Physiol. Res. 46: 9 – 13, 1997

Mesenteric Arteriovenous Differences in Glucose, Lactate and Insulin Concentrations in Rats and Humans

M.A. TORMO, J.C. MORENO, M. D. TORRES, J. E. CAMPILLO

Department of Physiology, Faculty of Medicine, University of Extremadura, Badajoz, Spain

Received January 22, 1996
Accepted August 29, 1996

Summary

The present study was aimed to investigate the mesenteric arteriovenous differences in blood glucose and lactate and plasma insulin in humans (n=8) and rats (n=10). Arterial (abdominal aorta) and mesenteric vein blood glucose and lactate (enzymatic methods) and plasma insulin concentrations (radioimmunoassay) were measured in patients during abdominal surgery and in normal rats. Blood glucose levels were significantly ($p<0.05$) higher in the abdominal aorta than in the mesenteric vein in both rats (9.2±1.0 vs 7.5±0.8 mmol/l) and humans (10.4±2.9 vs 8.5±2.7 mmol/l). Blood lactate levels were higher ($p<0.05$) in the mesenteric vein in both rats (3.7±1.3 vs 2.8±0.9 mmol/l) and humans (0.7±0.23 vs 0.1±0.05 mmol/l). Plasma insulin concentrations were identical in the aorta or mesenteric vein in both rats (314.4±162.0 vs 311.4±94.2 pmol/l) and humans (62.4±43.2 vs 61.8±48.0 pmol/l). In conclusion, both rat and human intestine retained a high proportion of arterially administered glucose and released lactate under the studied conditions.

Key words
Glucose – Lactate – Insulin – Human – Rat

Introduction

In addition to its endocrine secretory activity, the intestine may play an important role in glucose homeostasis because of its high glycolytic activity (Hanson and Parson 1976, 1978, Nicholls *et al.* 1983, Windmueller and Spaeth 1980, Abumrad *et al.* 1982, Tormo *et al.* 1988). A number of *in vivo* (Nicholls *et al.* 1983, Windmueller and Spaeth 1980, Abumrad *et al.* 1982) and *in vitro* (Tormo *et al.* 1988, Porteus 1980, Mallet *et al.* 1986) studies on experimental animals have shown that the intestine might utilize a high proportion of the arterially or luminally supplied glucose, and that lactate is one of the products of intestinal glucose metabolism. Most of the produced lactate returns to the portal circulation to be used in the liver (Niewoehner *et al.* 1984, Niewoehner and Nuttall 1989). The alteration of this metabolic process in diabetes (Jamal *et al.* 1984, Caspary 1973) could contribute to the overall metabolic derangement observed in diabetic patients. Little information is available, however, regarding the metabolism of glucose and production of lactate by the human intestine. The few reported studies were carried out by portal vein sampling, so the data only partially represent the proper intestinal metabolic events (Blackard *et al.* 1974, Björkman *et al.* 1990). Furthermore, because of the same technical difficulties, no studies are available in the literature concerning the *in vivo* uptake of insulin by human intestine. Consequently, we have investigated the arterial and mesenteric venous concentrations of blood glucose and lactate and plasma insulin in patients during abdominal surgery and in normal rats.

Material And Methods

The human part of the study was performed on eight overnight fasted (14 h) adult subjects (Table 1) during abdominal surgery under nitrous oxide anaesthesia. None of the patients was obese or suffering from diabetes mellitus. The study was performed in accordance with the principles of the Declaration of Helsinki and informed consent was obtained from the patients. The study protocol was reviewed by the institutional ethics committee. A 5 ml blood sample was first obtained from a tributary vein of the superior mesenteric vein using a 0.5 x 18 mm

needle, and then another 5 ml blood sample was obtained from the abdominal aorta using a 0.8 x 40 mm needle. An antecubital vein blood sample was obtained the day before as part of the pre-surgical protocol.

