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RANDOMIZED CLINICAL TRIAL OF DEXMEDETOMIDINE EFFICACY IN COMPARISON WITH KETOROLAC FOR PATIENTS WITH ACUTE RENAL COLIC IN THE EMERGENCY DEPARTMENT

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ABSTRACT

Background: To choose an analgesic choice for renal colic patients in the Emergency Department, sometimes is a challenge. This investigation focuses on comparing efficacy of parenteral dexmedetomidine versus intravenous ketorolac in pain relief of patients with acute renal colic pain. **Methods:** Two groups were studied consist of 160 patients in a study design of single blind clinical trial. 18-55 years old patients with acute colicky pain of renal stone origin which have been referred to Emergency Department were included in the study. The diagnosis were confirmed with non contrast abdominopelvic computed tomography. Case group (80 patients) received single-dose parenteral dexmedetomidine (200mcg/2ml vials) against the control group (80 patients) which received single-dose parenteral ketorolac (30 mg /ml vials) as gold standard treatment during 10 minutes. The pain score were evaluated with Visual Analogue Pain Scale (VAS) on arrival and 20, 40, 60 min after drug administration. Data analysis established using Mann-whitney U test and independent sample T test in both groups. **Results:** The study data showed administration of dexmedetomidine is more efficient in renal colic pain control immediately and during 60 minutes after administration rather than ketorolac. Although both ketorolac and dexmedetomidine trial group patients, achieved significant pain reduction in contrast to base line pain score in the minutes of 20 and 40 and 60, but analgesic effect of dexmedetomidine were more significant. ($p<0.001$). **Conclusion:** Dexmedetomidine may have been a choice for acute renal colic pain control.

Trial registration: Clinical Trials IRCT2015120625402N1.

KEYWORDS: Acute renal colic; Dexmedetomidine; Ketorolac; Visual Analogue Pain Scale (VAS); Pain severity.

INTRODUCTION

Renal colic pain generally creates by an increase in ureteropelvic pressure as aresult of complete or partial urethral obstruction.[1] Its prevalence is around 10-15%.[2] Control of pain is a main part of treatment of renal colic and administration of ketorolac as a NSAIDs, is a popular choice.[1] Dexmedetomidine is an anxiolytic, analgesic and sedative medication which is well known for its specificity of sedation without risk of respiratory depression.[3] Ketorolac may have side effects such as respiratory depression and confusion which may stop using drug as a consequence.[4]; This Study designated to evaluate efficacy of Dexmedetomidine in alleviation of Pain of renal stones.

METHODS AND MATERIAL

Trial Design

The trial has been randomized with 2 arms receiving intravenous dexmedetomidine and intravenous ketorolac as reference product. One hundred and sixty patients were allocated to 2 parallel groups (dexmedetomidine and ketorolac). Patients in case and control groups respectively received intravenous dexmedetomidine 200mcg/2ml vials (Hospira; USA) and intravenous ketorolac 30 mg /ml vials (Combino Pharm; Spain), with a dose of 1 gram in 100 ml normal saline during 10 minutes (a 1-h study period, Time Frame: 20 minutes interval) and measuring the pain intensity (PI) in the VAS and adverse events. All participants (160 patients with diagnosis of renal colic) ranging in age from 18 to 55 years attended the Emergency Department. The patients were required to have an abdominopelvic (A/P) computed tomographic (CT) scanning without contrast performed by a board-certified radiologist for definitely diagnosis of renal colic with kidney stone origin. They were enrolled in the trial from September 2015 to May 2016.

Based on history and physical examination, a complete sign and symptom data were collected. The time of pain onset and alleviating and aggravating factors And accompanying symptoms were documented. The patient younger than 18 years old and older than 55 years old excluded from the clinical trial; history of any drug sensitivity to opioids or NSAIDS, any accompanying history of renal or cardiac or hepatic or lung disease or seizure or metabolic disturbance, systolic hypotention less than 90 mmHg, any analgesic consumption within 6 hours of arrival, fever, pain visual scale less than 3, pregnancy, addiction, speech impairment,

any abdominal tenderness or rebound, history of gasterointestinal bleeding or ulcer and dissection or aneurism of abdominal aorta Were another exclusion criteria. (Figure 1).

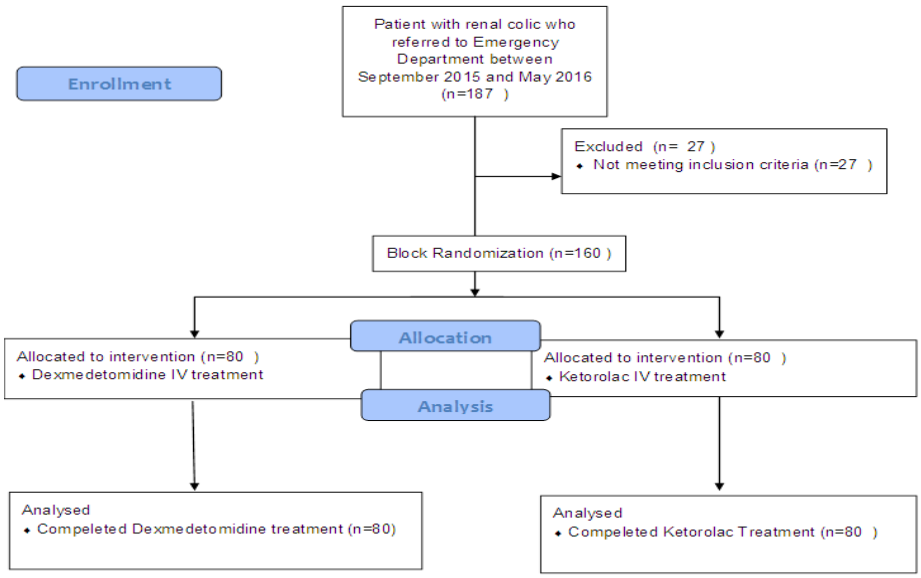

Fig. 1. Consort flow diagram of participants through randomized clinical trial of dexmedetomidine efficacy in comparison with ketorolac for patients with acute renal colic.

