Ondansetron for Primary Pain Relief in Ureteral Colic

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Üreteral Kolikte Ondansetronun Ağrı Kesici Rolü

Özet

Bu çalışmanın amacı 5-HT_3 antagonisti olan ondansetronun akut üreter koliğinin tedavisinde ağrı kesici olarak değerlendirilmesidir.

Bu çalışmaya mikroskobik veya makroskobik hematürisi olan, klinik olarak üreter koliği ve şiddetli veya orta derecede ağrısı olan 19 hasta alınmıştır. Bilinen böbrek veya karaciğer hastalığı, ondansetron allerjisi olanlarla, gebe veya laktasyonu olan hastalar bu çalışmaya alınmadı. Ağrıyı verbal veya vizüel analog skala (VAS) ile değerlendirdikten sonra IV 8 mg ondansetron uyguladık ve ağrı skoru her 15 dakikada bir kaydedildi. Şayet 60 dakika içinde anlamlı bir ağrı azalması başarılamadı ise ağrıyı kesmek için ikinci ilaç olarak IV meperidin kullanıldı.

Ondansetron başlıca ağrı kesici olarak 10 hastada etkili idi, buna karşılık 9 hastada ek ilaç gerekli oldu. Ondansetronun başarılı olduğu 10 hastada başlangıçtaki VAS 9.0±1.6 ve ondansetron uygulandıktan 60 dakika sonraki 1.0±1.8 idi.

Bu hazırlık çalışmasında akut üreter koliği olan hastalarda ondansetronun ağrı kesici özelliği kabul edilebilir bulundu. Ondansetronun bu hasta grubundaki antispazmodik ve analjezik etkisini değerlendirmek için çok sayıda hastada plasebo kontrollü çalışmalar yapılmalıdır.

Anahtar Kelimeler: *Üreteral kolik, ağrı kesici, ondansetron.*

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Abstract

The aim of this study is to evaluate the effectiveness of the 5-HT_3 antagonist, ondansetron, as a pain reliever in the treatment of acute ureteral colic.

Nineteen patients with severe or moderate pain who were clinically diagnosed as having ureteral colic associated with microscopic or gross hematuria were included in the study. Exclusion criteria were known kidney or liver disease causing dysfunction, known hypersensitivity to ondansetron, pregnancy and lactation. After pain assessment with a verbal scale and a visual analog scale (VAS), we administered 8 mg ondansetron intravenously and pain scores were recorded every 15 minutes. If significant pain relief was not achieved within 60 minutes, IV meperidine was given as rescue pain medication.

Ondansetron was effective as a primary pain reliever in ten patients, whereas nine patients required additional medication. In the ten patients in which ondansetron was successful, the mean VAS on admission was 9.0±1.6 and it was 1.0±1.8 after 60 minutes of ondansetron administration.

In this preliminary study, ondansetron was found to have acceptable pain relieving properties in patients with acute ureteral colic. Placebo-controlled studies with larger numbers of patients should be performed to assess ondansetron's antispasmodic and analgesic efficacy in this patient group.

Key Words: *ureteral colic, analgesia, ondansetron.*

Stone disease is one of the most common diseases of the urinary tract and a major health problem. Renal tract stones afflict more than 500,000 Americans each year, and 2-5 % of the general population may be expected to develop a urinary calculus during their lifetime (1). Reliable statistical data about renal stone disease do not exist in Turkey, but the prevalence is probably high due to traditional low fluid intake and the warm climate.

Ureteral colic is a symptom complex caused by the presence of upper urinary tract, usually ureteral calculi. Patients often present in acute distress from nausea, vomiting and excruciating

pain. Prompt and adequate pain relief is the primary goal of the emergency physician when treating such patients. Little has change from the early twentieth century when C. H. Chetwood recommended in 1916: "During the attack of renal colic, the patient may be benefited by hot baths, hot fomentations, suppositories of belladonna, and morphine and hypodermic injections of morphine according to the intensity and duration of the pain" (2). In addition to classic treatment with opioid medications; spasmolytics, spasmoanalgesics, and non-steroid anti-inflammatory drugs have been used for the relief of ureteral colic pain (3-10).

Serotonin (5-hydroxytryptamine, 5-HT) was discovered nearly half a century ago and has been shown to increase ureteral contractions (11). It is not clear however through which receptor it mediates its effects (12). 5-HT has been hypothesized to act as a potential neurotransmitter in human upper ureteral smooth muscle (12). Ondansetron is a selective 5- HT_3 receptor antagonist and is currently used in a variety of settings for the relief of nausea and vomiting (13-15). In this study we investigated the efficacy of ondansetron for primary pain relief in patients with ureteral colic presenting to the emergency department of a university medical center.

Materials and Methods

Population: Twelve men and seven women (age 18 to 80 years old) complaining of the acute onset of flank pain associated with microscopic or gross hematuria, and who were clinically diagnosed as having ureteral colic were included. Patients with known kidney or liver disease causing dysfunction, and known hypersensitivity to ondansetron were excluded, as were pregnant and lactating women.

