British Journal of Anaesthesia **87 (2)**: 316–19 (2001)

Another feature of TURP syndrome: hyperglycaemia and lactic acidosis caused by massive absorption of sorbitol

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Endoscopic transurethral resection of the prostate (TURP) can be complicated by absorption of a large volume of irrigation fluid. The clinical features of this complication are referred as the TURP syndrome. We report a case where hyperglycaemia and lactic acidosis complicated the TURP syndrome caused by the massive absorption (approximately 15 litres) of a sorbitol–mannitol irrigation solution. The proposed mechanism is a type B lactic acidosis related to the metabolism of sorbitol.

Br J Anaesth 2001; **87**: 316–19

Keywords: complications, lactic acidosis; surgery, prostatectomy; complications, TURP syndrome

Accepted for publication: March 19, 2001

The transurethral resection of the prostate (TURP) syndrome is caused by the passage of irrigating fluid into the vascular space. Depending on the nature and the amount of fluid absorbed, the TURP syndrome may affect many systems mainly through acute changes in vascular volume and plasma solute concentrations.[1 2] Sorbitol–mannitol solutions are widely used for TURP mostly because, unlike glycine, these two solutes are considered to be devoid of toxicity.[3] We report a case of massive absorption of a sorbitol–mannitol irrigating solution which was complicated by hyperglycaemia and type B lactic acidosis. The metabolism of sorbitol which led to this complication is also reviewed.

Case report

A 71-yr-old, 58 kg man with benign hyperplasia of the prostate was scheduled for TURP under regional anaesthesia. Apart from a history of transient cerebral ischaemic attacks, his medical history was unremarkable. His usual medication was aspirin and doxazosine. No premedication was given and spinal anaesthesia was achieved with 1.4 ml of 0.75% hyperbaric bupivacaine injected through a 22-gauge Whitacre needle at the L4–L5 interspace. A T-7 sensory block height was obtained followed by a slight decrease of systolic arterial pressure from 130 to 115 mm Hg which was judged to require no treatment. During the procedure, normal saline was infused in a peripheral vein, no sedation was given and the patient received supplemental oxygen by nasal prongs.

The prostate was resected using a Storz Iglesias resectoscope through a modified cystoscope continuously irrigated with a solution of 2.7% sorbitol and 0.54% mannitol (Abbott Laboratories, Montreal, Canada). The irrigation fluid bags were hung 60 cm above the operating table. Surgery proceeded without any problem for 50 min, the patient was calm and responsive, and his blood pressure, heart rate and oxygen saturation were normal. Then the patient complained of shortness of breath and his oxygen saturation decreased to 91%. At that point, a total of 24 litres of irrigation fluid had been used, 55 g of prostate tissue had been resected, and the decision was made to terminate surgery. During that time the patient became more dyspnaeic and his respiratory rate increased to 30 bpm. One hundred per cent oxygen was given by face mask and the oxygen saturation returned to 98% but the patient became restless. Blood was sampled for measurement of electrolyte concentrations. The patient was transferred to the recovery room where he was allowed to stay in the sitting position and his respiration was supported by non-invasive positive pressure ventilation. After that, he was more co-operative although he remained slightly drowsy. Throughout this period, sinus tachycardia was present but the patient's blood pressure remained within normal limits. Obvious signs of pulmonary oedema were present on the chest x-ray but, except for sinus tachycardia, no abnormality was present on the ECG. Furosemide 40 mg i.v. was given and an infusion of nitroglycerine was started. An arterial cannula was inserted and serial blood samples were collected for measurement of blood glucose, serum sodium and osmolality, pH, P_{CO_2}, P_{O_2}, bicarbonate and arterial blood lactate (Table 1). At the end of surgery, serum concentration of sodium was 97 mmol litre^{-1} and increased progressively in the recovery room. Blood glucose was normal at the end of surgery but increased steadily during

Table 1 Evolution of postoperative blood acid–base and chemistry values. *O_2 saturation at time 00:00 was measured by pulse oximetry. Subsequent O_2 saturations were measured by hemoximetry

