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Effect of bran particle size on gastric emptying and small bowel transit in humans: a scintigraphic study

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Abstract

Bran is an effective treatment for constipation but its use is often limited by heartburn and bloating. This study examined the effect of fine and coarse bran (15 g) on the gastric emptying and small bowel transit of a 325 kcal rice test meal. Twelve healthy volunteers underwent a three way cross over study, ingesting the technetium-99m labelled rice meal with or without 15 g of indium-111m labelled fine or coarse bran, in random order. Serial scintigraphic images were obtained to define gastric emptying and colonic arrival of label. Compared with control values (99 (9) minutes) (mean (SEM)), the time to 50% gastric emptying was significantly delayed by coarse but not fine bran, being 121 (6) and 104 (9) minutes respectively, $p<0{\cdot}05$, $n=12$. Fundal emptying was unchanged but both brans seemed to increase the proportion of isotope in the antrum at 90 minutes. Small bowel transit was slightly faster with both bran types but in this study the difference was not significant. Both the bran and rice labels moved down the gut without significant separation. Fine bran causes less disturbance of gastric physiology than coarse bran.

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High fibre diets are widely advocated as effective treatments for constipation[1–4] as well as metabolic disorders especially glucose intolerance[5] and obesity.[6] Bran is one of the commonest and most effective ways of increasing dietary fibre intake but intake may be limited by adverse effects including heartburn and postprandial bloating.[7] Bran, like many other sources of dietary 'fibre', delays gastric emptying of liquids[8] and reduces postprandial hyperglycaemia.[5] We have previously shown, however, using a similar test meal that both 15 g of coarse bran (particle size 2 mm) and 15 g of inert, non-viscous 2 mm plastic particles delay gastric emptying to a similar degree while the viscous gelling agent, ispaghula does not.[9] This suggested that the bran particle size might be an important factor in delaying gastric emptying.

The first aim of this study was to discover if grinding coarse bran to reduce its mean particle size from 2 mm to <0·7 mm would change this effect. Using our gamma scintigraphic technique also allowed us to examine whether the intragastric distribution of the meal was changed by the various forms of bran, as others have suggested that excessive antral filling may be associated with the sensation of bloating seen in functional dyspepsia.[10 11]

Our previous studies used ^{99m}Tc labelled rice, leaving open the question of whether this label readily separated from the meal residue. A subsidiary aim of this study was to assess the performance of the ^{99m}Tc rice label by separately labelling the bran with ^{111}In and comparing transit of the two labels down the gut.

Methods

Twelve healthy volunteers (seven male, five female, aged 19–23 years), free from gastrointestinal symptoms and taking no regular medication attended after an overnight fast on three occasions. Women were required to have a negative pregnancy test the day before study. The study was approved by Nottingham University Medical School Ethical Committee.

STUDY PROTOCOL

Two days before study subjects adhered to a 20 g fibre diet and avoided alcohol. On each study day they consumed one of three ^{99m}Tc labelled rice meals, A, B, or C (Table I) using a modified Latin Square design to overcome any order effects. After dosing radioactive markers (0·1 MBq ^{99m}TcDPTA soaked onto filter paper) were taped to the skin anteriorly where the mid-clavicular line met the right costal margin. Serial anterior and posterior 30 second scintigraphic images were then obtained for each isotope at 10, 20, 40, and 60 minutes, at 30 minute intervals for the next 2·5 hours, and thereafter hourly until 11 hours after dosing, when subjects were allowed home. Apart from water, subjects had no further food during the study day.

LABELLING

Rice meal

The rice meal was labelled by mixing into a rice pudding 25 g of freshly cooked rice soaked in $Na^{99m}TcO_4$ solution acidified with a few drops of 1 M HCl. Acidified $SnCl_2$ solution (1 g/l) was then added to coprecipitate $^{99m}TcO(OH)_{2+}$ with colloidal $Sn(OH)_4$. After leaving the mixture for 20 minutes the supernatant was then decanted and the rice

TABLE I *Test meal*

Meal A
325 kcal
220 g creamed rice pudding
25 g rice labelled with 5·0 MBq^{99m}Tc
10 ml condensed milk
34 g Robinson's seedless raspberry jam
100 ml concentrated orange juice
Meal B=A+14 g coarse bran labelled with 0·5 MBq^{111}In.
Meal C=A+14 g fine ground bran labelled with 0·5 MBq^{111}In.

remaining washed with 4×50 ml of water. The final wash eluted <3% label. Labelling efficiency varied between 45–65% and in each case the amount of rice added was adjusted to provide 5 MBq ^{99m}Tc per aliquot.

