Alimentary tract and pancreas

Jejunal water and electrolyte absorption from two proprietary enteral feeds in man: importance of sodium content

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SUMMARY Jejunostomy losses of Na⁺ and water during enteral nutrition after massive intestinal resection may be severe. We have attempted to analyse this practical problem by using an in vivo perfusion technique in healthy volunteers to study Na⁺, water and nutrient absorption from a short (25 cm) segment of jejunum during perfusion of an isotonic solution of the elemental diet Vivonex. Further solutions made from the amino acid and carbohydrate components of Vivonex were also perfused in part I of the study in order to determine the causes of the marked Na⁺ and water secretion seen during Vivonex perfusion. Low initial Na⁺ concentration was found to be the major determinant of net Na⁺ secretion, initial Na⁺ concentration correlating significantly with Na⁺ absorption (r=0.95, n=7 p<0.001). Water absorption correlated with net absorption of NaCl (r=0.82, n=7 p<0.01). There was, however, a better correlation with total absorption of NaCl plus amino acids (r=0.99, n=7, p<0.01). In part II of the study separate isotonic solutions of NaCl, glucose, and the polymeric diet, Ensure were also studied. Net sodium secretion occurred during glucose and Ensure perfusion, as predicted from their low Na⁺ concentration. Owing to rapid sucrose absorption from Ensure there was substantial luminal disappearance of osmotically active particles and hence marked water absorption, which was accurately predicted using the regression equation for water absorption derived in part I, substituting sucrose absorption for amino acid absorption. We conclude that the marked Na⁺ and water secretion observed during Vivonex perfusion is not a unique property of this amino acid based diet but is due to its low Na⁺ content.

The considerable absorptive capacity of the normal human colon means that increased ileal flow caused by secretion of fluid in the jejunum, small intestinal disease, or jejunal resection, does not cause diarrhoea unless colonic function is significantly impaired.3 There are a few difficult patients, however, who after massive bowel resection have only a short segment of jejunum remaining, in whom water and electrolyte losses via the jejunostomy may be of life threatening proportions.4,5 During the immediate postoperative period administration of predigested diets has been recommended6 in order to ameliorate the severe malabsorption of nutrients, water and electrolytes which inevitably ensues. Physiological studies in healthy volunteers have, however, shown considerable net water secretion into the jejunum during continuous nasogastric feeding of the elemental amino acid-based diet Vivonex,7 implying that jejunostomy losses would be increased by such a diet, perhaps because of secretion induced by its high concentration of free amino acids as has been recently reported with arginine.8 Interpretation of these findings is complicated by the unknown contribution of gastric and pancreatic outputs to the net water secretion observed. We have therefore re-studied this problem using a double-lumen perfusion system9 which incorporates a proximal occlusive balloon to exclude these secretions from the study segment. Preliminary studies10 showed that net water...
secretion occurred during jejunal perfusion with isotonic solutions of Vivonex while net water absorption was observed when isotonic solutions of the polymeric diet, Ensure, were similarly perfused. The aim of the present study was therefore to separately study the various components of Vivonex in order to identify the cause of the net water secretion and thereby to allow prediction of the feed composition which would maximise jejunal water and electrolyte absorption.

Methods

Subjects

After an overnight fast, 21 healthy volunteers were intubated with a standard multilumen perfusion tube assembly incorporating a 25 cm study segment with a proximal occlusive balloon. The tube was passed under fluoroscopic control until the infusion port lay 10 cm beyond the duodeno-jejunal flexure, when the occlusive balloon was inflated until the subject was just aware of it. Pancreaticobiliary secretions accumulating proximal to the balloon were aspirated via a proximal port to prevent contamination of the study segment. Perfusion of the study segment was then started at 20 ml/min. After a 30 minute period of perfusion with isotonic saline to flush out the test segment solutions were perfused in random order, usually four per subject, and after a 30 minute equilibration period, 3×10 minute samples were collected by syphoning into a container surrounded by crushed ice. Samples were immediately analysed for osmolality, pH, and free glucose, while the remaining assays were performed on a separate aliquot kept at −20°C. The constancy of polyethylene glycol (PEG) assays in the three consecutive aspirates (<10% variation about the mean) confirmed in each case that a steady state had been reached. Completeness of exclusion of pancreatic secretions was confirmed by assaying luminal amylase. Only two out of 68 study periods had detectable (>60 IU/l) amylase in the aspirate and these two were excluded from analysis. Whole body irradiation from fluoroscopy was <1 mrad, and the colonic dosage from 14C-PEG was estimated to be <1 mrad. All subjects gave their informed consent to take part in these studies which were approved by the Brent District Ethical Committee.