Table 1
Clinical data of the subjects

Sex	Age	Diagnosis	Peripheral venous glucose (mmol/l)
M	69	Cancer of caecum	5.1
M	42	Choledocholithiasis	5.4
F	42	Cholelithiasis	5.7
M	42	Cholelithiasis	7.3
F	62	Cholelithiasis	4.6
F	59	Cholelithiasis	6.0
M	77	Adherential syndrome	4.6
M	60	Cancer of stomach	5.9

Male Wistar rats (220–250 g) were maintained on a standard diet (composition: carbohydrates 57 %, proteins 17 %, lipids 3 %; metabolizable energy 2950 kcal/kg, Letica, Barcelona, Spain) with free access to water and housed in a room at 24±2 °C with lighting from 08:00 to 20:00 hours. Fasted (14 h) rats were anaesthetized with intraperitoneal sodium pentobarbital (60 mg/kg body weight, Nembutal, Serva, Heidelberg, Germany) and laparotomy was performed. A 2 ml blood sample was obtained from the mesenteric vein and then another 2 ml blood sample was immediately withdrawn from the abdominal aorta.

Both human and rat blood samples were immediately discharged into cold heparinized tubes. After centrifugation at 4 °C, the plasma was collected and stored at −40 °C until assayed. Glucose was measured in whole blood by a glucose oxidase-peroxidase method (Boehringer, Mannheim, Germany). Lactate was measured in whole blood by an enzymatic method (Richterich and Colombo 1983) after treatment of the blood with perchloric acid (0.66 mmol/l) added immediately after blood collection. Plasma insulin was measured by radioimmunoassay using human (Amersham, Buckinghamshire, UK) or rat (Novo, Copenhagen, Denmark) insulin as standards. Other plasma parameters (urea, creatinine, uric acid, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, gamma glutamyl transpeptidase (GGT), lactate dehydrogenase (LDH), creatinine phosphate kinase (CPK), cholinesterase, total proteins, albumin, total cholesterol and triglycerides) were measured in both rats and humans using standard automatized methods (Coulter Analyser CPA, Coulter Instruments, USA). All results are expressed as mean ± S.D. Statistical analysis was performed by the Wilcoxon test for paired values.

Table 2
Concentrations of glucose, lactate and measured in the abdominal aorta and in a mesenteric vein in rats (n=10) and humans (n=8)

		Aorta	Mesenteric vein
Glucose (mmol/l)	Rats	9.20±1.00	7.50±0.80*
	Humans	10.40±2.90	8.50±2.70*
Lactate (mmol/l)	Rats	2.80±2.70	3.70±1.30*
	Humans	0.10±0.05	0.70±0.23*
Insulin (pmol/l)	Rats	314.4±162.0	311.4±94.2
	Humans	62.4±43.2	61.8±48.0

** $p<0.05$ from the aorta*

Results

As shown in Table 2, the blood glucose concentration was significantly higher ($p<0.05$) in the abdominal aorta than in the mesenteric vein of both rats and humans. The venous reduction of blood glucose averaged 18.0±9.2 % in rats and 14.1±16.5 % in humans. The blood lactate concentration was higher ($p<0.05$) in the mesenteric vein than in the abdominal aorta in both rats and humans. The increase in blood venous lactate was 51.9±15.7 % in rats and 77.4±67.2 % in humans. Insulin concentrations were identical in

the plasma from the abdominal aorta or the mesenteric vein in both rats and humans. However, both arterial and venous plasma insulin levels were higher in rats than in humans ($p<0.05$).

No significant arteriovenous differences were found in the plasma levels of triglycerides, urea, creatinine, uric acid, bilirubin, or for the enzymes ALT, AST, alkaline phosphatase, GGT, LDH, CPK, or cholinesterase in both rats or humans (data not shown). In contrast, statistically significant arteriovenous differences were observed in total proteins, albumin and total cholesterol in both rats and humans. Venous total plasma protein concentration was increased by 5.17 ± 2.1 % in humans ($p<0.05$) and by 6.66 ± 0.58 % in rats ($p<0.01$) over the arterial values. Venous plasma albumin concentrations were higher by 6.37 ± 1.74 % in humans ($p<0.05$) and 4.99 ± 0.91 % in rats ($p<0.05$) than the arterial values (Table 3).

