Effect of glutamine on water and sodium absorption in human jejunum at baseline and during PGE₁-induced secretion

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Coëffier, Moïse, Bernadette Hecketswiler, Philippe Hecketsweiler, and Pierre Déchelotte. Effect of glutamine on water and sodium absorption in human jejunum at baseline and during PGE₁-induced secretion. J Appl Physiol 98: 2163–2168, 2005. First published January 20, 2005; doi:10.1152/japplphysiol.00761.2004. —Glutamine, a major fuel for enterocytes, stimulates water and sodium absorption in animal models of secretory diarrhea, but data in humans are still limited. The aim of this study was to investigate the effect of glutamine on jejunal absorption during hypersecretion in humans. In six healthy adults, the effects of glutamine on jejunal absorption were assessed with a triple-lumen tube on two occasions, at baseline and during PGE₁-induced hypersecretion (0.1 μg·kg⁻¹·min⁻¹) in a random order. Isoosmolar solutions containing polyethylene glycol 4000 as nonabsorbable marker were infused in the jejunum at 10 ml/min over 1-h periods: saline (sodium chloride 308 mmol/l), glucose-mannitol 45:45 mM, glucose 90 mM, alanine-glucose 45:45 mM, glutamine-glucose 45:45 mM, and glutamine 90 mM. Net absorptive and secretory fluxes were measured at steady state. At baseline, glutamine- and alanine-containing solutions induced a threefold increase of water and sodium absorption (P < 0.05); 90 mM glutamine stimulated water absorption more than 90 mM glucose (3.6 ± 0.6 vs. 1.9 ± 0.3 ml·min⁻¹·30 cm⁻¹, P < 0.05). PGE₁-induced hypersecretion was reduced (P < 0.05) by solutions of alanine-glucose, glutamine-glucose, and glutamine 90 mM (P < 0.05) and reversed to absorption by alanine-glucose and glutamine-glucose. Glutamine and alanine absorption was nearly complete and was not influenced by PGE₁. In conclusion, glutamine stimulates water and electrolyte absorption in human jejunum, even during experimental hypersecretion. In addition to the metabolic effects of glutamine, these results support the evaluation of glutamine-containing solutions for the rehydration and the nutritional support of patients with secretory diarrhea.

Indeed, neutral amino acids and dipeptides are cotransported with Na⁺ in the intestine by carriers that are different from the glucose-galactose carrier and may thus be added to the glucose-sodium ORS. Glutamine has been identified as a potential candidate to supplement or replace glucose in ORS (7, 23, 34). It was reported that L-glutamine stimulates sodium intestinal absorption in animals by a distinct and additive mechanism to that of glucose (29) and that this promising effect was maintained to some extent in animals with experimental diarrhea (33, 37). In addition, glutamine supports the metabolism of intestinal epithelial cells both as a major fuel and as a precursor for nucleic acid synthesis (39). Finally, glutamine is a major nitrogen carrier in vivo and plays a key role in the regulation of intestinal protein turnover (9) and lipolysis (12).

We previously reported the characteristics of L-glutamine absorption in human jejunum (12). In the present study performed in healthy subjects, the effect of L-glutamine on water and electrolyte jejunal absorption was assessed by means of an intestinal infusion method and was compared with the effects of glucose and alanine, at baseline and during an experimentally induced hypersecretion achieved by intrajejunal infusion of PGE₁.

SUBJECTS AND METHODS

Subjects. Six healthy, normal-weight nonpregnant young adults were recruited for the study (Table 1) and were instructed to maintain their usual levels of dietary intake and physical activity at home in the days preceding each study. They received detailed information on the purpose, methods, and potential risks of the protocol and gave their written consent before the study. The study protocol had been previously reviewed and accepted by the Ethics Committee of the Rouen University Hospital.

Materials. Natural L-glutamine, L-alanine, D-glucose, D-mannitol, and PGE₁ were obtained from Sigma (La Verpillière, France). The nasojejunal enteral tube consisted of three joined polyvinyl tubes. The upper tube was used for infusion of solutions (I); the two other tubes downward were used for aspiration of jejunal contents through a proximal (P) and a distal opening (D). The segment between I and P (mixing segment), and P and D (study segment) was 15 and 30 cm long, respectively. Tubes I and D were identifiable by fluoroscopy to facilitate adequate positioning of the device.

