Comparative Evaluation of Using Intranasal Desmopressin, Parenteral Diclofenac or their Combination in the Management of Acute Renal Colic Pain in Iraqi Patients

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Abstract

There is a suggestion that an antidiuretic hormone-induced decrease in diuresis might contribute to the rapid relief of the acute pain in renal colic. This study was designed to evaluate the efficacy of desmopressin nasal spray compared with diclofenac given intramuscularly in patients with acute renal colic. The study included 75 patients randomized into three different groups; group A received desmopressin (40 μg, nasal spray), group B diclofenac (75 mg) intramuscularly and group C, both desmopressin and diclofenac. Pain was assessed using a visual analogue scale (a 10-cm horizontal scale ranging from `no pain' to `unbearable pain') at baseline, 10, 20 and 30 min after administering the treatments. On admission, the pain level was the same in all three groups. At 10 min the pain decreased in all groups to a level that was not significantly different. At 20 min groups B and C had similar mean pain levels (5.8), whereas in group A it was 5.7. At 30 min, groups B and C scored 3.0 and 2.5 respectively, and group A 6.1. All three treatments were equally effective at 10 and 20 min but at 30 min there was a stabilization/slight increase in pain level in group A. In conclusion, these results indicate that desmopressin may be used to treat renal colic either alone or combined, increasing the analgesic effect of other drugs like diclofenac.

Key words: renal colic, intranasal desmopressin, diclofenac

Introduction

Renal colic is caused by an increase in pelvi-ureteric pressure secondary to an obstruction of the urinary tract. This increase in pressure causes a prostaglandins-mediated increase in renal blood flow and a subsequent increase in diuresis which, in turn, further increases intrapelvic pressure. Modulation of ADH is probably one of the most important mechanisms leading to an increased diuresis (1, 2) and one of the roles of prostaglandins (PGs) seems to be blocking the action of antidiuretic hormone (ADH) by interfering with cAMP-mediated signal transmission (3). NSAIDs (inhibitors of PG synthesis) have long been used as effective agents in the treatment of renal colic. They block other PG-induced effects, such as afferent arteriolar vasodilatation, which causes an increase in diuresis and consequently raises pelvic pressure. They also reduce local oedema and inflammation, and inhibit the stimulation of ureteric smooth muscle, which is responsible for increased peristalsis and subsequently increased ureteric pressure. There is a suggestion that an ADH-induced decrease in diuresis might...
contribute to the rapid relief of the pain of renal colic\(^6\). Desmopressin (1-desamino-8-D-argininevasopressin) is a synthetic structural analogue of ADH. Compared with ADH, it has a greater antidiuretic effect, a longer duration of action and reduced vasopressor activity. These properties make it a first-line drug for replacement therapy in central diabetes insipidus\(^5\) and a very effective agent in the treatment of nocturnal enuresis \(^6\). The marked antidiuretic effect of desmopressin is probably responsible for its efficacy in the treatment of renal colic \(^1\). Peripherally, it has been shown that desmopressin suppresses the spontaneous contractions of circular smooth muscle fibers in the renal pelvis of rabbits \(^7\). The same effect could be possible in humans. Some authors reported the role of desmopressin in stimulating the secretion of \(\beta\)-endorphins by the hypothalamus \(^8\)\(^-\)\(^11\), which could explain a possible additional central analgesic effect of the drug. To assess the efficacy of intranasal desmopressin in relieving the acute pain of renal colic caused by urolithiasis, we compared the analgesic efficacy of this drug with one of the most widely used NSAIDs in renal colic, diclofenac. We also compared desmopressin alone with desmopressin plus diclofenac. The study was enhanced by using the recently marketed intranasal spray form of desmopressin.

**Patients and Methods**

This prospective, randomized trial was conducted between May and June 2005 in the emergency department, Al-Nasirya General Hospital, and included 75 patients (45 men and 30 women, mean age 40.3 ± 3.4 years) admitted to the emergency service with renal colic caused by lithiasis and who had previously received no treatment. The patients were randomly assigned to three groups: group A received desmopressin 40 \(\mu\)g intranasally, group B diclofenac 75 mg intramuscularly and group C, both desmopressin and diclofenac. A detailed history was taken and the patients examined. The time of onset and duration of the pain and associated symptoms were recorded, with the number and dates of former episodes, the elimination of calculus and eventual previous documentation of stones by imaging. Vital signs and positive findings of the routine physical examination were evaluated and recorded. Patients with evidence of high blood pressure, coronary disease, rhinitis, influenza, anticoagulant therapy, and peptic ulcer, renal or liver failure were excluded from the study, as were any pregnant women. A visual analogue scale was used to assess the intensity of pain; this consisted of a 10-cm horizontal scale ranging from `no pain' to `unbearable pain', with values recorded to the nearest millimeter. The pain was assessed on admission and at 10, 20 and 30 min after therapy was administered. In all patients a plain X-ray of the urinary system was taken and any adverse reactions were recorded. The results, presented as mean ± SD, were assessed statistically by comparative statistics (one-way ANOVA).

