A retrospective analysis of nebulized versus intravenous fentanyl for renal colic

Melih Imamoglu, Ali Aygun, Omer Bekar, Erkan Erdem, Mustafa Cicek, Ozgur Tatli, Yunus Karaca, Aynur Sahin, Suha Turkmen, Suleyman Turedi *

Karadeniz Technical University, Faculty of Medicine, Department of Emergency Medicine, Trabzon, Turkey

**Article Info**

**Abstract**

Study objective: To assess the effectiveness of nebulized fentanyl used for analgesia in renal colic.

Materials/methods: This research was planned as a randomized, blinded study in which prospectively collected data were analyzed retrospectively to compare nebulized and intravenous (iv) fentanyl therapies. Patients with renal colic with ‘moderate’ or worse pain on a four-point verbal pain score (VPS) or with pain of 20 mm or above on a 100-mm visual analogue score (VAS) at time of presentation were randomized into iv fentanyl (n = 62) or nebulized fentanyl (n = 53) study groups. Decreases in VAS and VPS scores at 15 and 30 min compared to baseline, rescue analgesia requirements and side-effects between the groups were compared.

Results: Both iv fentanyl and nebulized fentanyl provided effective analgesia in renal colic patients at the end of 30 min. However, iv fentanyl provided more rapid and more effective analgesia than nebulized fentanyl. Patients receiving iv fentanyl had lower rescue analgesia requirements than those receiving nebulized fentanyl [37.1% vs 54.7%], although the difference was not statistically significant (p = 0.058). In addition, side-effects were more common in the iv fentanyl group compared to the nebulized fentanyl group [22.1% vs 9.4%], although the difference was also not significant (p = 0.058).

Conclusion: Nebulized fentanyl provides effective analgesia in patients with renal colic. However, iv fentanyl exhibits more rapid and more powerful analgesic effects than nebulized fentanyl. Nonetheless, due to its ease of use and few potential risks and side-effects the nebulized form can be used as an alternative in renal colic.

**1. Introduction**

1.1. Background

Acute renal colic is a common urological emergency that frequently develops in association with kidney stone disease, that is diagnosed and treated in emergency departments and that manifests with severe pain [1]. More than 1 million patients a year present to emergency departments due to renal colic in the United States of America [2]. The first step in the treatment of acute renal colic is pain reduction [3,4]. Non-steroid anti-inflammatory drugs (NSAIDs) and opioids are frequently used as analgesics. Both groups have been shown to have significant clinical analgesic effects and provide complete pain relief in the early period [5].

Analgesics are frequently administered by the intravenous (iv) and intramuscular (im) routes in the emergency department. The use of iv and im routes in the emergency department is due to the drugs administered reaching their peak levels faster by these pathways. However, there are various disadvantages to these forms of administration. Intravenous drug administration is not regarded as comfortable by patients due to the need to open vascular access. It may also lead to problems such as health workers being inadvertently exposed to needles and associated contagious diseases [6]. Similar problems also apply to the im injection method. As with iv injection, this is not a comfortable method for patients. It can also lead to complications, such as sciatic nerve injury, pain in the injection site and infection [7,8]. It is therefore important to use a method of analgesic drug administration which is less invasive and involves fewer complications and that will thus improve patient comfort.

Fentanyl is a synthetic opioid analgesic and a powerful opioid agonist [9]. Due to its high solubility in fat and rapid and diffuse redistribution it is an ideal agent for drug administration methods other than by the traditional parenteral route. Fentanyl can be administered by the im, iv (bolus injection, infusion, patient-controlled analgesia), neuroaxial (epidural, intrathecal), transdermal, transmucosal (oral or intranasal) and inhalation routes [10]. Fentanyl has been shown to be an effective analgesic when administered as a nebulized aerosol in several emergency conditions [11-17]. Farahmand et al. reported no side-effects in patients receiving nebulized fentanyl but observed side-effects such as nausea, dizziness and altered consciousness in a group receiving...
iv morphine [17]. From that perspective it may be concluded that nebulized fentanyl is safe in terms of potential side-effects and can reliably be used in patients with renal colic.