Solutions for enteral infusion. All solutions were prepared with sterile water in the morning of each study by the hospital pharmacy. The composition of the solutions is given in Table 2. Ionic composition and osmolality (300 mosmol/kg) were checked and adjusted if necessary before use. A control rehydration solution with 90 mmol/l glucose concentration was chosen, instead of 111 mmol/l, to allow the addition of high glutamine concentration without increasing markedly

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osmolarity; it has been reported that hypoosmolar solutions containing 90 mmol/l glucose were more efficient than solutions with 111 mmol/l glucose (16).

Perfusion protocol. Each subject was studied twice in the morning of 2 separate days, at baseline or during hypersecretion, in a random order, with a 15-day interval between studies. After a 12-h fast, subjects were intubated through the nose after local anesthesia (lidocaine), and the tube was allowed to migrate spontaneously across the pylorus; a few (1–3) h later, the correct position of the tube was assessed by fluoroscopic examination, with the infusion opening I being 10 cm beyond the duodenojejunal junction. The infusion was then initiated through infusion opening I.

In all studies, the six tested solutions were administered through tube I as follows: the control solution (saline) was infused first to assess basal absorption rate, and then other solutions [glucose 90 mM (glc90); glucose-mannitol (glc:man); alanine-glucose (ala:glc); glutamine-glucose (gln:glc); glutamine 90 mM (gln90)] were infused in a random order (Table 1). All the solutions were maintained at 37°C during infusion, which was achieved at a constant 10 ml/min rate over 60 min by means of a calibrated pump. Each 60-min infusion period consisted of a 30-min equilibration period, followed by three successive 10-min sampling periods during which samples were aspirated simultaneously from tubes P and D and collected on ice (aspiration was achieved by gentle and regular manual suction at a rate of 0.5 ml/min for each period during which samples were aspirated simultaneously from tubes P and D and collected on ice (aspiration was achieved by gentle and regular manual suction at a rate of 0.5 ml/min for each aspiration site). Separate aliquots of each sample were immediately centrifuged, were mixed with an equal volume of an ice-cold sulfosalicylic acid solution containing AGPA as an internal standard and centrifuged, other aliquots (0.5 ml) were mixed with an equal volume of an ice-cold sulfosalicylic acid solution containing AGPA as an internal standard and centrifuged, and the resulting deproteinized supernatant was frozen until analysis of amino acid concentration.

Intestinal hypersecretion was induced by infusion of PGE1 to mimic a secretory diarrhea with a pattern of water and electrolyte aspiration [(lidocaine), and the tube was allowed to migrate spontaneously across the pylorus; a few (1–3) h later, the correct position of the tube was assessed by fluoroscopic examination, with the infusion opening I being 10 cm beyond the duodenojejunal junction. The infusion was then initiated through infusion opening I.

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Glutamine and alanine increase water and electrolyte absorption at basal conditions. At baseline, a net absorption of water and electrolytes was observed (Table 3, Fig. 1). Water and electrolyte fluxes were significantly affected by administered solutions (P ≤ 0.05 for all, Friedman’s test). Solutions ala:glc, gln:glc, and gln90 induced a significant increase above control water and sodium absorption rates (Fig. 1). The gln90 solution did not stimulate significantly water absorption. The glc:glc and ala:glc solutions were the most effective and promoted water and sodium absorption threefold above control values; gln90 solution was significantly more potent than the equimolar pure glucose, glc90, solution (P < 0.05). Addition of 45 mM gln (glc:glc) or ala (ala:glc) to 45 mM glucose resulted in a twofold increase of water and sodium absorption compared with 45 mM glucose (glc:man). Chloride absorption (Table 3) was significantly increased by gln:glc and gln90 and potassium absorption by ala:glc and gln:glc solutions (both, P < 0.05). Glec90 solution did not significantly affect chloride and potassium fluxes.