**Results**

After the random assignment, each group includes 25 patients. The mean duration of pain was 15.07 h, with slight differences among the three groups (14.5, 19.8 and 12.7 in groups A, B and C, respectively). The mean number of previous episodes was 1.3 (1.5, 1.32 and 1.09, in A, B and C, respectively). There were no significant differences in age, blood pressure, radial pulse, or axillary temperature, or in the laboratory values, i.e. for factors related to urinary osmolarity. The intensity of pain at presentation was similar in all groups (table 1). After 10 min the pain scores were also similar, but at 20 min groups B and C had the same score, whereas group A had a higher score (5.3), and at 30 min, the scores were lower in groups B and C than in group A. In table (2) there were significant differences in pain score with time from baseline in all groups (P<0.01). Scores at 0, 10 and 20 min between groups were similar, but after 20 min the pain scores were lower in groups B and C. After 30 min, the differences between A and B, and between A and C, were significant (P<0.01). Although the differences between B and C were not significantly different, the score was lowest in group C. In Group A, there were significant differences between the first pain assessment and those at 10 and 20 min, but not after 30 min (i.e. pain increased after having diminished at 10 and 20 min).
Table 1. The changes in mean pain score in the three groups with time after administration of therapy.

<table>
<thead>
<tr>
<th>Response time (min)</th>
<th>Desmopressin 40µg</th>
<th>Diclofenac 75 mg</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.5±1.2a</td>
<td>7.7±2.0a</td>
<td>7.65±1.5b</td>
</tr>
<tr>
<td>10</td>
<td>5.7±0.9b</td>
<td>5.8±1.1b</td>
<td>5.8±1.0b</td>
</tr>
<tr>
<td>20</td>
<td>5.3±0.8b</td>
<td>3.8±0.6c</td>
<td>3.7±0.7c</td>
</tr>
<tr>
<td>30</td>
<td>6.1±0.9b</td>
<td>3.0±0.6d</td>
<td>2.5±0.3d</td>
</tr>
</tbody>
</table>

Values were expressed as mean ± SD, number of patients = 25 in all groups, values with non-identical superscripts (a, b, c, d) were considered significantly different P < 0.05.

Table 2. Number of responders to treatment and their percentage after administration of drugs.

<table>
<thead>
<tr>
<th>Response time (min)</th>
<th>Desmopressin 40µg</th>
<th>Diclofenac 75 mg</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>9 (36%)</td>
<td>21 (84%)</td>
<td>22 (88%)</td>
</tr>
<tr>
<td>20</td>
<td>8 (32%)</td>
<td>2 (8%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>30</td>
<td>1 (4%)</td>
<td>2 (8%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Total</td>
<td>18 (72%)</td>
<td>25 (100%)</td>
<td>25 (100%)</td>
</tr>
</tbody>
</table>

Number of patients in each group = 25.

Discussion

Treating renal colic with intranasal desmopressin 40 µg induced prompt pain relief, with significant decreases in pain scores after only 10 min. This effect was maintained at 20 min and then decreased slightly, in contrast to a former study (1) in which the effect lasted longer (thus reflecting the progressive intranasal absorption of desmopressin, with a plasma peak that can occur up to 4 h after administration, indicating a relatively slow absorption through the nasal mucosa) (10). Within group A (as in group C), there were apparently two subgroups of patients with marked differences in their response to therapy (table 2). Thus, although the mean response to therapy after 10 and 20 min was similar in the three groups, the response of individual patients showed that groups A and C had a greater proportion of patients with a marked decrease in their pain scores. Thus there seem to be two populations of individuals who will or will not respond to desmopressin. This was reported previously in two different studies (1, 2), in which 44% and 54% of patients, respectively, had complete pain relief. However, the underlying mechanism(s) are unknown; some authors suggest that it could be caused by individual variation in the intranasal absorption of desmopressin (10). Explaining these findings may detect factors that could be used to identify those patients in whom intranasal desmopressin may be more effective. As in a previous study (1), the administration of an NSAID with desmopressin was very effective in relieving pain, although the desmopressin was given before the NSAID and not simultaneously. NSAID action is more effective in the presence of higher plasma levels of ADH (4). In group C, none of the patients remain not responding to treatment after 20 min, which suggests that an NSAID with desmopressin may potentate each drug's analgesic effect, with no significant increase in adverse reactions. The mechanisms of action of NSAIDs and desmopressin were mentioned previously (8-12). The antiuretic effect of desmopressin is more intense than that induced by PG inhibition, but it is not caused by a decrease in renal blood flow. The antiuretic action of NSAIDs may in effect be nephrotoxic, by decreasing renal blood flow and the GFR (through an increase in preglomerular resistance) in an already obstructed, dysfunctional kidney. This functional compromise is not clinically detectable, as PG inhibitors act selectively on the obstructed kidney, leaving the contralateral organ unscathed and allowing serum creatinine levels to remain within normal limits (13). The ease of administration of desmopressin, its low cost, good tolerability and lack of clinically relevant side effects make it safe. Studies using desmopressin therapy for up to 3 years have shown no toxic reactions or significant changes in laboratory values. Thus the results of the present study suggest that desmopressin intranasal spray may be a useful addition to the therapy for renal colic, either alone or combined with NSAIDs. It is a safe drug which is easy to administer and apparently effective in treating renal colic. Other issues which need to be explored include the optimum dosage, method of use (i.e. in an ambulatory setting), whether there is a reduction in the need for diagnostic or
therapeutic interventions and whether it reduces the rate of hospital admissions. That there seem to be some patients who do not respond or respond only minimally to desmopressin needs further clarification; characteristics should be identified in this group which might explain their lack of response. In conclusion, these results indicate that desmopressin may be used to treat renal colic either alone or combined, increasing the analgesic effect of other drugs like diclofenac.

References