondary to increased intraluminal pressure. NSAIDs and opiod analgesic remain the main stay of treatment for acute ureteric colic.[7] The ideal practice for pain reduction in acute ureteric colic. Intravenous administration of analgesics, either NSAIDs or opioids.(5) The ideal analgesic is one with safe efficacy, few side effects as well as easy route of administration. The pharmacological treatment for pain in acute uretric colic patients depends on its intensity :in mild cases Paracetamol and Dypirone. NSAIDs and opiod analgesic are required in moderate to severe pain [15].

MATERIALS AND METHODS

Electronic Database PubMed was systemically searched for articles using the keywords, Uretric Colic, Nephrolithiasis, and Treatment of Renal Colic up till December 30, 2019. A total of 380 articles regarding these keywords were found. After excluding all studies, other than original research, a total of 186 were obtained. These articles were again wetted for their originality and purpose and a total of 12 articles were selected. It included Case Reports, Case Series, Original Research work, Short communications and letter to the editor. These articles were critically appraised for getting into conclusions for the present study.

RESULTS

Ganesan V *et al*., (2017) [15] conducted a study to determine the sensitivity and specificity of ultrasonography (US) for detecting renal calculi and to assess the accuracy of US for determining the size of calculi and how this can affect counselling decisions. They retrospectively identified all patients in their institution with a diagnosis of nephrolithiasis who underwent US followed by non-contrast computed tomography (CT) within 60 days. The use of plain abdominal film of kidney, ureter and bladder and US increases sensitivity (78%), but 37% (13/35) of patients may still be counselled inappropriately to undergo observation. They concluded that using US to guide clinical decision-making for residual or asymptomatic calculi is limited by low sensitivity and inability to size the stone accurately.

Shih MT *et al*., (2016) [16] conducted a retrospective study in evaluating the pain severity in renal colic in patients presented with excruciating flank pain and thus seek urgent medical care. This study aimed to determine correlations between clinical parameters and the perception of pain. 171 consecutive patients with initial presentation of renal colic due to a single ureteral stone were reviewed for the study. The Visual Analog Scale (VAS) was used to assess pain intensity at the time of colic. The mean size of the stones was 5.3 ± 2.2 mm, and 62% were found in the lower ureters. Medical expulsive therapy alone was effective in 48% of cases and the average time for stone passage was 9 ± 5 days with a high VAS score. BMI had a negative correlation ($P<0.01$). VAS is effective for evaluating individual discomfort, as it helps to assess patient's

perception of pain. They concluded that the study showed a lower BMI and smaller stones (<5 mm) tend to contribute to more severe colic pain which provided an information that was helpful in the clinical management of renal colic

Al-Jasmawy HO *et al*., (2015) [17] conducted a study to compare the efficacy of combined Tramadol with Diclofenac in comparison with the monotherapy treatment using Buscopan, Diclofenac or Tramadol in Renal pain control. They enrolled 160 patients of age 16-75 year with moderate to severe renal pain were treated in emergency department of Hilla Teaching General Hospital and private clinics. Baseline characteristics including age, sex and pain intensity after 10, 30, 60 minutes and 2 hours of drug treatment. Assessment of analgesic effect of the drugs was done by Numeric Rating Scale (NRS). Drug side effects were also reported. They concluded that for quick pain relief in renal colic, a combination of Intravenous Tramadol with Diclofenac Sodium is superior to each of them alone, Buscopan is least effective , with higher side effects.

Pickard R *et al*., (2015) [18] conducted a randomized controlled trials to test the effectiveness of smooth muscle relaxant drugs Tamsulosin and Nifedipine which assisted stone passage for people managed expectantly for ureteric colic and emphasized the need for high-quality trials with wide inclusion criteria. They recruited adults (aged 18–65 years) undergoing expectant management for a single ureteric stone identified by CT at 24 UK hospitals. Participants were randomly assigned by a remote randomization system to Tamsulosin 400µg, Nifedipine 30mg, or placebo taken daily for up to 4 weeks, using an algorithm with centre, stone size (≤5 mm or >5 mm), and stone location (upper, mid, or lower ureter) as minimization covariates. The primary outcome was the proportion of participants who did not need further intervention for stone clearance within 4 weeks of randomization, analyzed in a modified intention-to-treat population defined as all eligible patients for whom we had primary outcome data. No difference was noted between active treatment and placebo (p = 0·78), or between Tamsulosin and Nifedipine (p = 0·77). Serious adverse events were reported in three participants in the Nifedipine group (one had right loin pain, diarrhoea, and vomiting; one had malaise, headache, and chest pain; and one had severe chest pain, difficulty breathing, and left arm pain) and in one participant in the placebo group (headache, dizziness, lightheadedness, and chronic abdominal pain). Tamsulosin 400µg and Nifedipine 30 mg are not effective at decreasing the need for further treatment to achieve stone clearance in 4 weeks for patients with expectantly managed ureteric colic.