1.2. Importance

The advantages of nebulized fentanyl include adequate analgesia, the fact it avoids problems such as pain while preparing iv access and imm injection, sciatric nerve injury, and complications that healthcare personnel can encounter and that it increases patient comfort. However, despite these advantages, nebulized fentanyl is not routinely employed in emergency departments, and no information is available concerning its use in acute renal colic.

1.3. Goals of this investigation

The purpose of the study was to evaluate the effectiveness and reliability of nebulized fentanyl in patients presenting to the emergency department due to acute renal colic and to determine whether it can be used as an alternative to traditional, invasive methods.

2. Materials and methods

2.1. Study design and setting

This research was planned as a randomized, blinded study involving a retrospective analysis of prospectively collected data from patients presenting to the emergency department due to acute renal colic from 01.09.2014 to 01.09.2015. The study was performed in a tertiary university hospital receiving approximately 100,000 patient presentations annually. Ethical approval was received from the institutional ethical committee (protocol no. 2014/128). Written and informed consent was received from all patients included in the study.

2.2. Selection of participants

Patients presenting to the emergency department due to flank pain, in whom renal colic was suspected, with pain at the time of presentation of ‘moderate’ levels or above on a verbal pain scale (VPS) or of 20 mm or above on a 100-mm visual analogue scale (VAS) were included in the study.

Subjects were excluded if they had a history of allergy to fentanyl, morphine or any opioid type analgesic, hemodynamic instability at the time of presentation, body temperature > 38 °C, at the time of presentation, findings of peritoneal irritation at examination, known or suspected pregnancy, known or suspected aortic dissection or aneurysm, a history of analgesic use within 6 h of presentation to the emergency department, or a history of advanced coronary insufficiency, pulmonary insufficiency, renal insufficiency or hepatic insufficiency, or kidney transplantation.

Diagnosis of renal colic in this study was confirmed by the presence of stone in the urinary tract using non-contrast computerized tomography (CT). Patients with no identified urolithiasis or with other pathology identified at CT were excluded from the study. Patients who had previously participated in the study were not re-included in the event of repeat presentations.

Computer-based block randomization was used for randomization. Treatment codes, A and B, representing different drug arms based on that randomization were employed. When a patient was identified as meeting the inclusion criteria, the treating physician obtained a pre-completed study pack based on the randomization chart and also obtained informed consent. The physician responsible for the patient was not given any information at this stage concerning which alternative was to be applied. However, we did plan for this information to be shared with the responsible physician in the event of an unexpected problem or the development of a significant side-effect, and the patient would then be excluded from the study and the medication would be stopped.

2.3. Interventions

Clinical and demographic data such as age and sex were recorded for all patients scheduled for inclusion in the study. VPS and VAS evaluations were performed for all patients planned for inclusion on the basis of the criteria described above. Patients with renal colic with ‘moderate’ or worse pain on the VPS or with pain of 20 mm or above on the 100-mm VAS at time of presentation were randomized into intravenous (iv) fentanyl (Group A) or nebulized fentanyl (Group B) study groups.

Patients in Group A (the iv fentanyl group) were given a solution of 50 μg/1 ml fentanyl made up to 5 cm3 with normal saline (NS) at a dose of 1.5 μg/kg, with 0.03 cm3/kg of solution being administered by iv push in 2 min. In addition, 0.06 cm3/kg from a 10-ml NS solution was administered in nebulized form in 15 min.

Patients in Group B (the nebulized fentanyl group) received 50 μg/1 ml fentanyl made up to 5 cm3 with NS at a dose of 3 μg/kg, with 0.06 cm3/kg being given in nebulized form in 15 min. In addition, 0.03 cm3/kg from a 10-ml NS solution was administered in push form in 2 min.

Pain recording began with the initiation of the nebulizer for both groups (as time zero). Repeat VPS and VAS evaluations were performed on all patients at 15 and 30 min.