Study Design

This study consisted of two parts, in Part I (16 subjects) absorption from Vivonex was compared with the absorption from solutions consisting of the amino acid (AA) and carbohydrate (CHO) components of Vivonex, either alone, solution AA and solution CHO, or combined together, solution AA+CHO. The same solutions were also studied after dilution by approximately two-thirds (solutions AA(1), CHO(1), AA(1)+CHO(1)). In part II of the study (five subjects) water and solute absorption was observed from isotonic saline (NaCl), isotonic glucose-saline (glucose 254 mmol/l) and from isotonic solutions of the polymeric diet, Ensure (Abbott Laboratories, N Chicago, Ill, USA).

Composition of Test Solutions (Tables 1 & 2)

All solutions were prepared freshly on the day of the study, adjusted to isotonicity (290 mosmol/kg) and warmed to 37°C before infusion. All solutions contained 5 g/l of polyethylene glycol (PEG, mol wt 4000) labelled with 1 μCi/l 14C-PEG (Amersham International, Amersham, UK) which acted as a non-absorbable marker to allow calculation of water.

Table 1 Infusate composition (mean±SEM)
Jejunal water and electrolyte absorption from two proprietary enteral feeds in man

absorption. Details of the composition are given in Table 1. Unless otherwise specified all chemicals were AnalR grade from British Drug House (BDH Chemicals Ltd, Poole, England). The isotonic Vivonex solution comprised 108 g/l of the elemental diet Vivonex (Eaton Laboratories, Woking, UK). The glucose polymer solutions were made by dissolving known weights of the Vivonex glucose polymer (kindly provided by the manufacturers) in distilled water and making the solution up to 1 litre. The amino acid solutions were prepared so as to be identical to the manufacturer’s specifications by weighing out the individual amino acids (>98% pure, Sigma Chemical Co, St Louis, Mo, USA) and making the solutions up to 1 litre by adding distilled water. Each of these solutions were rendered isotonic by adding NaCl as required. Isotonic solutions of the polymeric enteral feed, Ensure, made by diluting the feed with distilled water, contained 82.2±0.7 mmol/l sucrose, 2.7±1.1 mmol/l free fructose, whole protein 26 g/l, unhydrolysed triglyceride 23.6 g/l and glucose polymer 61.3±3.6 g/l together with Na+ 26.5±2.0 and K+ 25.7±0.7 mmol/l. The carbohydrate source in Ensure is similar to that used in Vivonex, consisting of a range of glucose polymers, mean chain length 5–6 with 1–2% free glucose. The carbohydrate sources were analysed using a previously published HPLC method but using refractive index detection. Interfering substances were first removed from the Ensure solution by extracting the fat into a chloroform layer and precipitating whole protein using 10% sodium tungstate. Each source was shown to contain a similar range of glucose polymers (Gn where n equals the number of glucose monomers in each polymer), the ratio G1:G2:G3:G4:G5:G6 being 1:0.3:5.3:7.2:0:1:5:2:9 for Vivonex and 1:0.5:0:6:7:3:8:2:7:4:5 for Ensure. Thus the profile of oligosaccharides was similar though the technique does not allow comment on the distribution of higher molecular weight polymers. The amino acid component of Vivonex is a mixture of 18 essential and nonessential amino acids, both basic and acidic in the amounts shown in Table 2.

ASSAYS
Sodium and potassium were assayed by flame photometry, and 14C-PEG by liquid scintillation counting with a Packard Tricarb 2425 counter, using an internal standard to correct for quenching. Free glucose was assayed using the hexokinase method and free fructose assayed similarly after first converting fructose-6-phosphate to glucose-6-phosphate using phosphoglucoisomerase (BCL, Lewis, Sussex, UK). Total glucose (free glucose plus glucose in polymeric form) was also measured using the hexokinase method after hydrolysis of the glucose polymer by amylo-alpha 1–4, 1–6, glucosidase (BCL), using a pH2 buffer which allowed hydrolysis to be completed within one hour. Reproducibility of this method was good (coefficient of variation of repeated measures 2.8%, n=10) with a yield of 99% of the predicted value. Sucrose was measured enzymatically by incubating sucrose at pH 4.6 with beta-fructosidase (BCL, Lewis, Sussex), this produces equimolar amounts of glucose and fructose. The resulting rise in glucose concentration, measured using the hexokinase method, was taken to be the sucrose concentration. Alpha-amino nitrogen was assayed by the method of Goodwin and osmolality was measured by freezing point depression using an Advanced Osmometer, Model 3W (Advanced Instruments Ltd, Mass, USA). Freezing point depression only provides an accurate assessment of osmolality in dilute aqueous solutions and hence the values quoted for Ensure should be regarded as approximations only, because on freezing Ensure separates into a lipid and an aqueous phase.