Glutamine and alanine reverse net water secretion induced by PGE1 to water absorption. As expected, PGE1 intrajejunual infusion shifted basal water, sodium, chloride, and potassium net absorptive fluxes during infusion of saline to a secretory pattern (Table 3, Figs. 1 and 2). All tested solutions reduced water and sodium secretion to some extent (Fig. 2). However, this effect reached statistical significance only for the three amino acid-containing solutions (P ≤ 0.05, Dunn’s multiple comparison test compared with saline). Alanine-glucose and glutamine-glucose solutions even reversed net water secretion to an absorptive pattern (Fig. 2). Chloride and potassium fluxes were significantly affected by ala:glc and gln:glc solutions (Table 3).

PGE1 does not influence glucose, glutamine, and alanine absorption. Glutamine was very efficiently absorbed over segment I-P and segment P-D (Table 3). Glutamine cumulative absorption over 45 cm reached 87 to 99% of infused load in the basal state. Glutamine total absorption as well as its segmental absorption over P-D (Table 3) was strongly correlated to the rate of infusion and to the output entering the study segment at port P (r = 0.99, P < 0.05), thus indicating that glutamine jejunal absorption was not saturated in this range of concentration. PGE1-induced hypersecretion did not influence the segmental absorption of glutamine infused either alone (gln90) or in combination with glucose (glc:glc) (Table 3). Alanine and glucose cumulative absorption also reached nearly 100% over 45 cm and were not significantly altered by PGE1 infusion. At baseline, coupling ratios between sodium absorption and 90 mM glucose absorption averaged 1.1:1, and those between sodium absorption and 90 mM glutamine absorption averaged 1.2:1 (not significantly different). These coupling ratios were both enhanced during hypersecretion and averaged 2.1:1 and 1.7:1, respectively (not significantly different).

DISCUSSION

The present study demonstrates that glutamine is able to promote absorption more potently than glucose and that both substrates may be used in an additive way. Moreover, the stimulating effect of glutamine is maintained during an experimental stimulation of secretion mimicking a secretory diarrhea.

The intestinal infusion technique is an established method to assess water and electrolyte transport in human intestine and the effects of specific substrates, both in healthy humans (14,

Table 3. Net water, electrolyte, and solute fluxes in human jejunum

<table>
<thead>
<tr>
<th></th>
<th>Saline</th>
<th>glc:man</th>
<th>glc90</th>
<th>ala:glc</th>
<th>gln:glc</th>
<th>gln90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jĉ</td>
<td>78±27</td>
<td>180±36</td>
<td>167±66</td>
<td>415±165</td>
<td>401±98*</td>
<td>323±58*</td>
</tr>
<tr>
<td>Jk̂</td>
<td>6.3±1.3</td>
<td>21±7.2</td>
<td>19±7.8</td>
<td>30±9.3*</td>
<td>37±8.2*</td>
<td>22±4.3</td>
</tr>
<tr>
<td>JĥCO²</td>
<td>22±7.0</td>
<td>60±11</td>
<td>30±2.5</td>
<td>43±12</td>
<td>64±23</td>
<td>46±8.6</td>
</tr>
<tr>
<td>Js</td>
<td>106±34</td>
<td>130±42</td>
<td>73±12</td>
<td>71±16</td>
<td>90±16</td>
<td>223±24*</td>
</tr>
<tr>
<td>Jgln</td>
<td>100±16</td>
<td></td>
<td></td>
<td>16±2.5</td>
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PGE1-induced hypersecretion

Net absorptive (+) or secretory (−) electrolyte and solute fluxes (μmol·min⁻¹·30 cm jejunal segment⁻¹) in human jejunum at baseline and during PGE1-induced hypersecretion. Values are means ± SE (n = 6). Glucose (J(glc)), alanine (J(ala)), and glutamine (J(glnc)) fluxes were determined only for the respective solution. Dunn’s multiple comparison test: *P < 0.05 vs. saline. Paired Wilcoxon’s t-test: †P < 0.05 vs. glc:glc; ‡P < 0.05 hypersecretion vs. baseline for Jĉ and Jk̂.