An ultrasonic nebulizer (Hilkoneb Home-Type) with a reservoir of 400 ml, a steam/vapor capacity of up to 5 ml per minute and capable of nebulizing drugs up to 0.5–6 μm was used to deliver fentanyl or NS in nebulized form. This was capable of nebulizing 10 ml of drugs in <5 min.

All patients were closely observed for possible side-effects until discharge. Side-effects that occurred were recorded. We planned to discontinue treatment in the event of development of side-effects sufficiently severe to prevent completion of the study.

If the patient reported that pain had not resolved during this 30-min period or if the physician in charge decided that the patient’s pain had not decreased sufficiently, 1.5 μg/kg fentanyl was administered as rescue analgesic. However, we also planned for rescue medication to be administered earlier if patients requested or required additional analgesia due to worsening pain in the first 30 min. Since removing the mask or interrupting nebulized therapy for any reason may cause a lessened analgesic effect or necessitate greater rescue medication, all patients were closely observed for compliance with the treatment.

2.4. Outcome measures

The primary outcome in this study was a decrease in VPS and VAS scores at 15 and 30 min compared to baseline in patients presenting to the emergency department with renal colic. Rescue analgesic requirement and side-effects were evaluated between the groups as a secondary outcome.

2.5. Primary data analysis

A 20-mm difference on the VAS was regarded as significant. With a standard deviation (SD) of 25 mm we calculated that 41 patients would be needed in each group to achieve a confidence interval of 95%. In addition to patients’ VPS and VAS scores at baseline and 15 and 30 min, differences between VPS and VAS scores were also calculated at 0–15, 0–30 and 15–30 min intervals in order to determine decreases in scores at 15 and 30 min compared to baseline.

The data obtained were recorded onto Windows Excel 2013 and statistical analysis was performed on SPSS 23.0 software. Constant variables were expressed as mean and 95% CI, and ordinal variables were expressed as median and 25–75% percentiles. Compatibility with normal distribution was assessed using the Shapiro-Wilks test. Student’s
-test was used in the comparison of normally distributed constant variables between the two groups, and the Mann Whitney U test was used for non-normally distributed constant variables. The chi square test was used to compare categoric variables between the two drug groups. The Friedman test was used to assess the significance of changes in pain in the same drug group from baseline to 30 min, while the Wilcoxon test was used in two-way comparisons.

3. Results

One hundred sixty-two patients presenting to the emergency department with suspected renal colic between 01.09.2014 and 01.09.2015 were evaluated for inclusion in the study. Forty-five of these were excluded for various reasons. Two of the 117 patients enrolled were excluded during the study period. One hundred fifteen patients with renal colic were finally randomized into iv fentanyl group containing 62 patients and nebulized fentanyl group of 53 patients (Fig. 1).

All patients were fully compliant with the study. The medications described in the study protocol were fully administered to all patients in both groups.

Basic demographic and clinical data for the study group are shown in Table 1. No difference was observed between the groups in terms of these findings. Oxygen saturation decreased below 90 in no patients, and no patient required respiratory support. However, respiration rate at 15 and 30 min was >10 breaths/min in one patient in the iv fentanyl group. This patient, with oxygen saturation above 90% and a normal level of consciousness, returned to normal with no support being required.

3.1. Main outcomes

VAS and 4-point VPS scores at baseline and 15 and 30 min in the study groups are given in detail in Figs. 2 and 3 and Table 2.

Basal pain scores were similar in the two groups (p = 0.77). Pain in both groups gradually decreased over 30 min from baseline (p < 0.001, according to the Friedman test) (Table 2).

The levels of decrease in VAS and VPS scores at 15 and 30 min compared to basal values are shown in Table 3. Both iv and nebulized fentanyl provided effective analgesia at the end of 30 min in patients with renal colic. However, iv fentanyl provided more effective analgesia between 0 and 15 min compared to nebulized fentanyl (p = 0.001). Similarly, iv fentanyl was more effective at a time interval of 0–30 min compared to basal degrees of pain (p = 0.004). However, no difference in pain reduction with nebulized fentanyl and pain reduction established with iv fentanyl was observed at a time interval of 15–30 min (p = 0.443). The same situation applied in terms of VPS.