CALCULATIONS AND STATISTICS
Absorption of water and solutes were calculated from standard formulae and all values quoted are per 25 cm segment. Results in the text are expressed as mean ±SE and the significance of differences between matched/unmatched groups evaluated using the paired and unpaired ‘Student’s t’ tests respectively. Analysis of variance and linear regression analysis was carried out using a commercially available statistical package (Statspak, TeleVideo Systems Inc, Cal, USA) and the significance of the correlation coefficients so obtained evaluated using the F ratio. The significance of difference of observed versus predicted values were evaluated from the 95% confidence limits of the regression line using Students’ t test.

Results
SODIUM ABSORPTION
The studies in part I confirmed our previous work in showing large net sodium secretion into the study segment during jejunal perfusion with solutions of low initial Na+ concentration as shown in Table 3 in which solutions are arranged in order of increasing Na+ concentration. One way analysis of variance showed that there were highly significant differences between the various solutions (F=41.8, p<0.01). During perfusion of both isotonic Vivonex and the solution AA+CHO (initial Na+ concentrations 13.8±0.1 and 25.2±0.1 mmol/l) there was a large net secretion of Na+ into the lumen (35.0±2.4 and 28.9±4.2 mmol/h respectively, differences not significant). Diluting solution AA+CHO by ½ and
Table 3  Sodium and water absorption from test solutions (mean ±SEM)

<table>
<thead>
<tr>
<th>Solution</th>
<th>Infusate</th>
<th>Aspirate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vivonex</td>
<td>13±0.4</td>
<td>39±2.0</td>
</tr>
<tr>
<td>AA+CHO</td>
<td>25±2.0</td>
<td>47±3.0</td>
</tr>
<tr>
<td>AA+CHO(1) + CHO(1)</td>
<td>59±0.5</td>
<td>72±1.0</td>
</tr>
<tr>
<td>AA+CHO(1) + CHO</td>
<td>72±0.5</td>
<td>92±2.0</td>
</tr>
<tr>
<td>Cho</td>
<td>92±0.5</td>
<td>93±0.5</td>
</tr>
<tr>
<td>AA+CHO(1)</td>
<td>94±0.5</td>
<td>108±1.0</td>
</tr>
<tr>
<td>Cho</td>
<td>106±1.0</td>
<td>101±0.0</td>
</tr>
<tr>
<td>Part II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>15±0.5</td>
<td>34±2.0</td>
</tr>
<tr>
<td>Ensure</td>
<td>26±2.0</td>
<td>46±1.0</td>
</tr>
<tr>
<td>NaCl</td>
<td>14±0.5</td>
<td>147±2.0</td>
</tr>
</tbody>
</table>

* = Not significantly different from Vivonex; † = significantly different from Vivonex p < 0.01; ‡ = significantly different from Vivonex p < 0.001.

All values expressed per 25 cm segment, + = net absorption, − = net secretion.

making it isotonic by adding more NaCl (initial Na' concentration 59.5±0.5 mmol/l) resulted in a significant reduction in net Na' secretion which fell from 28.9±4.2 to 6.5±2.0 mmol/h, p < 0.01. Furthermore when all the amino acid and carbohydrate solutions studied in part I were considered together, Na' absorption (y) correlated strongly with the initial Na' concentration (x); y = -42.3 + 0.48x, r = 0.95, n = 7, p < 0.001 (Fig. 1). Sodium absorption in part II showed a similar relationship, with net secretion during perfusion of the low sodium solutions, -22±1.0 and -20±1.5 mmol/l for Ensure and glucose 254 mmol/l respectively. Perfusion with the high sodium, non-nutrient solution (NaCl 154 mmol/l) produced net Na' absorption of 8.6±1.7 mmol/h, which is significantly greater than that observed with the low Na' Vivonex (p < 0.01).

