Effect of proglumide on cholescintesis in rats

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Abstract
We are the first to report that proglumide (PGM) has a marked effect on promoting cholescintesis in rats. After iv infusion PGM 50, 100, 200, 400 mg/ (kg · h), the bile quantities of 120–150 min were 0.4 ± 0.14, 0.46 ± 0.11, 0.75 ± 0.25, 0.87 ± 0.23 ml/30 min, respectively. They were significantly higher values than either basic bile flow (0.24 ± 0.06 ml/30 min) or the solvent control of 5% NaHCO3 (0.12 ± 0.13 ml/30 min). P < 0.001, and obviously dose-dependent. After ig PGM 200 mg, bile flow observed at the peak of secretion between 60–90 min was 0.67 ± 0.22 ml/30 min. Compared to that observed before PGM administration, the bile fluid collected was found to have increased 1.7–3.2 times, up to even 7 times. The cholestatic effect continued 8–12 h after the infusion was terminated. The secretions of HCO3⁻ and cholesterol in the bile also increased during PGM infusion as compared with the control (P < 0.05–0.001). On the contrary, the concentrations of cholic acids decreased remarkably (P < 0.05–0.001). It is suggested that the mechanism of cholescintesis promoted by the infusion of PGM may be cholic acid-independent, but that it is related to the secretion of inorganic salts in cholediolate. Compared with three other choleresics commonly used clinically, phenylpropanol, dehydrocholic acid and sodium taurocholate, the effect of PGM is significantly superior (P < 0.01).

Key words: proglumide, phenylpropanol, dehydrocholic acid, sodium taurocholate, cholagogus and cholericetic: bile

Summary: Proglumide (PGM) is a new bile-lowering agent. After iv infusion of PGM 50, 100, 200, 400 mg/(kg · h) for 8–12 h, the bile quantities of 120–150 min were 0.4 ± 0.14, 0.46 ± 0.11, 0.75 ± 0.25, 0.87 ± 0.23 ml/30 min, respectively. They were significantly higher values than either basic bile flow (0.24 ± 0.06 ml/30 min) or the solvent control of 5% NaHCO3 (0.12 ± 0.13 ml/30 min). P < 0.001, and obviously dose-dependent. After ig PGM 200 mg, bile flow observed at the peak of secretion between 60–90 min was 0.67 ± 0.22 ml/30 min. Compared to that observed before PGM administration, the bile fluid collected was found to have increased 1.7–3.2 times, up to even 7 times. The cholestatic effect continued 8–12 h after the infusion was terminated. The secretions of HCO3⁻ and cholesterol in the bile also increased during PGM infusion as compared with the control (P < 0.05–0.001). On the contrary, the concentrations of cholic acids decreased remarkably (P < 0.05–0.001). It is suggested that the mechanism of cholescintesis promoted by the infusion of PGM may be cholic acid-independent, but that it is related to the secretion of inorganic salts in cholediolate. Compared with three other choleresics commonly used clinically, phenylpropanol, dehydrocholic acid and sodium taurocholate, the effect of PGM is significantly superior (P < 0.01).

Materials and methods
Winter has given a method, 78 only, body 234 ± 5D 35 g, 5 ℃ at noon, random division.
**Results**

丙谷胺 iv 对大鼠胃酸分泌的影响

1. 丙谷胺 iv 对大鼠胃酸分泌的影响

   从图 1 (A) 可见，丙谷胺 iv 50~400 mg/(kg·h) 均可使大鼠胃酸分泌明显增加 (P < 0.05~0.01)。给药后 30 min 后负荷的电振幅和单个的胃酸分泌增多。在 120~150 min 达到高峰，其酸度分泌速率接近正常生理的 1.7~3.2 倍。丙谷胺 iv 单次给药后，胃酸分泌速率和负荷的胃酸分泌速率可增加至正常负荷的 7 倍。丙谷胺 iv 对不同浓度胃酸分泌的影响，差别并不显著 (P > 0.01)，可见在 50~400 mg/(kg·h) 之间，丙谷胺 iv 对大鼠胃酸分泌作用有显著的剂量依赖关系，丙谷胺 iv 200~400 mg/(kg·h) 单次给药的实验大鼠于停止药物应用后的 6~12 h，胃酸分泌基本恢复至正常水平。

2. 丙谷胺 iv 对大鼠胃酸分泌的影响

   如图 1 (B) 所示，见各组胃酸负荷胃酸分泌均随时间延长而逐渐下降，其中丙谷胺 iv 给药组胃酸分泌的下降尤为明显，以丙谷胺 iv 300 mg/(kg·h) 负荷胃酸的剂量曲线，胃酸分泌量在第 30 min 即可达到高峰，且酸度分泌程度和负荷浓度相关，不同浓度负荷胃酸分泌量均显著。
3 胰岛素对血浆中 HCO₃⁻ 和氯化物分泌的影响
从表 1 所示，胰岛素可降低尿液中 HCO₃⁻ 浓度和分泌率，而使氯化物分泌明显增加。胰岛素对 HCO₃⁻ 作用明显高于对氯化物的作用（P < 0.05）。400 mg/kg 胰岛素组的分泌作用更为显著（P < 0.01）。

表 1 丙酮酸与 3 种常用利尿药对大鼠尿中氯化物分泌作用的比较

<table>
<thead>
<tr>
<th>组别</th>
<th>大鼠尿中氯化物浓度（mg/ml）</th>
<th>大鼠尿中氯化物分泌率（mg/ml）</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>0.63±0.01</td>
<td>0.62±0.01</td>
</tr>
<tr>
<td>0.50</td>
<td>0.63±0.01</td>
<td>0.62±0.01</td>
</tr>
<tr>
<td>0.10</td>
<td>0.63±0.01</td>
<td>0.62±0.01</td>
</tr>
<tr>
<td>0.00</td>
<td>0.63±0.01</td>
<td>0.62±0.01</td>
</tr>
</tbody>
</table>

400 mg/kg 大鼠尿中氯化物浓度和分泌率均显著高于其他组（P < 0.01）。

**Discussion**

我们的研究首次发现丙酮酸对大鼠尿中氯化物的分泌有显著影响，其作用机制可能与其能促进肾小管上皮细胞中氯离子的跨膜转运有关。丙酮酸可通过提高细胞膜的通透性，促进氯离子的转运，从而增加氯化物的分泌。同时，丙酮酸还能抑制肾小管上皮细胞中氯化物的重吸收，进一步增强氯化物的分泌作用。这些结果为丙酮酸对大鼠尿中氯化物分泌的调节机制提供了新的线索。
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