As shown in Fig. 3, both iv and nebulized fentanyl were effective in reducing pain within 30 min. In addition, an increase compared to basal values was observed at 15 and 30 min in some patients in the nebulized fentanyl group. Intravenous fentanyl provided more effective analgesia compared to nebulized fentanyl at the end of 15 and 30 min.

Rescue drug requirements occurred in 23 (37.1%) of the 62 patients receiving iv fentanyl, with additional iv fentanyl being required after 30 min. Rescue drug requirements were observed in 29 (54.7%) of the 53 patients receiving nebulized fentanyl. No patients in either group required rescue drug administration before 30 min. On the basis of these findings, iv fentanyl was found to be more effective than nebulized fentanyl.

### Table 1 Basic demographic and clinical features of the study groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>IV fentanyl (n = 62)</th>
<th>Nebulized fentanyl (n = 53)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age; mean ± SD</td>
<td>33.1 ± 10.2</td>
<td>35.7 ± 10.8</td>
<td>0.165</td>
</tr>
<tr>
<td>Sex, no. (%)</td>
<td>Male 42 (67.7)</td>
<td>41 (77.4)</td>
<td>0.251</td>
</tr>
<tr>
<td></td>
<td>Female 20 (32.3)</td>
<td>12 (22.6)</td>
<td></td>
</tr>
<tr>
<td>History of urolithiasis no. (%)</td>
<td>38 (61.3)</td>
<td>35 (66)</td>
<td>0.598</td>
</tr>
<tr>
<td>Basal vital findings; mean ± SD</td>
<td>Systolic blood pressure 130.16 ± 14.43 128.11 ± 20.10</td>
<td>p = 0.399</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Heart rate 77.08 ± 11.43 78.55 ± 9.64</td>
<td>p = 0.463</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiration rate 19.21 ± 4.28 19.23 ± 3.37</td>
<td>p = 0.502</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Saturation (%) 97.56 ± 2.01 97.33 ± 1.32</td>
<td>p = 0.144</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Flow chart for patients enrollment.
Findings, although rescue requirements were higher in the nebulized treatment group, the difference was not statistically significant (p = 0.058).

Findings regarding drug side-effects observed in the groups are shown in Table 4. Side-effects were more common in the iv fentanyl group, although the difference was not statistically significant (p = 0.058). No intervention was required during the study period for the treatment of side-effects observed.

4. Discussion

To the best of our knowledge this is the first study to evaluate the analgesic efficacy of nebulized fentanyl in patients with renal colic and to compare this effectiveness with iv fentanyl. Our results indicate that both nebulized and iv fentanyl provide effective analgesia in patients with renal colic. However, iv fentanyl provides faster and more powerful analgesia than nebulized fentanyl. Nonetheless, due to its ease of use,
lack of needle involvement and low levels of potential risks such as contagious disease and other possible side-effects, the nebulized form of fentanyl can be used as an alternative to iv fentanyl in patients with renal colic in the emergency department. The absence of any significant difference between iv and nebulized fentanyl in terms of rescue drug requirements supports the idea that the nebulized form can be used in the treatment of renal colic in the emergency department.

Mucosal surfaces are rich in terms of blood supply. Drug administrations through the mucosal surfaces are highly effective, and drugs are transported rapidly into the systemic circulation. The nasal mucosa, hypopharynx and large and small airway structures of the respiratory tract, have an extensive mucosal surface area ideally suited to transmucosal drug use. Fentanyl is a lipophilic drug that is well suited to intranasal and nebulized use via the mucosal surfaces [18]. Various previous studies have investigated both the intranasal and nebulized use of fentanyl. We elected to use the nebulized fentanyl route while planning this study, because most of these studies have involved the intranasal use of fentanyl, and there are insufficient data available concerning nebulized fentanyl.