Study Design: This was a non-randomized, open-label study using 8 mg IV ondansetron (Zofran®, Glaxo) in adult patients with ureteral colic pain. After initial evaluation, pain was assessed using a 4-point verbal rating scale that consisted of "none", "mild", "moderate" and "severe". Only patients who indicated 'moderate' or 'severe'pain were included in the study and informed consent was obtained. The change in pain score as quantified by a 10-cm visual analog scale (VAS) before and after drug administration was the primary outcome measure. If severe pain continued for at least one hour after administration of ondansetron, IV meperidine 5 mg was administered as a rescue pain relief agent.

Pain Assessment: Pain relief was considered significant if on the verbal scale severe pain was reduced to a degree of mild or no pain and moderate pain to no pain. The patient's pain level was evaluated using the 10-cm VAS immediately before ondansetron administration; at 15, 30, 45 and 60 minutes after administration; and before discharge from the emergency department.

The presence of calcification on the kidney/ureters/bladder (KUB) X-ray and hydronephrosis on ultrasound or intravenous urography (IVU), if performed, were recorded.

Analysis of Data

VAS scores are expressed as mean±SD and were analyzed using the Wilcoxon signed rank test.

Results

Of the nineteen patients eligible for inclusion in the study, eighteen reported 'severe' and one 'moderate' pain on presentation. After ondansetron administration three patients experienced pain relief within 15 minutes; two patients within 30 minutes; four patients within 45 minutes and one patient within 60 minutes. Rescue medication (meperidine) was required within 30 minutes for three patients, and within 45 minutes in five patients. One patient required an additional 15 minutes to experience significant pain relief.

Ten out of 19 patients (53 %) reported pain relief after ondansetron administration within 60 minutes. The mean values of these ten patients who did not need rescue medication at 0, 15, 30, 45 and 60 minutes after ondansetron administration were 9.0±1.6; 6.0±2.7; 5.0±2.9; 2.1±2.2 and 1.0±1.8 respectively. A significant decrease in the VAS of 10 patients was found after administering ondansetron at sixtienth minute ($p=0.005$). Nine patients needed rescue medication to achieve adequate pain relief.

The mean blood pressures of patients on presentation were 130±18 mm Hg systolic and 79±16 mm Hg diastolic. These values were 127±14.5 mm Hg and 76±15 mm Hg on discharge ($p=0.2$ and 0.15). The difference between patients'heart rates before (96±7 bpm) and after (90±6 bpm) treatment were statistically significant ($p=0.04$).

No adverse effects of the study drug were observed during the follow-up period in the emergency department.

Ultrasonography in 12 patients revealed shadowing consistent with urolithiasis in six, overt hydronephrosis in two, and mild pelvicaliceal dilatation in two patients. Three of four patients who underwent intravenous urography (IVU) had pelvicaliceal dilatation. Plain abdominal X-rays were obtained in all patients. Opacities consistent with urolithiasis were observed in nine patients, of which only five were verified with ultrasound or IVU.

Discussion

In this preliminary, open-label, non-controlled study, we found ondansetron to be useful for providing primary pain relief in a majority of patients with ureteral colic. This result is consistent with known neurotransmitter effects of serotonin in ureteral smooth muscle (12). Ondansetron has also been found to have biochemical properties similar to those of local anesthetic agents (16). Perhaps similar or other unknown mechanisms result in its pain-relieving effects in ureteral colic. In one clinical study of post-operative patients, Doenicke et al. found that ondansetron was no more effective than placebo in reducing pain (17).

One potential disadvantage of ondansetron's widespread use in this setting is its high relative cost compared to standard opioid medications. If future studies find ondansetron to be effective for nausea and vomiting in ureteral colic patients as well, potentially only one medication would be able to relieve ureteral colic's most prevalent symptoms. Administering one medication, in place of several, may result in decreased costs and fewer side effects. Larger, blinded studies should be done to analyze ondansetron's effects in these patients, as well as a cost-analysis comparing it to traditional treatment.

Despite the statistically significant lower pulse rate after ondansetron administration in this small group of patients, we feel that these changes were not clinically significant.

Although in recent years non-steroid anti-inflammatory drugs have been increasingly used for the acute management of ureteral colic pain, more effective agents are constantly being sought. One example is metoclopramide, classically used for the treatment of nausea and vomiting, but which has been shown also to have pain-relieving properties in patients with migraine headache. The anticholinergic agent, oxybutynin, has also been investigated in the treatment of ureteral and bladder spasms (18).

Ondansetron has several potential advantages over other agents in the management of patients presenting with acute ureteral colic. In this preliminary study, ondansetron was adequate as a pain reliever in about half the patients. Larger, double-blind, controlled studies are needed to determine its advantages over classical approaches in ureteral colic patients in the emergency setting.

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