Potassium Absorption
Apart from Vivonex and Ensure these solutions were all K' free and only small net secretion of K' was observed into the latter, ranging from 1.4±3.9 mmol/l. The relatively high initial K' concentration found in Ensure, however (25±0±7 mmol/l) resulted in a significant net K' absorption amounting to 10.6±1.0 mmol/h. The initial K' concentration of Vivonex (7-0±0.1 mmol/l) is close to blood levels and net absorption was not significantly different from zero (1.5±1.0 mmol/h).

Water Absorption
As for sodium absorption, analysis of variance showed highly significant differences between the seven solutions studied in part I (F = 318.8, p < 0.01 Table 3). Thus, whereas marked net water secretion was observed during perfusion of Vivonex and AA+CHO (118±6±14.4, 686±28.2 ml/h, difference not significant), this was not seen during perfusion of either the full strength amino acid solution (AA), or the two of three diluted solutions, AA(1), CHO(1), and AA(1)+CHO(1), water absorption being 19.9±10.7, 133±18.9, 103±8±12-4, and 69±1±2.5 ml/h respectively, all values being significantly greater than the water absorption observed during Vivonex perfusion, p < 0.01. Absorption from Ensure (118±6±16.3 ml/h was similarly significantly greater than from Vivonex (p < 0.01).

Intraluminal Osmolality
The concentration of glucose and fructose monomer rose significantly (Table 4) during perfusion of the glucose polymer and sucrose containing solutions and with the more concentrated solutions – that is, Vivonex, AA+CHO, and CHO, this was associated with small rises in intraluminal osmolality (1.8, 1.8, and 1.4% respectively). There were, however, no significant changes from the initial isotonicity with any of the other solutions.

Absorption of Carbohydrate (Table 4)
Glucose absorption during perfusion of the more dilute polymer containing solutions (CHO(1) and AA(1)+CHO(1)) appeared to be saturated as increasing the load by 50% (as in solutions CHO, AA+CHO, and Vivonex) did not increase absorption significantly. Further evidence that absorption was proceeding at a maximal rate is seen from the fact that absorption from the polymers was not significantly different from the absorption from the glucose.

Fig. 1. Correlation between initial Na' concentration (mmol/l) and net Na' absorption (mmol/l) for the seven amino acid and carbohydrate solutions studied in part I, r = 0.95, n = 7, p < 0.001.
As observed with glucose, absorption of amino acids appeared to be saturated at the lower concentrations used (103, 104 mmol/l) as no increase was noted when the amino acid concentrations rose to 140, 146, and 147 mmol/l. Analysis of variance showed a small but significant difference between solutions (F= 4.4, p<0.05). Further analysis showed that although adding carbohydrate to the amino acid solutions produced no change in amino acid absorption (AA v AA+CHO, and AA(1) v AA(1)+CHO(1), no significant differences), amino acid absorption from the most concentrated mixtures, that is, Vivonex and AA+CHO, was significantly less than from the most dilute solution AA(1), p<0.01.

**Relationship between water and solute absorption**

As already indicated, for the most part absorption occurred with only minimal (1–2%) changes in intraluminal osmolality. Water absorption can therefore be predicted to be approximately proportional to the luminal disappearance of osmotically active particles. As sodium secretion into the jejunum in vivo is known to be accompanied by approximately equal secretion of anions, usually Cl (16), the number of osmotically active particles (expressed as mosmol) entering the lumen due to this source can be approximated to by 2× net Na⁻ secretion in mmol x f, where f is the osmotic coefficient which corrects for non-dissociation (f=0.97–0.95 in the concentration range 10–100 mmol/l). Net sodium absorption (mosmol/h) correlated well with water absorption (W ml/h), r=0.82, n=7, p<0.01. This correlation could be improved further by including the luminal disappearance of other components of the various solutions. Owing to variable hydrolysis of the glucose polymer we were not able to calculate the osmotic effect of the polymer in the intestinal aspirates but this could be done for some of the other components of our solutions. By direct measurement of the osmolarity of the amino acid solutions we found the

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Glucose absorption (mean±SEM)</th>
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<tbody>
<tr>
<td>Solution</td>
<td>Free glucose concentration (mmol/l)</td>
</tr>
<tr>
<td></td>
<td>Infusate</td>
</tr>
<tr>
<td>Part I</td>
<td>Vivonex</td>
</tr>
<tr>
<td></td>
<td>CHO + AA</td>
</tr>
<tr>
<td></td>
<td>CHO</td>
</tr>
<tr>
<td></td>
<td>CHO (1)+ AA (1)</td>
</tr>
<tr>
<td>Part II</td>
<td>Glucose</td>
</tr>
<tr>
<td></td>
<td>Ensure</td>
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</tbody>
</table>

*Significantly different from AA(1), p<0.05.

