Effects of Ethanol on Sodium, 3-O-Methyl Glucose, and L-Alanine Transport in the Jejunum

YUH-JYH KUO, MS, and L.L. SHANBOUR, PhD

Ethanol has been reported to inhibit the absorption of amino acids and glucose (1-4) when administered into the intestinal lumen of the rat. The absorption of these organic substances is dependent to a considerable extent on the active transport of sodium across the intestine (5, 6). The mechanism of inhibition of glucose and amino acid transport which are linked with Na⁺ transport has not been completely documented. Although Dinda et al (7) found that 2.6% (v/v) ethanol inhibited glucose transport and mucosal (M) to serosal (S) Na⁺ flux but did not affect net Na⁺ flux in the hamster jejunum, it was still uncertain whether ethanol inhibited the active absorption of Na⁺, since neither M-to-S Na⁺ flux nor net Na⁺ flux could represent the active transport of Na⁺ due to the presence of electrochemical gradients across the mucosa in their studies.

Net absorption of Na⁺ is evident when D-glucose or 3-O-MG is present in the bathing bicarbonate Ringer solution (8) in the isolated rabbit jejunal mucosa. This in vitro technique was used in the present studies to determine the effects of ethanol on the fluxes of Na⁺, Cl⁻, and two actively transported but not metabolized organic solutes, 3-O-MG and L-alanine (5). The advantages of these studies are: (1) The net flux represents the active transport of the electrolyte or organic substance since the electrochemical gradients across the mucosa are maintained at zero. (2) The changes in unidirectional fluxes represent changes in permeability. (3) The changes in the electrophysiological parameters, including electrical potential difference (PD) and short-circuit current (Isc), can also be simultaneously detected.

It is well established that the effects of ethanol on intestinal function are dose dependent (1, 3, 7, 9, 10). Israel et al (4) have found that the ethanol concentration is about 1-3% in the human upper jejunum during moderate drinking. However, the concentration of ethanol in the jejunal lumen could increase to over 6% with prolonged alcohol consumption (11). Several concentrations of ethanol, 1.8, 3.0, and 5.4% were selected in this study because they would approximate the concentration present in the jejunal lumen when drinking table wine, one martini, and common spirits, respectively.
MATERIALS AND METHODS

New Zealand white rabbits (Oryctolagus cunicutus), weighing 1.5-3.0 kg, were anesthetized with intravenous administration of nembutal (approximately 25-50 mg/kg). The abdomen was opened and the jejunum just distal to the ligament of Treitz was excised. After dissecting off the serosa and muscularis (12), paired adjacent segments of the mucosal surfaces were mounted in Ussing type flux chambers with an aperture of 1 cm² between the two compartments. The mucosal and serosal surfaces of the tissues were bathed with 10 ml of identical ionic solutions of bicarbonate Ringer maintained at 37 °C with a thermoregulator. The solutions were gassed with 95% O₂-5% CO₂ and had the following ionic composition, in millimoles per liter: Na⁺, 141; K⁺, 10; Mg²⁺, 1.1; Ca²⁺, 1.25; Cl⁻, 127; HCO₃⁻, 25; H₂PO₄⁻, 0.3; HPO₄²⁻, 1.6. Control tissues were incubated in bicarbonate Ringer with 10 mM of glucose (J.T. Baker Chemical Co.) or 3-O-MG or L-alanine (Sigma Chemical Co.), and experimental tissues were similarly incubated with the exception that the bicarbonate Ringer solution contained 1.8, 3.0, or 5.4% (v/v) ethanol. All tissues were short-circuited throughout the course of the experiment, but the current was interrupted periodically to determine the spontaneous transmembrane PD. Potential difference and Isc across the tissue were determined as previously described (13).

After PD and Isc stabilized, a 50-μl aliquot of radioisotopic ²²Na, ³⁶Cl, [¹⁴C]-3-O-MG, or [¹⁴C]L-alanine (New England Nuclear, approximately 3 μCi) was added to the opposite sides of paired mucosae. A 1-ml sample was removed from the unlabeled half chambers and replaced with the same fresh and prewarmed solutions at 20, 35, and 50 min after the addition of the isotopes. The Isc and PD of paired tissues were not significantly different. Unidirectional fluxes of Na⁺, Cl⁻, 3-O-MG, or L-alanine were measured as the mean value of two consecutive 15-min periods (14) in one direction from one chamber and in the opposite direction from the other chamber. The ²²Na, ³⁶Cl, [¹⁴C]3-O-MG, and [¹⁴C]L-alanine were counted in a liquid scintillation detector (Nuclear Chicago). The concentration of chloride was determined by a chloridometer (Buchler) and that of sodium by a flame photometer (Brinkman).

The effect of hyperosmolarity on the electrophysiology of the isolated rabbit jejunal mucosa was determined by using 940 mM mannitol in the bicarbonate Ringer solution. The first 30 min served as control, then the bicarbonate Ringer solution of both mucosal and serosal sides was replaced with fresh bicarbonate Ringer (control group), 5.4% ethanol (930 mOsm/liter, Precision Osmette osmometer), or 940 mM mannitol, respectively. Potential difference and Isc were recorded every 5 or 15 min.

The values reported are means ± standard errors. Differences were considered significant if the P value calculated from the Student's t test was less than 0.05.

RESULTS

Figure 1 illustrates the effects of various concentrations of ethanol on PD, Isc, and Na⁺ fluxes in the rabbit jejunum. The PD across the jejunum was 5.9 ± 0.3 mV, the mucosal side negative. This value was slightly higher than reported by Fromm (8), which was probably due to the different procedure employed; ie, removing the jejunum when the rabbit was anesthetized rather than after the animal was killed. Ethanol, at a concentration of 1.8%, did not significantly alter either PD or Isc. However, both PD and Isc were significantly decreased when the concentration of ethanol was increased to 3.0 or 5.4%. The unidirectional flux of Na⁺ from mucosa (M) to serosa (S) was significantly greater than the unidirectional S-to-M flux of Na⁺, resulting in a net flux which represented active transport of Na⁺ (Δ Na⁺) from M to S during short-circuited conditions. There was no difference between the net flux of Na⁺ and the Isc. Sodium fluxes were not significantly altered in the presence of 1.8% ethanol; but there was a marked decrease in net flux of Na⁺ with 3% ethanol. Ethanol at 5.4%, in addition to inhibiting active Na⁺ transport, also increased uni-

---

Dig Dis 23:52-66, 1978


---

Digestive Diseases, Vol. 23, No. 1 (January 1978)