The effect of varying amounts of intravenous glucose on the metabolic changes after surgery

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Summary

The metabolic effects of saline, 30 g of glucose a day and 129 g of glucose a day were studied in patients after either cholecystectomy or highly selective vagotomy. In the saline group the blood ketone concentration increased to 3.3 mmol/l on the 5th day after surgery, but this increase was completely abolished by a daily intake of 129 g of glucose and almost completely so by 30 g of glucose. Urine nitrogen excretion expressed as nitrogen to creatinine ratio in the saline group increased from 42.5 to 66.2 by the third day after surgery, and there was a similar increase in the group given 30 g a day of glucose. However, 129 g/day of glucose completely prevented the increase in urine nitrogen, an effect which is similar to that reported in starving subjects given similar amounts of glucose. It is suggested that 129 g of glucose only prevents that part of the increase in nitrogen excretion which is due to starvation and that it has no effect on the increase in nitrogen excretion which happens as part of the metabolic response to surgery.

Introduction

After surgery, as during starvation, there is an increase in the concentration of ketone bodies in the blood (Benotti *et al.*, 1977; Craig *et al.*, 1977), and a loss of nitrogen from the body (Cuthbertson, 1936; Moore, 1953).

Glucose (150 g/day) prevents the increase in ketone bodies in the 3 to 4 days after surgery (Benotti *et al.*, 1977; Craig *et al.*, 1977) and abolishes the ketosis during starvation (Aoki *et al.*, 1975). The same amount of glucose reduces the nitrogen loss during starvation, but there are conflicting conclusions about its effect on nitrogen loss after surgery (Benotti *et al.*, 1977; Craig *et al.*, 1977).

This paper describes the effects of 129 g/day of

glucose and 30 g/day of glucose on the metabolite concentrations and urine nitrogen in patients after moderate uncomplicated surgery in order to clarify the conflicting results reported in the literature. The study was extended beyond 3-4 days until oral feeding was started on the 5th or 6th day.

Patients

Twenty-one patients were studied after elective abdominal surgery of moderate severity (cholecystectomy or highly selective vagotomy). None of the patients had diabetes or hepatic or renal failure. All the patients had an uneventful postoperative recovery without sepsis. None of the patients received heparin during the study. Patients were allocated to 3 groups. There were 5 males and 2 females in each group.

Protocol

Each patient was given 3 litres of fluid intravenously daily from the day of operation until the resumption of eating 5-6 days later. The saline group received 0.9% saline, the second group received 1% dextrose with 0.72% saline (30 g of glucose a day) and the third group received 4.3% dextrose with 0.18% saline (129 g of glucose a day).

Blood samples were taken between 8 a.m. and 9 a.m. each morning. Two ml of blood was added immediately to 2 ml of 10% trichloroacetic acid in hydrochloric acid for the measurement of ketones, glycerol and alanine. Consecutive 24-hr urine collections were made from the day of operation (day 0) for the measurement of nitrogen (urea plus ammonia) and creatinine.

Blood glucose was measured by an automated glucose oxidase method. Blood ketone bodies (acetoacetate and β -hydroxybutyrate) and alanine were determined enzymatically by a semi-automated

method using an LKB reaction rate analyser (Annan, 1974). Glycerol was also measured on an LKB reaction rate analyser using glycerol kinase. Urine nitrogen, measured as the sum of urea and ammonia, and urine creatinine were determined on a Vickers multichannel analyser M300. Urine nitrogen results were expressed as nitrogen/creatinine ratio. This ratio has been shown to reduce the variation between people which may arise as a result of body size (Swaminathan *et al.*, 1979).

The results in the groups were compared with the Mann Whitney U test and by Students 't' test. A probability value of 0.05 or less by both tests was taken to indicate a statistically significant difference between the groups.

Results

Table 1 shows the daily mean values of blood glucose, ketones, glycerol and alanine concentrations and urine nitrogen creatinine ratio in the 3 groups of patients.

The blood glucose concentration increased in all 3 groups on the first postoperative day (day 1). The blood glucose concentration returned rapidly to the original value in the patients given saline or 30 g of glucose, whereas it remained raised for 3–4 days in the patients given 129 g of glucose.