Bran

Some 1·5 kg of wheat bran (Holland and Barret Health Foods, Hinkley, Leicestershire, UK) was uniformly mixed and about 300 g completely ground, using a Kenwood Executive food liquidiser (Kenwood, Wilton, Hants, UK), yielding a powder that passed through a 710 μm sieve. This powder is referred to hereafter as fine bran. The unprocessed bran that had a particle size >200 μm was used for the coarse bran meal.

Labelling with ^{111}In was achieved by adding 0·5 MBq $^{111}InCl_2$ in acidified solution to a phosphate buffer solution (pH 6·2) and then adding 14 g of fine or coarse bran. At the buffer pH $^{111}InCl_2$ was rapidly hydrolysed to colloidal ^{111}In(OH), which adsorbed to the bran. Labelling efficiency was only 33–66% but once bound the link seemed stable as repeated washings eluted <5% of bound label.

The stability of both labels in a simulated gastric fluid was tested by incubating both rice and bran in continuously stirred saline containing 3·2 g/l pepsinogen (Sigma Chemicals, St Louis, Missouri) at pH ranging from 2–4 for three hours. Under these conditions 80% (range 75–90%) of the bran label and 78% (82–68%) of the rice label remained bound at three hours confirming their suitability for our study in which gastric emptying was largely complete by three hours.

ANALYSIS OF SCINTISCANS

The radioactive markers over the hepatic region were used to align serial scans. A region of interest (ROI) programme was used to obtain total abdominal, total gastric, fundal, antral, and colonic counts for both isotopes. In each case the whole series of images was reviewed before outlining each organ. The gastric image was divided into antrum and fundus by drawing a line to bisect the angle created at the incisura. Where this was not clear the line was drawn on the initial images to bisect the area of the gastric region of interest with a line running perpendicular to the axis of the stomach. Geometric mean counts were then calculated for each region from anterior and posterior counts corrected for background and decay.

Regional time activity curves were then constructed and gastric emptying assessed from time to 50% emptying of whole stomach (T_{50}GE) and also for fundus separately ($T_{50}GE_{fundus}$). Similarly mouth to caecum transit was assessed from time to 50% colonic filling (MCTT). Small bowel transit was then calculated from the difference MCTT$-T_{50}$GE. Intragastric distribution of the rice label was assessed by calculating the ratio of antral/fundal counts. The ^{111}In/^{99m}Tc ratio at various times during emptying was computed, expressing each as a percentage of initial dose, giving a number close to unity, which permitted assessment of whether there was any significant separation of the two labels. Total exposure to ionising radiation amounted to 0·64 mSv.

STATISTICS

Non-parametric statistics were used, the Wilcoxon signed ranks test for paired comparisons, and the Spearman's rank correlation coefficient to assess correlation.

Results

All subjects successfully completed the three studies and in all cases clear images of the stomach and colon were obtained. Apart from mild headache there were no adverse reactions to the meals. Gastric images using the ^{99m}Tc label were much superior to those obtained with ^{111}In and only these permitted clear definition of the fundal and antral regions. There was no evidence of separation between the bran and rice label, the ^{111}In/^{99m}Tc ratio for the whole stomach remaining unchanged over the period of gastric emptying (Table II). We have therefore reported the times to half emptying of gastric and half filling of the colonic regions for the ^{99m}Tc label (Table III) as our best estimates of meal transit.

Gastric emptying of ^{99m}Tc from the whole stomach (T_{50}GE) was linear, with minimal lag in all cases. Emptying from the fundus occurred initially more rapidly causing an initial increase in antral counts, which then stabilised as the rate of emptying from the pylorus increased to match the rate of transfer from fundus to antrum. Emptying of both meals from the fundus occurred at a similar

TABLE II *Ratio ^{111}In/^{99m}Tc in whole stomach during emptying at 0, 60, and 120 minutes*

Bran type	*0 Minutes*	*60 Minutes*	*120 Minutes*
Fine	1·00	0·85 (0·13)	0·92 (0·04)
Coarse	1·00	0·99 (0·01)	1·04 (0·02)

No significant difference from time 0 for either bran type at either 60 or 120 minutes. Data presented as mean (SEM).

