INVESTIGATIVE UROLOGY

Role of papaverine hydrochloride administration in patients with intractable renal colic: randomized prospective trial.

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Objectives: To evaluate the therapeutic effect of papaverine hydrochloride in the treatment of patients with renal colic pain unresponsive to conventional treatment.
Methods: From March 2007 to January 2008, a total of 561 patients with severe renal colic pain due to a ureteral stone were treated with conventional agents (hyoscine-N-butylbromide and diclofenac sodium) in the emergency and urology departments. Of these 561 patients, 110, with no response to the treatment and persistent severe pain, were randomized into 3 groups for additional treatment. The patients in group 1 (n = 37) received intravenous hyoscine-N-butylbromide, those in group 2 (n = 37) received papaverine hydrochloride, and those in group 3 (n = 36) received pethidine. Before and after treatment, all patients completed a visual analog scale (VAS) questionnaire, with a scale of 0 (no pain) to 10 (maximal complaint), to measure their subjective pain. The mean VAS score of each group was compared with that of the other groups.
Results: The pretreatment mean VAS scores of all 3 groups were not significantly different statistically from each other (4.02 +/- 1.20, 4.36 +/- 1.97, and 4.27 +/- 1.50; P > .05). However, after treatment, the mean VAS scores of the patients treated with papaverine (0.93 +/- 0.29) and pethidine (0.81 +/- 0.38) were significantly different from those of the hycosine group (3.67 +/- 2.21; P < .001). However, the mean VAS scores of groups 2 and 3 were comparable (P = .67). Unlike opioids, no papaverine-related severe side effects were observed.
Conclusions: Our results indicate that papaverine hydrochloride can used in an effective manner in the management of renal colic pain in patients unresponsive to commonly used conventional agents.

Editorial Comment

Out of 561 patients with severe renal colic due to ureteral stone treated with hyoscine-N-butylbromide and diclofenac sodium, 110 who did not responded to the treatment were randomized into 3 groups for additional treatment.

The treatment protocol for these 3 groups consisted of a second repeat dose of intravenous hyoscine-N-butylbromide (20 mg in 250 mL 0.9% physiologic saline) administered within 20 minutes to group 1 (n _ 37); papaverine HCl (60 mg in 250 mL 0.9% physiological saline) administered intravenously within 20 minutes to group 2 (n _ 37); and pethidine (50 mg in 250 mL 0.9% physiologic saline) administered intravenously within 20 minutes to group 3 (n _36). No general side effects associated with hyoscine-Nbutylbromide or papaverine HCl administration was noted. However, a mild degree of bradycardia and hypotension occurred in 2 patients (5.5%) in the pethidine group, as well as mild to moderate degree of sedation in 13 patients (36%). The authors found that the severity of the pain was significantly diminished in the papaverine and pethidine groups (without significant difference between then).

The authors speculated that smooth muscle relaxation could be accepted as the main factor for papaverine action; nevertheless, the exact underlying mechanism of action could not be derived from the present study. The authors also proposed that possible changes caused by decreased renal output following the renovascular hemodynamic changes could also be responsible for this clinical effect.

It was concluded that although the classic and established conventional management of renal colic pain is highly effective, before second line opioid application, papaverine administration might be a valuable alternative for these patients.

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An in vitro study on human ureteric smooth muscle with the alpha1-adrenoceptor subtype blocker, tamsulosin.

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Objective: To study the effects of tamsulosin on ureteric contractions and its effects on the basal tone of human ureteric specimens, as clinical trials with tamsulosin have shown promising results in the spontaneous expulsion of lower ureteric calculus, but the mechanism of action of tamsulosin in the expulsion of ureteric calculus has not been elucidated in in-vitro studies on human ureters.
Materials and Methods: Human mid-ureteric specimens were obtained from live kidney donors. The specimen was transported in Krebs' solution and the isometric contraction of human ureteric smooth muscle was recorded in the presence of tamsulosin. Ureteric rings from 19 kidney donors were studied.
Results: At 100 microm tamsulosin the frequency of ureteric contraction was blocked completely, or the contraction frequency was reduced in 89% of specimens. There was no change in the frequency or in the amplitude of contraction in the remaining specimens. The basal tone of the ureter was reduced in 16% of the specimens.
Conclusion: Our results suggest that peristaltic activity in human ureteric smooth muscle is inhibited by tamsulosin. The effect of tamsulosin on basal tone is marginal.

Editorial Comment

Previous studies hypothesized that tamsulosin relaxes the ureteric smooth muscle, thereby facilitating the spontaneous passage of stone. Clinical studies demonstrated that tamsulosin decrease the colic pain and the number of colic episodes. Nevertheless, the exact mechanism of action is still controversial. The authors found that tamsulosin decreased or completely blocked the peristaltic contractions in 17 of 19 ureteric specimens studied in vitro. However, tamsulosin did not produce a decrease in baseline tension in 16 of 19 specimens. The results of this work support that the mechanism of action of tamsulosin is the inhibition of peristaltic contractions, and do not support the hypothesis that it causes a relaxation of ureteric smooth muscle.

In conclusion, the present study elegantly demonstrates that peristalsis in human ureter is inhibited by tamsulosin.

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