Rectal hyperpolarization following intestinal bypass for obesity

J. RASK-MADSEN¹, P. BRIX JENSEN, AND J. O. LUND

From the Medical Department F and the Department of Clinical Physiology, Glostrup Hospital, Glostrup, Denmark

SUMMARY The electrical potential difference across the rectal mucosa in six shunt-operated women was compared with that obtained in 26 normal females. The potential difference was considerably increased in all the patients, whereas the plasma concentrations and the transmural fluxes of sodium, chloride, and potassium were within normal ranges. Based on measurements of plasma renin and plasma aldosterone concentrations in three of the patients, the possibility of secondary hyperaldosteronism could be ruled out.

Intestinal bypass for obesity is followed by frequent diarrhoeas, which are probably caused in part by the action of bile salts on the colonic epithelium (Hofmann, 1967). It seemed of interest, therefore, to investigate whether the transmural potential difference generated by rectal mucosa (Geall, Spencer, and Phillips, 1969; Dalmark, 1970; Edmonds and Godfrey, 1970) would reflect the recently reported changes in colonic absorptive capacity induced by bile acids (Mekhjian, Phillips, and Hofmann, 1971). In addition to measurements of the rectal potential difference, the plasma concentrations of Na⁺ and K⁺, and the transmural fluxes of electrolytes in six shunt-operated females, we have measured the plasma concentrations of aldosterone and renin in three of the patients, as the potential difference might also be influenced by secondary hyperaldosteronism provoked by sodium depletion (Edmonds, 1967; Edmonds and Richards, 1970), if any, induced by the pronounced loss of faecal fluids.

Patients and Methods

Six consecutive patients, all females between 20 and 48 years of age, were investigated four to 28 months after intestinal bypass for obesity (preoperative weight 101 to 139 kg). All had an end-to-side jejuno-ileostomy, the anastomosis being established

between jejunum 37 cm distally to the ligament of Treitz and ileum 10 cm proximally to the junction of the ileum with the colon. The patients were in a good general condition at the time of the investigation, and so were the 26 normal females, who comprised healthy volunteers and patients in a medical ward without any recognized disease of the large bowel, liver, kidneys, or circulatory system. None of the controls or the patients studied received corticosteroids, diuretics, or lithium salts. A single patient (case 4) had been treated with cholestyramine (Cuemid) for a fortnight two months before the investigation, and another patient (case 1) was currently being treated with digoxin for auricular fibrillation. The individual weight loss obtained by the patients so far, as well as the number of daily bowel movements, are given in the table. Measurements of the transmural potential difference were performed in all patients postoperatively, and in a single patient (case 6) preoperatively as well. Blood samples were obtained simultaneously with the potential difference after about half an hour of rest for determination of sodium, potassium, aldosterone, and renin in plasma. The experimental nature of the investigation was explained to all patients.

The transmural potential difference was measured at sigmoidoscopy by a modification of the method previously described (Rask-Madsen, Baastrup, and Schwartz, 1972) connecting one of two balanced calomel half-cells (Radiometer, Copenhagen) directly to the negative input of the recorder (Servogor S-RE 541, Goerz Electro, Vienna, internal resistance 10⁸ ohm, measuring current <10⁻⁷ Amp) and to a

¹Requests for reprints should be addressed to J.R.-M., Medical Department F, Glostrup Hospital, DK-2600 Glostrup, Denmark.

Case	Months after Operation	Total Weight Loss (kg)	No. of Bowel Movements Daily	PD (mV)	Concentration in Plasma				Transmural Electrolyte Flux ($n\text{-equiv} \times \text{min}^{-1} \times \text{cm}^{-2}$)				
					Na ⁺ m-equiv/l	K ⁺ m-equiv/l	Aldosterone (ng/100 ml)	Renin ($\mu\text{g/ml}$)	Na ⁺ Net	Na ⁺ out of Lumen	Na ⁺ into Lumen	Cl ⁻ Net	K ⁺ Net
1	28	37	5-6	-65	143	3.6	—	—	—	—	—	—	—
2	15	50	1-2	-65	142	4.0	—	—	176	232	56	208	-53
3	9	15	5-6	-67	142	3.8	4.1	31	—	—	—	—	—
4	9	31	2-7	-80	139	3.8	<1.5	11	241	343	102	249	-175
5	7	42	6-8	-55	140	4.3	—	—	175	316	141	236	-140
6	4	14	5-6	-69 ¹	142	4.2	3.8	9	254	299	45	298	-130
Healthy subjects	mean $\pm$ SD			-46 $\pm$ 3					238 $\pm$ 111	308 $\pm$ 120	70 $\pm$ 49	283 $\pm$ 99	-141 $\pm$ 70
	range			(-41)-(-55)	134-144	3.6-4.8	3-18	6-60					