Ethical Aspects

Study design ethical issue approval was granted by the ethics committee of Ahvaz Jundishapur University of Medical Sciences (IR.ajums.rec.1394.430). The patients signed a written informed consent at the baseline visit of this trial. Also the Iranian Clinical Trial registry Number has been allocated(IRCT2015120625402N1).

Outcome Evaluations

Pain score(Visual Analogue Scale) has been evaluated at arrival and in the minutes 20, 40, and 60 after drug administration. The VAS scoring concept has been explained to the patients to mark a number ranging from 0(no pain) to 10(most severe pain) using a graded ruler. Any adverse reactions were documented.

Randomization and Blinding

Participants were categorized into 2 groups (case and active control) by block randomization, assigning 80 patients to each group. A sample size of 80 participants in each group was

sufficient to figure out a 50% decrease in VAS scores. Not only the researchers and the patients but also data analysts were blinded to the drug allocations.

Statistical Analysis

Data were analyzed using Mann Whitney U test and sample T test with a confidence interval of 95%. Statistical analysis performed with SPSS 20 and a P value of 0.05 considered as clinically significant.

RESULTS AND DISCUSSION

Renal colic patients were divided to two 80 person case and control groups for treatment with dexmedetomidine and ketorolac (a sum of 160 patients of the 2 arms). Distribution of basic characteristics, such as sex and age and weight of the patients of case and control groups were not statistically significant. (Table 1).

Table 1. Demographic data and basic characteristics of patients who received dexmedetomidine or ketorolac Baseline characteristics

	Dexmedetomidine (n=80)	Ketorolac(n=80)	p value
Age, years (mean, SD)	34.15 ± 9.29	32.35 ± 7.24	0.405
Weight, kilograms (mean, SD)	72.62 ± 11.14	71.90 ± 9.73	0.894
Gender **Male (n, %)**	59 (73.75%)	49 (61.25%)	0.792
Female (n, %)	21 (26.25%)	31 (38.75%)	

The mean VAS at the time of admission in the dexmedetomidine and ketorolac groups were 9.3±0.9 and 9.3±0.7, respectively (p=0.22). Twenty minutes after the first injection, the mean VAS decreased to 6.2±1.4 and 7.5±1.5 in the dexmedetomidine and ketorolac groups, respectively.

Pain score alleviation, in dexmedetomidine trial group was more significant rather than ketorolac trial group, comparing with their baseline pain severity score. ($p<0.001$). The mean pain severity score significantly decreased in the minute of 20 after drug prescription in both Dexmedetomidine and Ketorolac groups. Also the mean Pain severity score, 40 minutes after administration of dexmedetomidine was [mean (SD)= 3.2 (1.5); $p<0.001$] and in the ketorolac group was [mean (SD)= 6.1 (1.7); $p<0.001$]. Pain severity was considerably different between case and control trial groups and also in contrast to the baseline pain score in the minutes 20

and 40 after drug administration($p<0.001$). The mean pain score in the minutes 60 after drug receiving were 4.1 ± 2.5 and 6.3 ± 1.8 in dexmedetomidine and ketorolac groups, respectively. In the other hand, the pain intensity score 60 minutes after the drug prescription was significantly lower in those who received dexmedetomidine when compared to ketorolac ($p=0.01$) (Table 2).

Table 2. Mean reduction of pain scores in two groups (compared with 0, 20, 40, and 60 minutes)

Pain Score after drug administration	Group A	Group B	P Value
Pain score min 0 (mean±SD)	9.3±0.9	9.3±0.7	0.22
Pain score min 20 (mean±SD)	6.2±1.4	7.5±1.5	0.00
Pain score min 40 (mean±SD)	3.2±1.5	6.1±1.7	0.00
Pain score min 60 (mean±SD)	4.1 ± 2.5	6.3 ± 1.8	0.01

According to the findings of the present study, treating acute renal colic with intravenous dexmedetomidine 200mcg/2ml had significantly higher success rate in pain control after 20 min and this effect was maintained at 40 and 60 min after injection in comparison to intravenous Ketorolac 30 mg/ml when compared to baseline pain scoring.

A large number of different medications have been suggested for renal colic pain management consist of opiates, NSAIDS, Paracetamol, lidocaine, Hyoscin Butyl Bromide, Phloroglucinol, Drotaverine, Papaverine Hydrochloride, Aminophylline, Nitrates, Calcium Channel Blockers, Alpha blockers. Efficacy of some of these medications is the point of controversy.[5] But Taherinia et al. showed different changes of pain relief of their treatment based on ages.[6] Lopes and their colleague revealed the acceptable effects of desmopressin for pain relief of renal colic.[7] Esmailian et al. concluded that the concurrent prescribtion of morphine sulfate-citalopram result in more success rate in pain management of patients with renal colic.[8] Although this study demonstrated probable benefits of application of parenteral dexmedetomidine as a novel treatment for renal colic; yet more research should be conducted to clarify its efficacy.

CONCLUSION

It seems that the dexmedetomidine can be an efficacious analgesic choice for renal colic pain control in comparison to ketorolac for use in Emergency Departments.

Conflict of interest

There is no conflict of interest.

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