Parameter	Time after end of surgery (h:min)									
	00:00	01:00	01:30	02:00	02:30	03:00	03:30	04:00	04:30	05:00
Glucose (mmol litre^{-1})	5.3	9	13.4	16.6	17.9	18.1	16.5	14.8	12.8	11
Na (mmol litre^{-1})	98	104	108	110	111	112	115	115	118	119
P_{O_2} (mm Hg)		108	62	59	117	129	118	202	62	99
O_2 saturation* (%)	98	97	91	91	97	96	96	98	91	96
pH		7.31	7.29	7.30	7.32	7.32	7.34	7.35	7.32	7.37
Bicarbonates (mmol litre^{-1})		18.4	18.4	17.4	18	19.4	19.5	20.2	19.4	20.4
Lactate (mmol litre^{-1})		4.3	5.3	6.8	5.9	5.5	5.7	5.9	6.5	6.4
Osmolality (mmol kg^{-1})					286				280	

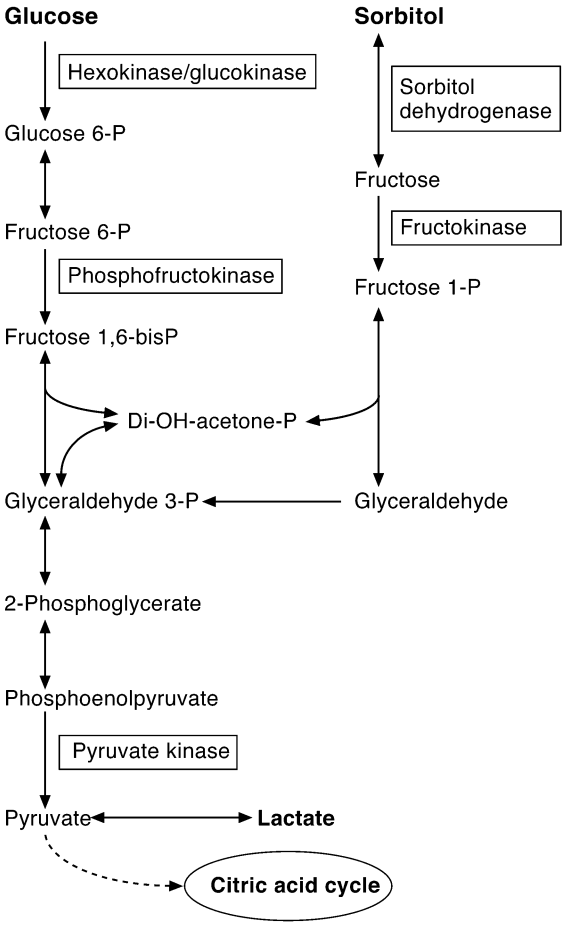

Fig 1 Pathways of glycolysis (Embden-Meyerhof pathway) and fructolysis along with major regulatory steps in the metabolism of glucose and sorbitol towards lactate production (see text). For simplicity and clarity purposes, four regulatory enzymes of glucose synthesis from lactate (gluconeogenesis) have been omitted from the figure.

the first hours after surgery. This was treated with i.v. human insulin and progressively improved. Blood-gas analysis done shortly after the end of surgery showed metabolic acidosis with elevated blood lactate. In the first few hours the acidosis increased, then slowly corrected without specific therapy but arterial lactate remained elevated for the whole recovery room stay. The pulmonary oedema improved rapidly and both nitroglycerine and ventilatory assistance were easily weaned in less than 3 h. Apart from postoperative nausea and vomiting which was treated with droperidol and ondansetron, the patient improved rapidly. He made an uneventful recovery and was discharged home 2 days later.

Discussion

Sorbitol and mannitol are electrically non-conducting but osmotically active solutes that are added to irrigation fluids to decrease the risk of massive intravascular haemolysis.[1 2] Because these solutions are devoid of the risk of hyperammonaemia and hyperglycinaemic encephalopathy associated with glycine solutions, they are widely used in urologic endoscopic surgery.[3] With these solutions, the clinical signs and symptoms of the TURP syndrome are believed to be caused by the massive absorption of fluid and the resulting hyponatraemia and hypo-osmolality and not by any toxicity of sorbitol or mannitol.[1 3] To the best of our knowledge, this is the first report of hyperglycaemia and lactic acidosis associated with absorption of sorbitol–mannitol irrigation solution.

