Use of human growth hormone in treatment of nesidioblastosis in a neonate

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SUMMARY Growth hormone was effective in reducing the glucose requirement in an infant with nesidioblastosis. He was suffering from fluid overload secondary to glucose and water infusions necessary to maintain blood glucose. Early pancreactectomy is the preferred treatment in severe cases, but human growth hormone has a place in preoperative management.

A neonate with hyperinsulinism was referred to us. He was being treated with intravenous dextrose and diazoxide but was oedematous and in heart failure. Water overload may arise from the treatment of hyperinsulinism with dextrose solutions. Diazoxide is known to cause sodium retention, and this compounds the problem. To reduce his glucose requirement we treated him with human growth hormone.

Case report

The boy was the third full term child of Asian parents who are first cousins. At delivery he weighed 3900 g and looked like the baby of a mother with gestational diabetes. He became symptomatically hypoglycaemic at four hours and was treated with intravenous glucose. To maintain his blood glucose concentration above 2 mmol/l (36 mg/100ml) he was treated with increasing amounts of intravenous glucose and oral feeds. Hydrocortisone 4 mg/kg/day intravenously and on four separate occasions glucagon 100 μg/kg did not have any apparent effect. By the sixth day his carbohydrate requirement (oral feeds plus intravenous) had risen to 23 mg/kg/min, but he was still having periods of symptomatic hypoglycaemia (Figure). He was subsequently found to have an insulin concentration of 38 IU/l, with a blood glucose concentration of 2.3 mmol/l (41.5 mg/100ml).

He was referred to Birmingham Children’s Hospital on the sixth day. He was in heart failure with pulmonary oedema, a patent ductus arteriosus, and some peripheral oedema. The liver was two and a half centimetres below the costal margin. During the previous 12 hours he had received 260 ml/kg/day of fluid. Treatment with hydrocortisone was stopped. His heart failure was treated with frusemide for 24 hours, and he was started on human growth hor-
mone one unit twice daily subcutaneously. The dose was reduced after five days to one unit daily but his symptoms returned and the carbohydrate requirement increased (Figure).

After 22 days he underwent a near total pancreatectomy (Mr J J Corkery), preserving only a small ‘collar’ of pancreas around the pancreatic duct/duodenal junction. Previous experience with pancreatectomy in the treatment of this condition has suggested that preservation of more pancreatic tissue is followed by relapse of hyperinsulinism. Nesidioblastosis was confirmed on histological examination. Currently, aged 9 months, he is on three units of insulin a day and pancreatic supplements.

Discussion

Many drugs have been used in the treatment of hyperinsulinism in the neonate. Diazoxide usually with chlorthiazide has been most commonly used but often fails to maintain euglycaemia without glucose infusion. A complication of this management is heart failure, and we have seen this twice in cases treated here recently. It may be a more common problem. When this neonate arrived with an already compromised cardiac state we felt justified in using growth hormone.

The first drug to be used in the treatment of hyperinsulinism was bovine growth hormone, which though initially effective was immunogenic. The development of human growth hormone preparations led to successful treatment in adults with hyperinsulinism, but this was soon superseded by diazoxide. The reported experience of human growth hormone in hyperinsulinism in infants is limited. Soyka et al describe the successful use of growth hormone in an infant of 3 months who had been symptomatic since birth. Aysnley-Green et al used it unsuccessfully in an infant of similar age, after subtotal pancreatectomy. This is the first case report to show that growth hormone can be effective in the treatment of hyperinsulinism in the neonate. This dose proved to be effective but is somewhat arbitrary. It would be expected to lead to grossly raised growth hormone concentrations in the blood, and the twice daily regimen would fit with known pharmacokinetics. There seemed to be a delay in onset of action of roughly 12 hours from injection to full effect. There was a similar delay in stopping of action when the dose was reduced.

We are not proposing the use of human growth hormone for the long term management of hyperinsulinism. It has proved to be an effective alternative to diazoxide and chlorthiazide, however, in maintaining normoglycaemia while pancreatectomy is arranged.

References


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