Payandermenhr P *et al*., (2014) [19] conducted a study to compare the efficacy and safety of Sublingual Buprenorphine with Intravenous Morphine for renal colic in emergency department using a double blinded , Randomized Controlled Trial. They enrolled patients of age 18- 55 yrs who had clinical diagnosis of renal colic. Patients received either 2mg Sublingual Buprenorphine with an IV placebo or 0.1mg/kg IV Morphine Sulfate with a sublingual placebo. Of 69 patients analyzed, 37 had received Buprenorphine, 32 had taken Morphine. NRS pain scores were reduced cross time by administration of both Buprenorphine (9.8 to 5.22 and then 2.30) and morphine (from 9.78 to 4.25 and then 1.8), significantly (p< 0.0001). Dizziness was more frequently reported by the Buprenorphine group (62.1% versus 37.5%, p< 0.05). They concluded that Sublingual Buprenorphine (2mg) was effective as Morphine Sulfate

(0.1 mg/kg) in renal colic pain management.

Dash A *et al*., (2012) [20] conducted a randomized, single-blind study comparing single intramuscular doses of Drotaverine Hydrochloride (80 mg) versus Diclofenac Sodium (75 mg) on 100 patients (50 in each arm) presenting to the emergency department (ED) with renal colic. Subjects with inadequate pain relief at 30 minutes received rescue intramuscular Tramadol (100 mg). Pain intensity was recorded using a visual analog scale (VAS), which is the primary outcome measure of this study, before drug administration and 30 and 60 minutes afterwards. The need for rescue medication and the presence of adverse effects were considered as secondary outcome of the study. The VAS decreased significantly with both Drotaverine (52.4%) and Diclofenac (49%) at 30 minutes. Reduction of VAS at 60 minutes was 61.3% with Drotaverine in comparison to 60.4% with Diclofenac. Forty-five patients (90%) in the Drotaverine group and 44 (88%) in the Diclofenac group found the therapy effective. The need for rescue medication was in five patients of the Drotaverine group and six patients in the Diclofenac group. They concluded that there was no significant difference in safety profile in the study groups and the efficacy and safety of Drotaverine as analgesic in renal colic is non inferior to Diclofenac and may be used as an alternative or add-on therapy to currently available options.

Salameh S *et al*., (2011) [21] conducted a study to compare the analgesic efficacy of Intramuscular Diclofenac and Tramadol in treatment of renal colic in the emergency department. A prospective, randomized trial was conducted in 100 patients with a clinical picture of renal colic. Diagnosis was confirmed by non contrast abdominal computed tomography. Subjects were randomized to receive a single Intramuscular injection of either 75mg Diclofenac or 100mg Tramadol. Ninety seven patients were included, of these 48 received Diclofenac and 49 received Tramadol. They concluded that Diclofenac was significantly more effective than Tramadol in reducing the severity of pain at 30 minutes as measured on a 10-cm visual analog Intramuscular Diclofenac as a single agent for the treatment of renal colic is more effective than Intramuscular Tramadol in our patients. Intramuscular Tramadol may be an alternative when contraindications preclude the use of Diclofenac.

Evan AP *et al*., (2010) [22] conducted a study to analyze weather all stones share similar presenting symptoms, and urine super saturation with respect to the mineral phase of the stone is essential for stone formation. However, recent studies using papillary biopsies of stone formers have provided a view of the histology of renal crystal deposition which suggests that the early sequence of events leading to stone formation. And they concluded that there appear to be three pathways for kidney stone formation: (1) overgrowth on sites of Randall's plaque, (2) growth on plugs from dilated ducts of Bellini, and (3) in free solution. The majority (approximately 75%) of CaOx stones is formed attached to sites of Randall's plaque and represents all ICSF patients.

Holdgate A *et al.,* (2004) [23] conducted a randomized controlled trial comparing systematic review of relative efficacy of NSAIDs and Opioids in the treatment of acute renal colic. 20 trials totally 1613 participants were enrolled for the study. Patient rated pain, time of pain relief, need for rescue analgesia, rate of recurrence of pain, adverse events were observed for outcomes. Both NSAIDs and Opioids led to clinically important reduction in patient

reported pain scores. Patients treated with NSAIDs were significantly less likely to require rescue analgesic than with opioids. Trial showed higher incidence of adverse event in patients treated with opioids. They have concluded that patients receiving NSAIDs achieved greater reduction in pain scores and are less likely to require further analgesia in short term than those receiving opioids. Opioids particularly Pethidine are associated with a higher rate of vomiting.