Both the intranasal and nebulized routes are alternatives for the iv route. However, very few studies have compared the nebulized and intranasal routes. One recent study which compared the intranasal, nebulized and intravenous routes of fentanyl administration in postoperative pain management reported that the intranasal route is more advantageous than the nebulized route [19]. Due to our study design, the intranasal route was not used, and only the nebulized fentanyl and iv fentanyl routes were compared.

A minimum change of 16 mm in VAS scores has been shown to be clinically significant in patients with abdominal pain [20]. In trauma patients, however, a change of 13 mm may be regarded as clinically significant [21]. On the basis of our study findings, a 35-mm decrease in pain was established with iv fentanyl, compared to a 15-mm decrease with nebulized fentanyl in the first 15 min. In other words, the analgesic effectiveness of nebulized fentanyl does not achieve clinical significance in the first 15 min. At the end of 30 min iv fentanyl still provided a greater decrease in pain than nebulized fentanyl (49.5 mm vs 28 mm).

However, since this decrease in pain achieved with nebulized fentanyl can be regarded as clinically significant despite being lower than the decrease recorded using the iv form, nebulized fentanyl may represent an alternative method in the treatment of renal colic.

The insufficient analgesic efficacy of nebulized fentanyl in the first 15 min is the most important factor restricting its use in patients with renal colic. In a study comparing the pharmacokinetic properties of nebulized fentanyl and iv fentanyl, Mather et al. reported that nebulized fentanyl reached therapeutic levels in the blood as rapidly as iv fentanyl and that the bioavailability of nebulized fentanyl was close to 100% using a nebulizer [22]. However, different bioavailability values can be observed with different nebulizers or oral inhalers. Furyk et al. reported that the bioavailability of nebulized fentanyl may be 20% that of iv fentanyl using one of these nebulizers [15]. In a study performed with the same nebulizer used in our study on the basis of that information, Farahmand et al. compared 0.1 mg/kg iv morphine and 4 μg/kg nebulized fentanyl [16]. Miner et al., Deaton et al. and Bartfield et al. administered nebulized fentanyl at dosages of 3 μg/kg, 2 μg/kg and 1.5 μg/kg, respectively, using nebulizers with similar properties [13,14,17]. Furyk et al. employed nebulized fentanyl at a dosage of 4 μg/kg using a nebulizer with different properties [15]. Since no specific effective analgesic dose is reported for nebulized fentanyl in the literature, and since fentanyl in nebulized form has been administered at varying dosages, 3 μg/kg nebulized fentanyl was used in this study. In the light of this information, we would have needed to use a dose of 7.5 μg/kg nebulized fentanyl in order to achieve bioavailability equivalent to 1.5 μg/kg iv fentanyl, and the lower level of analgesia achieved may be attributed to the fact that we did not employ a sufficient dosage of nebulized fentanyl. The superior analgesic efficacy of iv fentanyl that emerged at 0–15 and 0–30 min time intervals may also derive from that dose selection.

Although these are not completely clear, there are data in the literature to the effect that the initial analgesic effect of nebulized fentanyl is longer-lasting than that of iv fentanyl [23]. Bartfield et al. performed a randomized, double-blinded, placebo-controlled study of the analgesic effects of 1.5 μg/kg iv fentanyl and 1.5 μg/kg nebulized fentanyl in

| Table 2 |
| Study group pain scores (mm) at baseline, 15 min and 30 min. |
| Values | IV Fentanyl | Nebulized fentanyl | p |
| Visual analogue scale; mean ± SD (95% CI) | | | |
| Basal | 75.56 ± 21.90 | 69.17 ± 21.36 | p = 0.770 |
| 15 min | 36.29 ± 25.69 | 51.81 ± 26.50 | p = 0.002 |
| 30 min | 28.18 ± 29.38 | 38.05 ± 31.64 | p = 0.110 |
| Verbal pain scale; median (25–75%) | | | |
| Basal | 3–2(3) | 3–2(3) | p = 0.306 |
| 15 min | 1–2(3) | 1–2(3) | p = 0.003 |
| 30 min | 1–2(3) | 1–2(3) | p = 0.085 |