Table I Clinical data and values of the potential difference across the rectal wall, the transmural electrolyte fluxes, and concentrations of sodium, potassium, aldosterone, and renin in plasma of six shunt-operated females compared with the corresponding values obtained in normal subjects

¹ Transmural PD was -47 mV before operation.

vein of the forearm via a 154 mM NaCl salt bridge, whereas the other half-cell connected the positive input of the recorder with the exploring KCl salt bridge. The terminal porous plug of the KCl salt bridge was placed directly on the mucosa via the sigmoidoscope at various distances from the anus, and the transmural potential difference was continuously traced by the recorder.

The method of dialysis of faeces (Wrong, Metcalfe-Gibson, Morrison, Ng, and Howard, 1965) *in vivo* adapted for absorption studies by Edmonds (1971) was used for the estimation of transmural electrolyte fluxes. The composition of the solution in the dialysis tubes used to measure the electrolyte movements was 0.9% NaCl containing tracer doses of ²²Na. Concentrations of sodium and potassium were measured by flame photometry, whereas chloride was determined colorimetrically (Schales and Schales, 1941). The ²²Na activity (approximately 0.5 μCi ²²Na per litre) was measured in a sodium iodide well scintillation counter. Plasma renin concentrations were obtained by the method of Giese, Jørgensen, Nielsen, Lund, and Munck (1970), and plasma aldosterone was measured by radioimmunoassay. The original method of Mayes, Furuyama, Kern, and Nugent (1970) was slightly modified, as separation of free and bound aldosterone was performed by gel centrifugation.

Statistical analysis for the p values was by a two-tailed Wilcoxon test for two samples (Wilcoxon and Wilcox, 1964). The values of the potential difference and electrolyte fluxes in the controls are means $\pm$ SD.

Results

The individual values for the transmural potential

difference in shunt-operated patients as well as the mean values of the controls based on measurements in 26 healthy females are given in the table. The values in the patient group were significantly greater than those of the controls ($P < 0.001$), and there was no overlap. The magnitude of the potential difference appears to be independent of the weight loss and the time elapsing since the operation. The values for sodium and potassium concentrations in plasma were within the normal ranges, and so were the rates for sodium, chloride, and potassium fluxes across the rectal wall (SD based on 17 normal individuals Rask-Madsen and Jensen, 1973). Also the rates for bidirectional sodium fluxes were insignificantly different from those of normal subjects (Rask-Madsen and Jensen, 1973).

When measured, the plasma renin concentration was within the normal range. Plasma aldosterone was found to be subnormal in one case, and in the lower part of the normal range in the remaining two cases.

Discussion

The most interesting feature in the results of the present study is the pronounced augmentation of the transmural potential difference. The reason for the observed changes of mucosal polarization is unclear, but local changes in the molecular configuration of the mucosal membranes or their enzymes, induced by the surface active bile acids, as well as hormonal factors might be involved.

After the intestinal bypass described above, bile acid absorption by the ileum is reduced, and more bile acids reach the colon producing diarrhoea (Hofmann, 1967). Mekhjian *et al* (1971) tested human bile acids for their influence on electrolyte absorption in the human colon, and found that

dihydroxy bile acids inhibit absorption of sodium, chloride, and potassium, or even induce reversible secretion of these ions dependent on the concentration. In rabbit ileum it has been shown also that sodium influx across the mucosal border is inhibited by exposure of the mucosal surface to bile salts (Frizzell and Schultz, 1970). However, inhibition of sodium absorption, which is believed to be the source of the transmural potential difference in colon (Cooperstein and Brockman, 1959; Curran and Schwartz, 1960; Grady, Duhamel, and Moore, 1970), should predictably reduce this potential difference. Our results for transmural electrolyte flux measurements showed no significant alterations from normal. Secretion of chloride, which might result in great negative potentials, did not occur.

Although frequent diarrhoeas involving loss of water with the faecal fluids may lead to increased release of vasopressin, it has been demonstrated (Levitan and Mauer, 1968) that this hormone administered intravenously causes a decrease in colonic net sodium absorption. The possibility of secondary hyperaldosteronism, which is a known cause of increased potential difference across the human rectal mucosa (Edmonds and Richards, 1970), has been excluded by the simultaneous measurement of plasma aldosterone and plasma renin concentrations in three out of six cases. For the time being we can, consequently, give no explanation for the rectal hyperpolarization found in all patients studied. Prospective investigations of electrolyte metabolism and electrical polarization in response to intestinal bypass for obesity are in progress.

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