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and diarrheic patients (4, 28, 41). The triple-lumen tube method used in this study is more accurate than the double-lumen tube to measure segmental fluxes (4, 27). The intrinsic limitation of the intestinal infusion technique comes from the limited length of intestine under study, which does not allow a definite extrapolation of data on the full length of intestine. However, the jejunum is a major site for intestinal absorption, and most of nutrients are absorbed up to 75% over 50 cm of jejunum (42); more specifically, glutamine is absorbed almost 70% over 30 cm jejunum (12); thus the present study on 30 cm already gives a reasonable estimate of the major part of glutamine-related water and electrolyte absorption. Hypersecretion induced by PGE$_1$ was chosen because infusion of PGE$_1$ in human jejunum induces a reproducible pattern of water and electrolyte secretion, which resembles much that of cholera (4, 26). Moreover, intestinal hypersecretion induced by cholera enterotoxin may be mediated in part by an increased local production of prostaglandins (2, 41). The infusion rate of PGE$_1$ used in this study ($0.1 \mu$g·kg$^{-1}$·min$^{-1}$) was selected to induce a marked hypersecretion, yet without saturation of secretory pathways (38). The resulting water secretion (Fig. 2) was in the medium range of that reported in the jejunum of cholera patients (4).

The effects of glutamine on water and electrolyte absorption have been well established in experimental models. Indeed, glutamine stimulates sodium and water absorption in rabbit (1, 15, 20) and diarheic patients (4, 28, 41). The triple-lumen tube method used in this study is more accurate than the double-lumen tube to measure segmental fluxes (4, 27). The intrinsic limitation of the intestinal infusion technique comes from the limited length of intestine under study, which does not allow a definite extrapolation of data on the full length of intestine. However, the jejunum is a major site for intestinal absorption, and most of nutrients are absorbed up to 75% over 50 cm of jejunum (42); more specifically, glutamine is absorbed almost 70% over 30 cm jejunum (12); thus the present study on 30 cm already gives a reasonable estimate of the major part of glutamine-related water and electrolyte absorption. Hypersecretion induced by PGE$_1$ was chosen because infusion of PGE$_1$
of a proton/dipeptide cotransport (11). Alanyl-glutamine con-
tide alanyl-glutamine was more effective than a glutamine- 
toxin in rats (24), an experimental ORS containing the dipep-
tide alanyl-glutamine. In the present study, the 90 mM glutamine solution stimu-
ated sodium and water segmental absorption more potently 
than the 90 mM glucose solution in baseline. Because coupling 
ratios between sodium and both solutes are similar, this could 
be explained in part by a higher segmental absorption of glutamine compared with glucose (Table 3). In vitro studies 
with Ussing chambers have suggested that glutamine stimu-
lates to a variable extent both electrogenic sodium absorption 
electroneutral NaCl absorption (1, 29, 32). These two 
components of sodium transport cannot be distinguished in 
vivo. However, the superiority of glutamine over glucose could 
come in part from its ability to promote chloride absorption and consequently electroneutral NaCl absorption, whereas glucose 
effect is limited to the electrogenic glucose-sodium cotrans-
port. In hypersecretion-induced conditions, gln:glc and gln90 
increased water and sodium absorption compared with saline, whereas glc90 did not significantly affect fluxes. With the 
glutamine-glucose solution, the net water and sodium absorp-
tive fluxes were about twofold those observed with glucose. 
This result confirms in vitro experiments (13, 29, 31) showing 
that glutamine and glucose have additive effects on sodium 
absorption, which reflects the existence of separate sodium-solute co carriers for glucose and glutamine at the apical mem-
brane of enterocytes (31), with no competitive effect of glucose 
on glutamine intestinal absorption (13).

The alanine-glucose ORS also stimulated water and sodium 
absorption, which is in accordance with previous data (24, 41). 
The effects of alanine-glucose and glutamine-glucose solutions 
on sodium absorption were almost identical, suggesting that at 
the tested amino acid concentration (45 mM), sodium absorp-
tion results mainly from a solute-sodium cotransport of similar 
capacities. It has been suggested in some experiments that 
alanine and glutamine may be transported by the same carrier 
in rat enterocytes (6), but other studies indicate that glutamine 
transport may be carried by several distinct Na+-dependent (A, 
N, Y') and Na+-independent (L) transport systems, whereas alanine is transported mainly by the Na+-dependent ASC 
system (31). During a secretory diarrhea induced by cholera 
toxin in rats (24), an experimental ORS containing the dipep-
dide alanly-glutamine was more effective than a glutamine-
containing ORS on water and sodium absorption; this could be 
explained by a stronger effect of the dipeptide on sodium 
absorption compared with any constitutive single amino acid 
(31), by the additive effects of alanine and glutamine generated 
by the intraluminal hydrolysis of the dipeptide, or by the effect of 
a proton/dipeptide cotransport (11). Alanyl-glutamine con-
taining ORS have not been evaluated in humans.