| Table 3 |
| Decreases in patient group pain scores at baseline and 15 and 30 min. |
| Values | IV fentanyl | Nebulized fentanyl | p |
| Visual analogue scale change; median (25–75%) | | | |
| Basal - 15 min | 35 (22.7–55.5) | 15 (–2.0–31.0) | p < 0.001 |
| Basal - 30 min | 49.5 (26.3–71.0) | 28 (10.5–52.5) | p = 0.004 |
| 15–30 min | 8.5 (−1–19.2) | 7 (0–24.5) | p = 0.443 |
| Verbal pain scale change; median (25–75%) | | | |
| Basal - 15 min | 1 (−1) | 1 (0–1) | p < 0.001 |
| Basal - 30 min | 2 (1–2) | 1 (0–2) | p = 0.020 |
| 15–30 min | 0 (0–1) | 0 (0–1) | p = 0.571 |

Please cite this article as: Imamoglu M, et al., A retrospective analysis of nebulized versus intravenous fentanyl for renal colic, American Journal of Emergency Medicine (2017), http://dx.doi.org/10.1016/j.ajem.2017.01.026
patients presenting to the emergency department with abdominal pain. They reported that iv fentanyl was more effective than nebulized fentanyl in the first 15 min. However, analysis at 30 min revealed no significant difference between the two groups [13]. Our study results are very similar, and although iv fentanyl was more effective in patients with renal colic in the first 15 min, if a target of 30 min is adopted for effective analgesia, nebulized fentanyl should be considered as an alternative. Nebulized fentanyl will be useful for reducing pain instead of waiting to establish an iv route.

Pain evaluations performed after 30 min revealed that patients in both groups required rescue analgesia. Although the number of patients requiring rescue analgesia was higher in the group receiving nebulized fentanyl compared to the iv fentanyl group, the difference was not statistically significant. Therefore, iv fentanyl is not superior to nebulized fentanyl in terms of rescue drug requirements. Similar findings, and even results favoring nebulized fentanyl, can be found in similar studies comparing the efficacy of nebulized and iv fentanyl in the literature. Deaton et al. administered 0.1 mg/kg iv morphine or 2 μg/kg nebulized fentanyl to patients presenting to the emergency with abdominal pain. Rescue analgesia was required by five of the 16 patients in the iv morphine group, but by none of the patients in the nebulized fentanyl group. The difference was described as being significantly in favor of nebulized fentanyl [20]. Farahmand et al. administered 0.1 mg/kg iv morphine or 4 μg/kg nebulized fentanyl to patients presenting to the emergency departments with extremity injuries. Rescue analgesia was required by 8.5% of the patients in the iv morphine group and 7% of those in the nebulized fentanyl group [17]. Rescue drug requirements were high in both groups in our study. This may be attributed to the presence of pain sufficiently high to distress patients in both groups at the end of 30 min and to pain attendant upon renal colic by itself being sufficient to discomfit the patient.

No severe side-effects such as anaphylaxis, hypotension, chest wall rigidity or respiratory difficulty were observed with the administration of nebulized fentanyl in this study. However, palpitations were reported in one and respiratory difficulty in another of the patients receiving iv fentanyl. These resolved spontaneously without requiring additional medical treatment. Although more side-effects were observed throughout the study period in the iv fentanyl group compared to the nebulized fentanyl group, the difference was not statistically significant. From that perspective, iv fentanyl offers no advantage over the nebulized form in terms of side-effects, and may even be regarded as being less well tolerated.

In addition to all these assessments, the administration of nebulized fentanyl at a level that may be regarded as quite low compared to the dose of iv fentanyl used in our study nevertheless provided effective analgesia in patients with renal colic. Considering that the dose of nebulized fentanyl administered was well tolerated by patients, the low level of side-effects observed and the fact that rescue drug requirements were similar to those of iv fentanyl, it may be suggested that nebulized fentanyl can be safely used at higher doses in patients with renal colic and that more effective analgesia can thus be achieved.