TABLE III *Regional transit data*

	Control	*Coarse bran*	*Fine bran*
Gastric			
T_{50}GE	99 (9)	121 (6)*	104 (9)
$T_{50fundus}$	36 (6)	32 (4)	33 (5)
T50			
Colon filling	467 (31)	453 (29)	438 (30)
Small bowel	368 (28)	333 (26)	334 (28)

*=p<0·05. Data presented as mean (SEM).

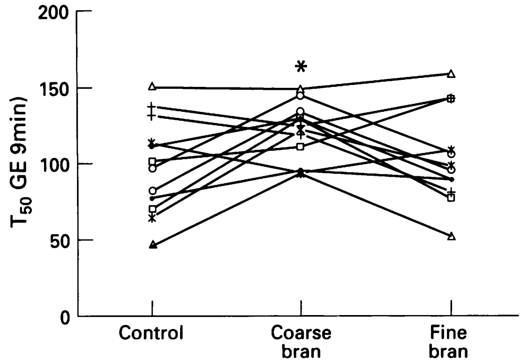

Figure 1: Effect of coarse or fine bran on $T_{50}GE$ (time to 50% emptying of test meals). Coarse but not fine bran significantly delayed emptying compared with control ($p<0{\cdot}05$, $n=12$).*

rate as assessed by $T_{50}GE_{fundus}$ but emptying of the whole stomach was significantly delayed by coarse but not fine bran (Table III, Fig 1). This implies that the delay occurred at the level of the antrum. The antral/fundal ratio of the ^{99m}Tc label rose with time as emptying proceeded and label was transferred from fundus to antrum before emptying (Fig 2). When gastric emptying was half completed (90 mins), the antral/fundal ratios (mean (SEM)) were as follows: control 2·7 (1·2), fine bran 3·4 (1·2), and coarse bran 3·9 (2·3). Although these differences failed to reach significance when the two bran study results were averaged giving a more reliable mean, 3·7 (1·4), this value was significantly greater than control, $p<0{\cdot}05$.

There was no difference in time to 50% colonic filling for either bran preparation. As in previous studies small bowel transit tended to be accelerated by coarse bran but this effect was small and not significant ($p=0{\cdot}16$) in this study.

Time to 50% colonic filling as assessed by the two isotope methods also correlated well (Fig 3) showing that at all levels of the gut the bran and rice labels moved together.

Discussion

Both labels remained with the relevant meal components both in in vitro and in vivo studies. After ingestion both ^{111}In and ^{99m}Tc passed down the gut together permitting clear imaging of the stomach and colon. The rice meal is presumably well homogenised during consumption forming a single phase, highly viscous chyme containing both liquid and solid components of the meal. Under these circumstances there is no apparent gastric sieving[12] and little opportunity for label to become separated from the bulk of the meal.

These studies confirm earlier findings by ourselves[9] and others[8 9] that coarse bran delays gastric emptying. We have also shown that the main effect was at the level of the antrum with fundal emptying apparently unchanged.

The mechanism of action has been thought to be increased viscosity of gastric contents,[13] which reduces pyloric flow. Increased viscosity reduces sedimentation of solids in liquids and thus impairs the ability of the antrum to preferentially empty liquids faster than solids (gastric sieving).[14] Coarse bran has a greater water holding capacity than fine bran[15] and when combined with our rice pudding meal there was an obvious increase in viscosity. Another obvious difference relates to particle size. The antropyloric mechanism seems to be able to selectively prevent the passage of particles greater than 2 mm diameter and may well have retarded the passage of coarse bran particles, whose size may have been increased further by adsorption of other meal components. This may account for our previous finding that inert, non-viscous plastic particles also delayed gastric emptying[16] while the gelling agent ispaghula did not.