Table 3
Concentrations of total proteins, cholesterol and albumin in the abdominal aorta and the mesenteric vein in rats ($n=10$) and humans ($n=8$)

		Aorta	Mesenteric vein
Total Proteins (g/dl)	Rats	5.72 ± 0.16	6.10 ± 0.16*
	Humans	6.71 ± 0.22	7.05 ± 0.18*
Albumin (g/dl)	Rats	3.02 ± 0.08	3.17 ± 0.09*
	Humans	3.56 ± 0.24	3.71 ± 0.20*
Cholesterol (mg/dl)	Rats	53.2 ± 3.2	56.4 ± 3.2*
	Humans	183.1 ± 21.6	190.1 ± 21.7*

** $p<0.05$ from the aorta*

Discussion

To our knowledge, this is the first report in the medical literature on glucose, lactate and insulin arteriovenous differences in human intestine *in vivo*. It furthermore demonstrates that arteriovenous differences behave similarly in rats and humans. Nobody, until now, has measured glucose uptake by the human intestine. Several studies which measured splanchnic glucose uptake by means of a hepatic venous catheter technique (Waldhäusl *et al.* 1983, Ferrannini *et al.* 1985), have determined intestinal, hepatic, splenic, and pancreatic glucose consumption, etc. The work that comes closest to our study is that of Björkman *et al.* (1990) on five post-operative patients, where glycaemia levels were measured simultaneously in the brachial artery and catheterized portal vein. Under basal conditions, the arteriovenous difference was 0.12 ± 0.02 mmol/l. These are lower values than those found in the present study. Nevertheless, it should be kept in mind that in our study the conditions were slightly hyperglycaemic because of the continuous intravenous infusion, of glucose (3.3 g/100 ml) and saline (0.3 g/100ml). In the work of Björkman *et al.* (1990), if one considers only the arterial glucose values which are similar to ours (10 mmol/l) then one obtains arteriovenous glucose differences of around 2 mmol/l (the exact value was not supplied by the authors), that are identical to those found by us. It is difficult to integrate the present results with other studies that measured the splanchnic consumption of glucose by means of the hepatic venous catheter technique, since this technique underestimates glucose production by the liver (Windmueller and Spaeth 1980). Glucose production determined by 3-^{3}H-glucose is 20 % greater than the net glucose output measured by catheter technique (Wennlund *et al.* 1986). The published data, especially those obtained in moderately hzperglzcaemic conditions (Abumrad *et al.* 1982) are compatible with those measured in our study which suggest, that the gut is an important site of glucose disposal in both rats (Hanson and Parson, 1976, Tormo *et al.* 1988) and humans (Björkman *et al.* 1990).

The mesenteric blood lactate concentration was 0.9 mmol/l (rats) and 0.5 mmol/l (humans) higher than in the aorta. Our results thus support previous *in vivo* (Windmueller and Spaeth, 1980, Abumrad *et al.* 1982) and *in vitro* (Tormo *et al.* 1988, Niewoehner and Nuttall 1989) observations suggesting that the intestine transforms a substantial proportion of the metabolized glucose into lactate that then returns to the portal circulation. The study which was performed on patients

with a portal vein catheter (Björkman *et al.* 1990) did not show any significant difference between arterial and portal venous lactate levels in the basal state. In our study, aorta lactate levels are lower than peripheral vein lactate levels (0.5–1.5 mmol/l). The conditions of general anaesthesia, including the maximal muscular relaxation imposed by abdominal surgery, would explain the low lactate plasma values reported in this study in man.

The increase in protein concentrations observed in mesenteric venous plasma suggests a certain amount of haemoconcentration in the mesenteric vein that is probably associated with intestinal secretory processes. This implies that values measured in mesenteric venous plasma should be corrected by a small unknown concentration factor. If this were done, plasma insulin concentrations measured in the mesenteric vein in both rats and humans would be slightly lower than the corresponding values measured in the aorta, and obviously the increase in arterial plasma lactate levels would be slightly lower and the reduction of glucose levels in venous blood would be higher that those reported in this study.

In conclusion, the present results suggest that both rat and human intestine retain a high proportion of arterially supplied glucose, and release lactate under basal conditions.

Acknowledgements

We gratefully acknowledge the collaboration of the Service of General Surgery of the Hospital Universitario Infanta Cristina, Badajoz, Spain.