254 mmol/l solution observed in part II of the study. Thus in spite of exclusion of pancreatic amylase, hydrolysis was not rate limiting to glucose absorption from the glucose polymers under the conditions of this study and free glucose actually accumulated in the lumen (Table 4). One way analysis of variance showed that there was no significant difference in glucose absorption between Ensure, Vivonex, CHO, AA+CHO, CHO(1), and AA(1)+CHO(1) F = 2.18, NS (Table 4). Because substantial amounts of sucrose derived fructose were also absorbed from Ensure (55.8±6.4 mmol/h) however total carbohydrate absorption (glucose + fructose) was significantly greater than that seen during perfusion of all the other solutions, being 178.3±18.8 mmol/h, p<0.01.

**Absorption of amino acids** (Table 5)

As observed with glucose, absorption of amino acids appeared to be saturated at the lower concentrations used (103, 104 mmol/l) as no increase was noted when...
The expression for the osmotic effect of absorbing amino acid absorption in the human jejunal mucosa is unimportant since others have clearly demonstrated that this is not a significant factor in the presence of luminal amylase activity. Hence, the effect on luminal osmolality of hydrolysis is balanced by the opposing effect of glucose absorption. Thus, our findings merely reflect the fact that at the rather high concentrations used, and in the absence of luminal amylase, the effect on luminal osmolality of hydrolysis is balanced by the opposing effect of glucose absorption. This, however, must remain speculative as owing to partial hydrolysis of the glucose polymer it was not possible to accurately calculate its osmotic effect in the intestinal aspirates from its measured concentration in mmol/l of glucose. No such problems existed with the sucrose component of Ensure and including this in the calculations markedly improved our prediction of net water absorption.

The large influx of Na⁺ and water into the jejunal mucosa during our perfusions is normally of little significance as these Na⁺ ions will be actively absorbed in the ileum and colon. In patients with massive intestinal resection and only a jejunal remnant however, these secretions will be lost as jejunal effluent and such losses may be life threatening. Further studies will be necessary to determine whether the relationship described here would also be valid in the presence of normal Na⁺-rich pancreatic secretions. With this proviso, however, our data would lead us to recommend in such patients the use of isotonic feeds containing a relatively high initial Na⁺ concentration (at least 90 mmol/l) together with glucose polymer, sucrose and amino acids or oligopeptides to stimulate Na⁺ absorption.

Our finding that glucose absorption from the polymer was as high as that from glucose 245 mmol/l even without pancreatic amylase, was initially surprising. As the chromatogram of the polymer showed however, the partial hydrolysates of corn starch which are widely used in commercial feeds do contain substantial amounts of low molecular weight oligosaccharides in the range G2–G6 which can be readily hydrolysed to glucose by brush border enzymes even in the absence of pancreatic amylase.

The impairment of amino acid absorption in the most concentrated amino acid and carbohydrate mixtures was unexpected and needs repeating as the numbers are small. It may reflect, however, the impairment of amino acid absorption at very high luminal concentrations first described by Mathews and Laster, and emphasises the point that the use of...
very highly concentrated feeds may not necessarily result in maximal absorption in the short bowel syndrome.

Finally it is worthy of note that substantial increases in maximal carbohydrate absorption resulted when sucrose was added to the nutrient solutions. This confirms the practical importance of the original fundamental observations of Holdsworth and Dawson,24 that in man fructose and glucose are absorbed by non-competing transport mechanisms. Sucrose is a palatable and osmotically efficient way of providing fructose and hence improving carbohydrate absorption in patients with markedly reduced small bowel mucosal surface area and as our data shows, also considerably enhances water absorption.

We would like to thank our biochemist Dr G K Grimble for his expert advice and Mrs B E Higgins for her technical assistance.

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