This delay in gastric emptying, together with a possible impairment of nutrient absorption in the intestine may delay the intragastric redistribution, which normally occurs as nutrients enter the duodenum.[17] This could explain the tendency towards higher antral/fundal ratios seen with bran. Experimentally antral distension has been associated with a sensation of distension and bloating,[18] which are of course common in patients consuming bran, as well as those with

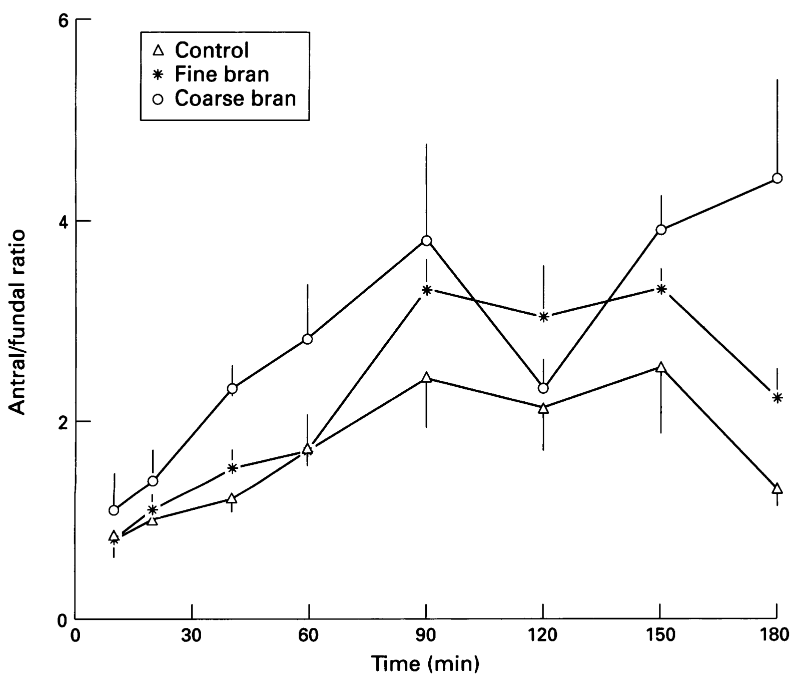

Figure 2: Ratio of counts in antrum/fundus versus time. There was a tendency for the ratio to be higher with both bran types, which was significant at 90 minutes ($p<0{\cdot}05$, $n=12$, see text). There was, however, no significant difference between the two bran preparations.

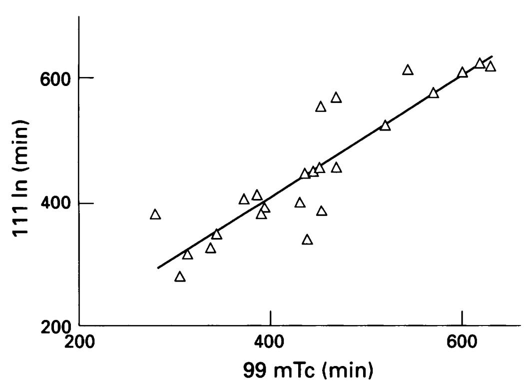

Figure 3: Correlation between colonic arrival of 50% of rice (^{99m}Tc) and bran (^{111}In) labels showing a close correlation, $r=0{\cdot}9$, $n=24$.

functional dyspepsia who have been shown to also show an increased antral/fundal ratio.[10]

Although this study used an identical meal to our previous study there was an important difference in subsequent feeding. In this study we permitted only water whereas previously we provided a sandwich lunch (600 kcal) and afternoon tea four and seven hours after the test meal. This may well account for the fact that although the delay in gastric emptying seen was nearly identical (24 versus 22%) the change in small bowel transit (29% reduction, $p<0 \cdot 01$) was much more noticeable in the previous study[9] than in this study (8% reduction, $p=0 \cdot 16$). This suggests that the accelerating effect of bran depends on its ability to enhance the propulsive effect of eating on ileal motility. This may be caused by water trapping or to a direct effect of bran particles on small bowel motility.

The most significant effect seen in both studies, the consistent delay in gastric emptying, may well account for the heartburn and bloating commonly noted as a side effect of bran containing meals.[7 19] Although limiting its use in the treatment of constipation, this effect may be exploited for therapeutic benefit in a number of ways. Firstly, high fibre meals delay the onset of hunger and by enhancing satiety[6] can be used as part of a weight reducing diet.[20] Secondly, the delaying effect of fibre may also be exploited to reduce precipitous gastric emptying in the dumping syndrome[21 22] and to reduce postprandial hyperglcaemia.[5] This last effect may be beneficial in improving the control of blood sugar in diabetic patients by slowing the rate at which glucose containing foods enter the duodenum. Finally, as the laxative effect of fine bran is only marginally reduced compared with the coarse variety it may be reasonable to recommend fine bran in the treatment of constipation if compliance is limited by heartburn or bloating.

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