The Effect Of Pinaverium Bromide On Gallbladder Motility In Humans

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ZET

Ön nesilarda Pinaverium Bromide’nin Safra Kesesi Motilitesi Üzerine Etkisi


Çalışmaya 20 sağlıklı görevlendi. Safra kesesi volümleri ultrasonografik olarak ölçüldü. Bazal ölçümler yapıldıktan sonra 10 ar kişilik gruplar halinde ölçüllülere 5 mg pinaverium bromide veya placebo, sabah oral yoldan verildi. 1 saat sonra 60 dakika süre ile 15 dakikada bir ölçümler yineleldi. Tüm hastalarda açık sahra kesesi volümü pinaverium bromide ile bazal ölçüme göre % 38-67 oranında (p<0.05-p<0.001) kontrolde göre ise % 36-66 (p<0.05-p<0.001) oranında artış gösterdi.

Sonuçta pinaverium bromide’nin safra kesesi kontraksiyonunu azalttığı ve bunun klinik olarak bilers diskinezili ve ağrı hastalarda kullanılabileceğini sonucuna varildı.

Anahtar kelimeler: Safra kesesi motilite, Pinaverium Bromide.

SUMMARY

Calcium antagonists which block the influx of calcium into muscle fibers also inhibit contraction. Thus, drugs that control the entry of calcium into cell by acting as calcium channels would inhibit gastrointestinal hypermotility and spasm. Pinaverium bromide (a calcium channel blocker) is used to relieve pain, spasm and motility disturbances of the gastrointestinal tract. Therefore we investigated the effect of pinaverium bromide on fasting gallbladder volume in normal subjects.

Twenty healthy volunteers participated in this study. The gallbladder volumes were measured using ultrasonography. After the basal measurement was taken, the subjects received either 5 mg pinaverium bromide (n:10) or a placebo (n:10) per oral in the morning hour before rescanning. The gallbladder was rescanned in 15 min intervals for 60 min. In all subjects, pinaverium bromide increased fasting gallbladder volume by 38 %-67% compared to the baseline (p<0.05 and 0.001) and by 36%-66% compared to the placebo group (p<0.05 and p<0.001). In conclusion, pinaverium bromide significantly affects gallbladder contraction. This effect of pinaverium bromide may be of clinical usefulness in patients with biliary dyskinesia and pain.

Key Words: Gallbladder motility, Pinaverium Bromide.

INTRODUCTION

The gastrointestinal submucosa is surrounded by two perpendicular layers of smooth muscle fibers. The inner, circular muscle layer is responsible for concentric contractions and segmentation of the digestive tract, while the outer, longitudinal layer is responsible for the progression of intestinal contents. Together they induce peristalsis and ensure harmonious transit. The outer envelope is called serosa.'
Table 1: Effect of Pinaverium Bromide on Gallbladder Volume

<table>
<thead>
<tr>
<th>Groups</th>
<th>The mean volume after administration of therapy in different time (Min)</th>
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<tbody>
<tr>
<td>Control</td>
<td>Baseline 60 75 90 105</td>
</tr>
<tr>
<td></td>
<td>17.6±8.2 20.3±10 20.1±9.8 18.9±9 19.2±10</td>
</tr>
<tr>
<td>Pinaverium</td>
<td>18.8±4 27.9±10TT 27.9±10TT 29.2±12TTTT 31.4±11TTTT</td>
</tr>
</tbody>
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US: No significance
*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 difference from control
*p<0.01, **p<0.001, ***p<0.0001 difference from baseline

Calcium antagonists show clearly different selectivities for the 3 types of smooth muscles. While nifedipine and diltiazem are used clinically in the treatment of angina and hypertension (vascular smooth muscle), verapamil in the treatment of angina and cardiac tachy arrhythmia (cardiac muscle) and flunarizine in the treatment of migraine, pinaverium bromide is used to relieve pain, spasm and motility disturbances of the gastrointestinal tract (by acting on the gastrointestinal smooth muscle).

A study has been reported concerning the use of nifedipine, verapamil or diltiazem in a limited number of patients in the treatment of dyskinesia of the sphincter of Oddi.