In the patients given saline the blood ketones increased from 144 $\mu\text{mol/l}$ before operation to 3323 $\mu\text{mol/l}$ on the 5th day and then fell rapidly towards the control values when oral feeding was started. The ketone concentration increased much

less in the patients given 30 g of glucose and not at all in the patients given 129 g of glucose a day. The blood glycerol concentration in patients given 129 g of glucose a day was lower on the 3rd and 4th day after operation, but this difference was not statistically significant.

The alanine concentration in blood decreased progressively during the 5 days after operation equally in the 3 groups, and then increased after oral feeding was started. The nitrogen/creatinine ratio increased after surgery in the patients given saline. In patients given 30 g of glucose/day, the nitrogen/creatinine ratio was lower but the difference was not statistically significant. In patients given 129 g of glucose the values decreased after surgery and were significantly lower than in the other 2 groups on days 3, 4 and 5.

Discussion

During starvation there is an increase in blood ketone bodies, and a decrease in blood alanine (Ruderman, Aoki and Cahill, 1976). These changes happened in the surgical patients given saline, and could be due to starvation. Foster *et al.* (1978) have suggested, however, that the changes in the concentrations of ketones and alanine were greater during starvation than after surgery. Dudley, Masterton and Nayman (1965) and Dudley (1968) have suggested that the loss of nitrogen after surgery is also due to starvation. However, the nitrogen excretion increased after operation, whereas it decreases during starvation (Aoki *et al.*, 1975; O'Connell *et al.*,

TABLE 1. Comparison of metabolite concentration in the three groups. Results are: mean ($\pm$ s.e.mean)

	0	1	2	3	4	5	6
Glucose (mmol/l)							
Saline	5.3 (0.53)	6.1 (0.41)	5.3 (0.44)	4.1 (0.21)	4.1 (0.20)	3.8 (0.26)	6.7 (0.3?)
30 g glucose	4.7 (0.38)	6.7 (0.40)	5.3 (0.21)	4.8 (0.13) x	4.5 (0.12)	4.5 (0.35)	6.5 (0.89)
129 g glucose	4.5 (0.39)	6.9 (0.56)	6.3 (0.17)	6.0 (0.36) x	5.7 (0.38) x	5.8 (0.44) x	6.1 (0.64)
Total Ketones ($\mu\text{mol/l}$)							
Saline	144 (12)	459 (121)	1084 (198)	2007 (468)	2362 (553)	3323 (553)	1154 (523)
30 g glucose	184 (83)	189 (35)	353 (70) x	541 (110) x	862 (214) x	1208 (375) x	607 (184)
129 g glucose	468 (142) x	142 (47) x	217 (75) x	236 (47) x	204 (47) x	210 (43) x	368 (151) x
Glycerol (mmol/l)							
Saline	66 (13.4)	77 (14.8)	76 (12.2)	78 (24.6)	82 (21.9)	84 (14.2)	54 (18.0)
30 g glucose	29 (6.7)	62 (5.9)	58 (9.3)	63 (8.4)	61 (21.1)	74 (23.3)	70 (29.0)
129 g glucose	59 (4.8)	59 (14.2)	42 (4.1)	36 (6.2)	43 (6.3)	50 (8.2)	78 (21.7)
Alanine (mmol/l)							
Saline	520 (48)	383 (55)	324 (49)	259 (36)	238 (41)	244 (28)	352 (83.0)
30 g glucose	471 (40)	351 (64)	296 (37)	273 (47)	294 (54)	255 (36)	323 (68.0)
129 g glucose	426 (19)	426 (39)	330 (43)	302 (21)	266 (31)	292 (35)	349 (39.0)
N ₂ /Creatinine							
Saline	42.5 (12.0)	41.6 (3.9)	54.2 (6.3)	66.2 (8.0)	61.2 (6.0)	59.7 (7.6)	44.4 (2.8)
30 g glucose	39.0 (2.1)	40.0 (2.7)	43.5 (2.6)	45.3 (4.2)	52.8 (5.5)	52.0 (5.5)	40.7 (8.2)
129 g glucose	46.2 (3.5)	50.1 (3.6)	44.8 (2.7)	35.4 (2.7) x	33.9 (3.7) x	33.2 (4.5) x	31.6 (4.0) x

(x) Significantly different from the saline group by Students 't' test and by Mann-Whitney U test.