In the present study, an apparent stoichiometric ratio of 
about 1:1 for sodium-glucose and glutamine-glucose cotrans-
port has been estimated, which is in accordance with classical 
experiments in rabbit ileum but probably underestimates the 
true absorptive glutamine:sodium ratio; other studies have 
suggested that a ratio of 2:1 was closer to the actual transepi-
thelial influxes (3, 5, 13, 20, 29). Indeed, glutamine transport 
across intestinal brush-border membrane is only partly sodium 
dependent (36). Thus the actual Na+-glutamine coupling ratio 
is probably higher than 1.2:1 at baseline and than 1.7:1 at the 
hypersecretory state, because of an enhanced paracellular Na+
efflux (33).

Finally, glutamine was almost completely absorbed along 
the 45-cm-long jejunal segment. This confirms our previous 
observations that, in this range of infusion rate (27 and 54 
mmol/h), glutamine absorption is ~70% over 30 cm jejunum 
(12). The estimated Km for glutamine absorption in human 
jejunum is 2.3 mmol/min, i.e., 139 mmol/h (12); thus even the 
highest infusion rate in the present study is far from saturating 
glutamine absorption. Interestingly, glutamine absorption was 
not affected by experimental hypersecretion (Table 3); this is in 
accordance with experimental studies showing maintained glu-
lose (8) or glycine (21) absorption during cholaera and with the 
clinical observations that glucose- or amino acid-linked sodium 
absorption is maintained in cholera patients (4, 28). Glucose 
and alanine were also almost completely absorbed, even during 
PGEJ infusion; only a very high PGEJ infusion rate decreased 
glucose absorption ~25% in other studies (26).

In conclusion, glutamine promotes sodium absorption in 
human jejunum both at baseline and during hypersecretion, an 
effect that is additive to that of glucose. Moreover, glutamine 
absorption is maintained during hypersecretion. Thus, in addi-
tion to its beneficial effect on intestinal fluid and electrolyte 
transport, glutamine could be efficiently administered to diarr-
heic patients via the enteral route, as a specific component of 
the nutritional therapy of associated malnutrition.

REFERENCES

1. Abely M, Dallet P, Boisset M, and Desjeux JF. Effect of cholera toxin 
on glutamine metabolism and transport in rabbit ileum. Am J Physiol 
Gastrointest Liver Physiol 278: G789–G796, 2000.
2. Argenzio RA, Rhoads JM, Armstrong M, and Gomez G. Glutamine 
stimulates prostaglandin-sensitive Na(+)H(+) exchange in experimental 
3. Armstrong WA. Cellular mechanisms of ion transport in the small 
4. Banwell JG, Pierce NF, Mitra RC, Bingham K, Caranasos G, and 
Keimowitz R. Intestinal fluid and electrolyte transport in human cholera. 
Glutamine transporter in crypts compensates for loss of villus absorption 
in bovine cryptosporidiosis. Am J Physiol Gastrointest Liver Physiol 281: 
6. Bradford NM and McGivan JD. The transport of alanine and glutamine 
into isolated rat intestinal epithelial cells. Biochim Biophys Acta 689: 
7. Carneiro-Filho BA, Bushen OY, Brito GA, Lima A, and Guerrant R. 
Glutamine analogues as adjunctive therapy for infectious diarrhea. Curr 
8. Carpenter CC, Sack RB, Feeley JC, and Steenberg R. Site and 
characteristics of electrolyte loss and effect of intraluminal glucose in 
and Déchelotte P. Enteral non-essential amino acids stimulate protein 
synthesis and glutamine decreases ubiquitin mRNA level in human duo-