Mannitol is a sugar alcohol derived from mannose that is not metabolized and is rapidly excreted by glomerular filtration in the kidney.[4] Sorbitol is a natural C6-sugar alcohol found in many fruits. It is metabolized to fructose by sorbitol dehydrogenase in the liver and to a lesser extent in the kidney (Fig 1).[4] One might anticipate that high doses of sorbitol could induce toxic effects similar to fructose toxicity such as lactic acidosis, hyperuricaemia and hyperglycaemia. Lactic acidosis following fructose infusions may be caused by a combination of several mechanisms. First, in the presence of both fructose and glucose, the formation of fructose 1-phosphate is favoured by the higher fructokinase activity compared with the lesser capacity of hexokinase plus glucokinase to phosphorylate glucose. Second, the fructolysis of fructose 1-phosphate by aldolase bypasses phosphofructokinase, the first regulatory enzyme along the glycolysis pathway towards pyruvate and lactate formation. Third, fructose 1-phosphate and fructose 1,6-biphosphate stimulate pyruvate kinase, the second regulatory step of glycolysis.[4] The hyperglycaemia observed in this case may be explained by the much higher activity of fructokinase that favours the formation of fructose 1-phosphate over glucose 6-phosphate, thus restraining glucose metabolism while favouring fructose metabolism towards pyruvate and lactate and providing substrate for gluconeogenesis.[4 5] Indeed, in the isolated liver perfused with fructose, about 50–75% of the fructose is retrieved as glucose and the rest as lactate and pyruvate.[6 7]

Causes of lactic acidosis are classified as type A where poor tissue oxygenation is present and type B where tissue oxygenation is preserved.[8] In such a case of TURP syndrome presenting with pulmonary oedema, metabolic acidosis when present is usually attributed to type A lactic acidosis caused by hypoxaemia and tissue hypoperfusion. Our patient never presented hypotension or significant oxygen desaturation, thus making a type A aetiology unlikely. Sorbitol and fructose are among the numerous causes of type B lactic acidosis. For instance, fructose was abandoned for parenteral nutrition several years ago because of associated metabolic disturbances similar to those encountered in this case.[9 10] Furthermore, Buijs and van Zuilen have reported a time course of blood glucose, lactate and acid–base disturbances remarkably similar to this case in a patient who received 250 ml of 30% sorbitol (7.5 g) for brain volume reduction.[11] In the present case, based upon the serum concentration of sodium at the end of surgery, the calculated volume of irrigation solution

absorbed was approximately 15 litres and the amount of sorbitol absorbed can be estimated at around 40 g, many times the amount previously reported to cause type B lactic acidosis.[11] Finally, a milder case of lactic acidosis during TURP has been recently reported with a low volume absorption (500 ml) of a sorbitol–mannitol solution and might also be explained by the same mechanism.[12]

The clinical presentation of lactic acidosis varies greatly. In type A, the signs and symptoms of the underlying problem dominate the clinical picture. However patients with type B may present with a variety of symptoms such as hyperventilation, malaise, weakness, nausea, vomiting, abdominal pain and progressive mental clouding.[8] These symptoms are frequently encountered in the TURP syndrome but are usually believed to be caused by hypervolaemia and hyponatraemia. Many of these symptoms were present in this case and were at least in part caused by lactic acidosis, especially in the recovery phase when hypervolaemia and hyponatraemia were improving while blood lactate was still elevated. It should be noted that both type A and B lactic acidosis may occur simultaneously. Hypoxaemia and hypoperfusion are often present in the TURP syndrome and will prevent the entry of pyruvate into the citric acid cycle, thus further increasing production of lactate.

In summary, we report a case where hyperglycaemia and lactic acidosis complicated the TURP syndrome caused by the massive absorption of a sorbitol–mannitol irrigating solution. We suggest that blood glucose and arterial lactate concentration should be measured when an important absorption of sorbitol–mannitol is suspected and that type B lactic acidosis is a possible cause of metabolic acidosis in such cases.

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