In a very wide class of calcium antagonists, pinaverium bromide therefore holds a special place: as a calcium antagonist, it shares a number of pharmacodynamic and electrophysiological properties with other molecules belonging to this class, but, as a drug targeted selectively at the gastrointestinal tract, it is different from the previous cardiovascular calcium antagonists. The properties of pinaverium bromide have been studied at the clinical, cellular and molecular levels. Several pharmacological studies in man show the relaxation of the sphincter of Oddi in patients with biliary dyskinesia after having received pinaverium bromide.

The aim of this study is to show the effect of pinaverium bromide on fasting gallbladder contractions in normal subjects.

MATERIAL AND METHODS

Twenty healthy volunteers (mean age 45±12 years, all within ± 12% of ideal body weight) agreed to participate in the study after the protocol and test procedures had been explained to them. All the subjects completed the protocol.

Scans were performed at 9 am after a 12 h fast. After the baseline measurement was taken the volunteers received either 5 mg pinaverium bromide (n:10) or a placebo (n:10) per oral in the morning one h before scanning. The gallbladder was rescanned in 15 min intervals for 60 min.

The gallbladder volumes were measured using ultrasonography. Using a 3.5 or 5 MHz transducer, real time ultrasound scans were obtained with Siemens Sonoline SL-2 3.5 MHz. Subjects were scanned supine in the right anterior oblique position by a radiologist trained in ultrasonography. The gallbladder was visualized in the longitudinal and transverse planes, and measurements of the maximum length, width, and height were taken in duplicate. The volume of the gallbladder was subsequently calculated using the ellipsoid method (volume=0.52×length×width×height).

The results are expressed as mean±SEM unless otherwise stated. For statistical analysis, the wilcoxon signed-rank test or Mann Whitney-U test was used where appropriate. The level of significance was set at p<0.05.

RESULTS

As shown in table 1, the fasting gallbladder volumes of the control group were 17.6±8.2; 20.3±10; 20.1±9.8; 19.2±10 ml at the baseline after 60, 75, 90, 105 min respectively. The fasting gallbladder volumes of the pinaverium group were 18.8±4 ml 27.9±10; 29±12; 31.4±11; 34.8±13.2 ml at the baseline after 60, 75, 90, 105 min respectively. In all subjects, pinaverium bromide increased the fasting gallbladder volume by 48% (p<0.01), 55% (p<0.01), 67% (p<0.001), 85% (p<0.0001) compared to the baseline, and by 37% (p<0.05), 45% (p<0.01), 66% (p<0.001), 81% (p<0.0001) compared to the placebo group after 60, 75, 90, 105 min respectively (Table 1, Figure 1).

DISCUSSION

This study demonstrated that pinaverium bromide significantly decreased
the fasting gallbladder contraction in healthy subjects. Until now no study had addressed directly the effect of pinaverium bromide on gallbladder motility. Several pharmacological studies in man show the relaxation of the sphincter of Oddi in patients with biliary dyskinesia after having received pinaverium bromide. 

In a calcium-free medium in vitro, gastrointestinal tract segments stop contracting because of the lack of calcium influx into smooth muscle fibers and the rapid exhaustion of intracellular stocks. Calcium antagonists, which block the influx of calcium into muscle fibers, also inhibit contraction. Thus, drugs that control the entry of calcium into the cell by acting as calcium channels would inhibit gastrointestinal hypermotility and spasm, regardless of the hormonal or neuronal supracellular control mechanisms involved.

Calcium antagonists show clearly different selectivities for the 3 types of smooth muscles. While nifedipine and diltiazem are used clinically in the treatment of angina and hypertension (vascular smooth muscle), verapamil in the treatment of angina and cardiac tachyarrhythmia (cardiac muscle) and flunarizina in the treatment of migraine, pinaverium bromide is used to relieve pain, spasm and motility disturbances of the gastrointestinal tract (by acting on the gastrointestinal smooth muscle).

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In conclusion, pinaverium bromide significantly affects gallbladder contraction. This may be of clinical usefulness in patients with biliary dyskinesia and pain.

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