LETTER TO THE EDITOR

Cabergoline and gallbladder motility in healthy men

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Cozzi et al. (1) have shown that cabergoline, a synthetic ergoline derivative with an extremely long half-life (2, 3), is effective in the management of acromegalic patients resistant to somatostatin analogs, suggesting that cabergoline is a worthy therapeutic tool in these patients: it can be administered by the oral route and is much less expensive. Dopaminergic drugs are characterized by a poor gastrointestinal tolerability, especially nausea, vomiting and constipation: these effects occur early during treatment, and seem to be less frequent with cabergoline than with bromocriptine (4). Other drugs which can induce constipation, like opioids and somatostatin analogs, often reduce gallbladder motility (5, 6). The aim of this study was to evaluate the effect of cabergoline on gallbladder motility in healthy men.

According to a protocol approved by the local ethics committee and performed following the Good Clinical Practice of the European Community, ten healthy men aged 24.1 ± 0.59 years (mean ± S.E.) were admitted at 0700 h on the first day at the Unità di Farmacologia Clinica of Istituto San Raffaele where they remained for 48 h.

At 0800 h on the second day they received a single dose of cabergoline (Dostinex, Pharmacia Upjohn, Milan, Italy: 1 mg tablet) before breakfast.

During the period of hospitalization, all subjects received a standard 1800 calorie diet (20% at breakfast at 0800 h, 40% at lunch at 1300 h, 40% at dinner at 2000 h).

Ultrasound scanning for the evaluation of the gallbladder volume (ml) was performed by the same physician on both days of the study immediately before lunch (V0) and 1 and 2 h after lunch (V60 and V120 respectively). Evaluation of gallbladder volume was obtained using a real-time linear array, 3.5 MHz measuring the greatest longitudinal, transverse and sagittal diameters. Gallbladder size was calculated according to Everson’s formula (7) (volume = \( \frac{1}{6} abc \), where \( a \) is the longitudinal diameter, \( b \) is the transverse diameter and \( c \) is the sagittal diameter). Gallbladder emptying was assessed by evaluating the difference between two consecutive readings.

Data are expressed as the mean ± S.E. at each time interval (V0, V60, V120) and the comparisons were performed using Student’s t-test for paired data. \( P \) values <0.05 were considered statistically significant.

Table 1 shows that gallbladder volume was greater on day 2 than on day 1 at 60 min, but not at 120 min, suggesting a delay in gallbladder emptying during the first 60 min.

Drugs which induce constipation, like opioids and somatostatin, can reduce gallbladder motility; in this study we found that cabergoline delays but does not reduce gallbladder emptying. The mechanism of action of cabergoline in delaying gallbladder emptying is a matter of speculation: dopamine and bromocriptine act on the gastrointestinal tract through interaction with dopaminergic and with \( a_2 \)-adrenergic receptors (8). Other possibilities include interaction with hormones which stimulate gallbladder motility such as cholecystokinin, neuropeptide Y, secretin, substance P, or with hormones which inhibit gallbladder motility such as pancreatic polypeptide, somatostatin or vasoactive intestinal polypeptide (9, 10).

In conclusion acute administration of cabergoline delays, but does not block, gallbladder emptying, and therefore cabergoline, under chronic administration is unlikely to promote gallstones.

Table 1. Gallbladder volumes (ml, means ± S.E.) in subjects evaluated after no drug (day 1) and after cabergoline (day 2).

<table>
<thead>
<tr>
<th>Time intervals (mins)</th>
<th>Gallbladder volumes</th>
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<tbody>
<tr>
<td></td>
<td>No drug day 1</td>
</tr>
<tr>
<td>V0</td>
<td>13.5 ± 0.67</td>
</tr>
<tr>
<td>V60</td>
<td>6.16 ± 0.70</td>
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<tr>
<td>V120</td>
<td>2.9 ± 0.51</td>
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</tbody>
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References

3 Andreotti AC, Pianezzola E, Persiani S, Pucciariello MA, Strolin Benedetti M & Pontiroli AE. Pharmacokinetics, pharmacodynamics, and tolerability of cabergoline, a prolactin-lowering drug, after administration of increasing oral doses (0.5, 1.0 and 2.0 mg).

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