Short communication

Effect of 4-hydroxyandrost-4-ene-3,17-dione (formestane) on the bile secretion and metabolism of 4-\(^{14}\)C-cholesterol to bile acids

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Abstract:

4-Hydroxyandrost-4-ene-3,17-dione (formestane) is a selective aromatase inhibitor. It is indicated for postmenopausal patients with advanced breast cancer.

The aim of the present study was to investigate the effect of 4-hydroxyandrost-4-ene-3,17-dione on the bile secretion and metabolism of 4-\(^{14}\)C-cholesterol to bile acid.

The experiments were carried out in the ovariectomized and sham-operated female Wistar rats. Formestane (20 mg/kg, \(\text{im}\), daily) was administered to animals for 2 weeks. Twenty four hours after the last drug administration, rats were anesthetized with ethyl urethane.

4-\(^{14}\)C-cholesterol (740 kBq/kg, s.a. 2.28 GBq/mmol) was infused for 1 min by catheter inserted into the jugular vein. Bile samples were assayed for total \(^{14}\)C radioactivity. \(^{3}\)C-bile acids were determined in bile (after thin-layer chromatographic separation) by the use of isotopic technique with liquid scintillator.

Previous studies showed that systemic adverse effects occurred in about 12% of patients following intramuscular drug administration. Many of them such as hot flushes, vaginal spotting and emotional lability were related to the mechanism of action of formestane i.e. estrogen suppression. Lethargy, rash, nausea, dizziness, indigestion, ataxia, cramps and facial swelling have also been reported.

The results of the present study have shown that formestane administered to the female ovariectomized rats decreased the bile secretion and diminished conversion of 4-\(^{14}\)C-cholesterol to trihydroxy bile acids. The decreased synthesis of trihydroxy bile acids and increased concentrations of cholesterol and lithocholic acid in bile may be associated with increased risk of gallstone formation.

**Key words:**

formestane, cholesterol, bile