Hidas G *et al*., (2010) [24] conducted study on preoperatively assess the composition of urinary stones by using dual-energy Computed Tomography (CT), with postoperative in vitro x-ray diffraction analysis as the reference standard. In conclusion, uric acid, cysteine, and calcium stone composition may be reliably predicted in vivo on the basis of dual-energy CT findings. They concluded that a single dual-energy CT examination may contribute to not only the identification but also the chemical characterization of stones in the urinary tract, and it may add to the information available from non enhanced conventional CT performed for evaluation of nephrolithiasis

Cannon GW *et al*., (2000) [25] conducted the study to compare the clinical efficacy of Rofecoxib, a specific inhibitor of Cyclooxygenase 2 (COX-2), with that of Diclofenac in patients with OsteoArthritis (OA) and to evaluate the safety and tolerability of Rofecoxib. Rofecoxib was well tolerated and provided efficacy that was clinically comparable, according to predefined statistical criteria, to that of 150mg of Diclofenac per day in this 1-year study. Specific inhibition of COX-2 provided therapeutic efficacy in OA. Rofecoxib at dosages of 12.5 and 25mg demonstrated efficacy that was clinically comparable to that of Diclofenac, as assessed by all 3 primary end points according to predefined comparability criteria. Results from secondary end points were consistent with those of the primary end points. There were small statistical differences favoring Diclofenac for 2 of the end points. All treatments were well tolerated.

Nagatsuka C *et al*., (2000) [26] done a study to investigate whether preemptive multimodal analgesia (Diclofenac, Butorphanol, and Lidocaine) was obtained during Sagittal Split Ramus Osteotomy (SSRO). 82 healthy patients (ASA-I) undergoing SSRO were randomly assigned to 1 of 2 groups, the preemptive multimodal analgesia group (group P, n = 41) and the control group (group C, n = 41). This study was conducted in a double-blind manner. Patients in group P received 50 mg rectal Diclofenac Sodium, 10ug/kg intravenous 0.1% Butorphanol Tartrate, and 1% Lidocaine solution containing 10ug/ml epinephrine for regional anesthesia and for bilateral inferior alveolar nerve blocks before the start of surgery. Postoperative pain intensity at rest was assessed on a Numerical Rating Score (NRS) in the Post anesthesia Care Unit and on a Visual Analogue Scale (VAS) at the first water intake (FWI) and at 24, 48 and 72 hours after extubation. They concluded that there was significantly lower value in group P than in group C, whereas there were no significant differences at FWI, 24, 48, and 72 hours after extubation in both groups. Pre-emptive multimodal analgesia was not observed in this study.

DISCUSSION

On critical appraisal of the published articles it was visualized that Renal Stone is one of the clinical disorder worldwide affecting up to 5% of the population. From the past two decades the prevalence has hiked from 3.2% to 5.2%. In developed countries the lifetime risk is 10-15% on

other hand in Middle East it has strikes over 20-25%. Renal stones are common in both sexes and estimated as 5% of American women and 12% of men at any point in their life with male – female ratio of 2:1.

The main etiological reason for having stone formation is that the insoluble substances causes formation of crystals which grows and aggregate due to the super saturation of urine. The major causes Dehydration, Hyperparathyroidism, Hyperoxaluria, Hyperuricaemia, Hyperuricosuria, Infection, Cystinuria, Renal Tubular Acidosis, Polycystic Kidneys, Medulary Sponge Kidneys. Apart from these, deficiency of Vitamin A, decreased urinary citrate, inadequate urinary drainage and urinary stasis, prolonged immobilization are responsible for stone formation.

The major causes for Ureteric Colic are due to Renal Calculi. Pain can be mainly categorized as Nociceptive pain and Neuropathic pain, but in case of ureteric colic the patients are more prone to have nociceptive pain, among 90% of patients with renal calculi experience this type of pain and is frequently encountered in emergency department (EDs). In some cases this pain may be due to passage of calculi through the urinary tract.

Our study concluded that IV Diclofenac sodium is superior to IV Tramadol as an effective analgesic with minor side effects in patients with Acute Ureteric Colic. Diclofenac sodium with a rapid onset of action lead to consistent improvement in reducing the colicky pain in patients associated with Renal Calculi. Tramadol showed higher rate of side effect such as nausea, vomiting, dizziness and constipation when compared to Diclofenac sodium. The rapid improvement ofclinical symptoms of Diclofenac Sodium treated patients may also be due to its indirect smooth muscle relaxant properties

CONCLUSION

Even though Nephrolithiasis is a very common condition with high prevalence and recurrence rate the number of studies conducted in this field is not up to the mark. Also the exact flow chart for the treatment of Uretric Colic associated with Nephrolithiasis still needs to be studies in detail. As Nephrolithiasis is a recurring condition and as a whole lot of patient factors can affect its recurrence, the effect of patient education in its prevention can be studied and explored in future.

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