References

ABUMRAD N.N., CHERRINGTON A.D., WILLIAMS P.S., LACY W.W., RABIN D.: Absorption and disposition of a glucose load in the conscious dog. *Am. J. Physiol.* **242:** E398–E406, 1982.

BLACKARD W.C., NERLSON N.C., ANDREWS S.S.: Portal and peripheral vein immunoreactive glucagon concentrations after arginine or glucose infusions. *Diabetes* **23:** 199–202, 1974.

BJÖRKMAN O., ERIKSSON L.S., NYBERG B., WAHREN J.: Gut exchange of glucose and lactate in basal state and after oral glucose ingestion in postoperative patients. *Diabetes* **39:** 747–751, 1990.

CASPARY W.F.: The effect of insulin and diabetes mellitus on the absorptive function of the small intestine. *Digestion* **9:** 248–263, 1973.

FERRANNINI E., BJORKMAN O., REICHARD G.A., PILO A., OLSON M., WAHREN J., DEFRONZO R.A.: The disposal of an oral glucose load in healthy subjects. A quantitative study. *Diabetes* **34:** 580–588, 1985.

HANSON P.J., PARSON D.S.: The utilization of glucose and production of lactate by in vitro preparations of rat small intestine. *J. Physiol. Lond.* **255:** 775–795, 1976.

HANSON P.J., PARSON D.S.: Factors affecting the utilization of ketone bodies and other substrates by rat jejunum: effects of fasting and of diabetes. *J. Physiol. Lond.* **278:** 55–67, 1978.

JAMAL A., KELLET G. L., ROBERTSON J.P.: The effect of glucose on the activity of phosphofructokinase in the mucosa of rat small intestine. *Biochem. J.* **218:** 458–464, 1984.

MALLET R.J., KELLEHER J.K., JACKSON M.J.: Substrate metabolism of isolated jejunal epithelium conservation of three-carbon units. *Am. J. Physiol.* **250:** C191–C198, 1986.

NICHOLLS T.J., LEESE H.J., BRONK J.R.: Transport and metabolism of glucose by rat small intestine. *Biochem. J.* **212:** 183–187, 1983.

NIEWOEHNER C., NUTTALL F.Q.: Disposition of a glucose load in fed rats and rats adapted to a high-carbohydrate diet. *Am. J. Physiol.* **256:** E811–E817, 1989.

NIEWOEHNER C.B., GLIBOE D.P., NUTTALL F.Q.: Metabolic effects of oral glucose in the liver of fasted rats. *Am. J. Physiol.* **246:** E89–E94, 1984.

PORTEUS J.W.: Glutamate, glutamine, aspartate, asparagine, glucose and ketone-bodies metabolism in chick intestinal brush-border cells. *Biochem. J.* **188:** 619–632, 1980.

RICHTERICH R., COLOMBO J.P.: Piruvato y lactato. In: *Quimica Clinica. Teoria, Práctica e Interpretación*,. R. RICHTERICH, J.P. COLOMBO (eds), Salvat, Barcelona, 1983, pp. 292–297.

TORMO M.A., ZUBELDIA M.A.G., MONTERO J.L., CAMPILLO J.E.: In vitro study on the contribution of the rat intestine-pancreas to glucose homeostasis. *Diabetologia* **31:** 916–921, 1988.

WALDHÄUSL W.K., GASIC S., BRANTUSCH-MARRAIN P. NOWOTNY P.: The 75-g oral glucose tolerance test: effect on splanchnic metabolism of substrates and pancreatic hormones release in healthy man. *Diabetologia* **25:** 489–495, 1983.

WENNLUND A., FELIG P., HAGENFELDT L., WHAREN J.: Hepatic glucose production and splanchnic glucose exchange in hyperthyroidism. *J. Clin. Endocrinol. Metab.* **62:** 174–180, 1986.

WINDMUELLER H.G., SPAETH A.E.: Respiratory fuels and nitrogen metabolism *in vivo* in small intestine of fed rats. Quantitative importance of glutamine, glutamate and aspartate. *J. Biol. Chem.* **255**: 107–112, 1980.

Reprint requests
J.E. Campillo, Departamento de Fisiología, Facultad de Medicina, Universidad de Extremadura, Apartado 108, 06071 Badajoz, Spain.