1974; Ruderman *et al.*, 1976) so that even after moderately severe surgery the nitrogen loss is much greater than in simple starvation of the same duration.

Muscle protein has been suggested as the origin of much of this excessive loss of nitrogen after surgery (Frawley, Antz and Howard, 1955; Cuthbertson, McGin and Robertson, 1939; Levenson and Watkin, 1959). Alanine is the principal amino acid released during muscle breakdown (Felig, 1975), so that if the nitrogen lost after surgery came from muscle there should be an increase in the blood alanine concentration. However, the alanine concentration decreased after surgery in the present patients as in previous reports (Dale *et al.*, 1977; Schønheyder, Bone and Skjoldborg, 1974). The similar decrease in blood alanine after trauma has been attributed to an increased clearance of alanine (Alberti, Batstone and Johnston, 1977). The authors suggest that the changes in blood alanine concentration after surgery are due to changes in the rate of entry of alanine into the blood (Swaminathan, unpublished). The simultaneous decrease in alanine release and increase in urinary nitrogen excretion in the surgical patients given saline indicates that either an increased proportion of the urine nitrogen was coming from some source other than muscle or that a greater proportion of the alanine reaching the liver is metabolized to urea rather than being incorporated into proteins, i.e. a decrease in protein synthesis. The findings of O'Keefe *et al.* (1974) that protein synthesis is decreased after abdominal surgery supports the latter suggestion.

It is well known that body size can influence the loss of nitrogen after surgery (Moore and Ball, 1952). The authors have previously shown that nitrogen loss after surgery is related to fat free mass or 24 hr urinary creatinine excretion, and expressing the results as nitrogen to creatinine ratio will reduce the variation due to body size (Swaminathan *et al.*, 1979). Furthermore, this ratio will also reduce errors due to incomplete collection. This ratio was used in the present study to compare the nitrogen loss between groups.

Patients after surgery are regularly given glucose containing solutions and the metabolic state in these patients therefore includes the effects of glucose. The 4.3% glucose solution, which is the solution usually used in surgical practice, supplies 129 g of glucose (2167.2 J) a day and was sufficient to raise the blood glucose, and prevent the rise in ketones and urine nitrogen (Table 1). The 1% solution which supplied 30 g of glucose (502.1 J) a day was sufficient to prevent the rise in ketones but it did not diminish the increase in nitrogen (Table 1). Neither solution had any effect on the fall in blood alanine. The reduction in blood ketones after 1%

dextrose solution was not associated with any effect on blood glycerol and was therefore probably due to inhibition of ketone production in the liver rather than inhibition of lipolysis. The recent work of Elkeles, Chalmers and Hambley (1978) suggests that this effect of glucose could be due to an increased secretion of insulin.

Conclusions reported in the 2 previous studies on postoperative patients of the effect of dextrose on urine nitrogen excretion have been conflicting (Craig *et al.*, 1977; Benotti *et al.*, 1977), but as

TABLE 2. Reduction in urine nitrogen excretion by glucose during fasting and after surgery

	Amount of glucose	Reduction in urine nitrogen* % mmol/day
Starvation		
O'Connell <i>et al.</i> , 1974	150	37.0 280
Post op.		
Benotti <i>et al.</i> , 1977	150	35.5 315
Craig <i>et al.</i> , 1977	150	33.5 350
Present series	129	40.5 290

*Reduction in urine nitrogen was calculated as the mean difference from the group given no calories.

Table 2 shows, the reduction in urine nitrogen in those 2 studies was similar and the difference in conclusion arose from interpretation of the statistical significance of the findings. The present results are similar to those in both the previous studies and when the 3 studies are combined the average reduction in urine nitrogen excretion is 300 mmol/day. This is similar to the reduction in urine nitrogen in starved subjects given similar amounts of glucose (Table 2). This finding suggests that in the patients after surgery the glucose is preventing that part of the nitrogen excretion which is due to starvation and it has no effect on the excessive nitrogen excretion which happens as part of metabolic response to surgery. If this is the case, then it further suggests that these 2 components of nitrogen loss are due to different metabolic mechanisms.

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