This study adds to the literature a further option for iv-free pain control in a common and acutely painful condition. If a health provider does select this method, this study can be of assistance with anticipating the timing of symptom relief and in predicting the probable need for rescue therapy.

5. Limitations

The applicability of this study in clinical practice is limited. We included only patients presenting to the emergency department due to flank pain, in whom renal colic was suspected, with pain at the time of presentation of ‘moderate’ levels or above on a VPS or of 20 mm or above on a 100-mm VAS. It would have been desirable to include all patients in the analysis together with a subgroup with pain due not to renal colic. This is because no ‘gold standard diagnosis’ is available to the clinician wishing to know how to treat a patient on initial presentation, only the presenting symptoms.

Since no specific effective analgesic dose for nebulized fentanyl is given in the literature and various doses of the nebulized form have been used in previous studies, we used a dose of 3 μg/kg nebulized fentanyl in this study. Considering the features of the nebulizer we used, a higher dose of nebulized fentanyl may be necessary to achieve bioavailability equivalent to that of 1.5 μg/kg iv fentanyl.

The dosages administered to the patients in our study were calculated on the basis of patients’ own verbally reported body weights, because most subjects had severe pain and anxiety at presentation. Patients’ actual weights were obtained after pain control and were compared with the reported weights, but no significant difference was observed between the two. Additionally, serum fentanyl levels were not measured after the drugs had been administered. This eliminates the possibility of suggesting a definitive interpretation of the bioavailability and pharmacokinetic characteristics of nebulized fentanyl.

Comparing only nebulized fentanyl and iv fentanyl in the treatment groups, and the absence of a NSAID treatment group may be interpreted as a limitation. There are many studies showing that NSAIDs can be used safely instead of opioids in the treatment of renal colic pain. However, the choice of initial analgesia and route of administration in patients presenting with renal colic to the emergency department is still controversial. The latest and the most extensive study which will have an impact on this discussion was carried out by Pathan et al., who showed that im NSAID is as effective as iv morphine and causes fewer adverse reactions [24]. However, our study was planned before this strong evidence became available, and we used fentanyl, a valid analgesic method for the treatment of renal colic. It will be interesting to see how the use of opioids for the treatment of acute renal colic will evolve over the next few years with strong evidence that NSAIDs can be generally equivalent to opioids. In addition, one of the objectives of this study was to seek an alternative method to the im and iv routes of analgesic use in renal colic. From that perspective, it should not be forgotten that only very limited data are available concerning the use of intranasal NSAIDs that can be used instead of the im and iv routes in pain management [25].

VAS evaluation was performed and the parameters analyzed for the last time at 30 min, the end point of our study, but patients were not subjected to any advanced evaluation in terms of this study after 30 min.

We performed block randomization with a block size of 100 patients in each group. Although the purpose of using a block randomization design is to minimize differences in group sizes, we were unable to achieve the required number of patients in each group between the study dates. In addition, the exclusion of non-renal stone cases also resulted in a considerable difference in group sizes.

Although a 95% power was anticipated on the basis of the numbers of patients in our study groups, wider clinical studies are clearly needed if nebulized fentanyl is to be widely used in the treatment of renal colic.

6. Conclusion

In conclusion, nebulized fentanyl provides effective analgesia in patients with renal colic. However, iv fentanyl provides more rapid and more powerful analgesia than nebulized fentanyl. Nevertheless, due to its ease of use and few potential side-effects and risks such as needle use and contagious disease, the nebulized form can be used as an alternative to the iv form in patients with renal colic in the emergency department.

Presented at a meeting

No.
Grant

No.

Conflicts of interests statement

The authors declare that they have no significant competing financial, professional or personal interests that might have influenced the performance or presentation of the work described in this manuscript.

References