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Nifedipine-induced Hyperglycaemia in an Infant : A Case Report

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Summary

Jobran Al Qhtani, Abdulla A Al Harthi, Yousef Fatinni, Ahmed Al Barki, Sulaiman Al-Fifi, Asindi A Asindi, Saad Al Daama. Nifedipine-induced Hyperglycaemia in an Infant: A Case Report. *Nigerian Journal of Paediatrics* **2001;28:18.** This case report describes reversible hyperglycaemia in a severely ill six-month old Saudi boy treated with nifedipine for hypertension. Hyperglycaemia became manifest on the second day of treatment with nifedipine and was not dose-related. Following discontinuation of the drug, the patient rapidly became euglycaemic. It is concluded that the hyperglycaemia was induced by nifedipine. This side effect of nifedipine has been reported in adults but the present case would appear to be the first of a similar report in a child. We suggest that dehydration due to hyperglycaemia-induced osmotic diuresis can constitute a risk to small infants on nifedipine, hence it should be used with caution on outpatient basis.

Introduction

NIFEDIPINE, a dihydropyridine, is currently one of the widely used antihypertensive agents in adults, but experience of its use in children appears to be limited.[1,2] Its side effects which include dizziness, hypotension, flushing and headaches, are due largely, to excessive vasodilatation.[3] Other untoward effects include constipation, peripheral oedema, cough, wheezing and pulmonary oedema. Animal studies have identified hyperglycaemia as an additional complication,[4,5] while in isolated cases, a rise in the blood glucose level has been observed in humans especially adult diabetics receiving nifedipine for concomitant hypertension.[6,7] We are unaware of any documentation of high blood glucose levels as an adverse reaction in children being treated with the drug. This report describes a six-month old Saudi infant who rapidly became hyperglycaemic while on treatment with nifedipine for hypertension in Assir Central Hospital, Saudi Arabia.

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Case Report

A six-month old Saudi male was admitted on 26/6/99 to the paediatric intensive care unit (PICU) of Assir Central Hospital for the treatment of 25 percent scalded burn of the perineum and thighs. According to the parents, he accidentally sustained the injury while being bathed under a running tap of hot and cold water. The scalded area was managed routinely with open dressing and antibiotics. On the tenth day of hospitalization, he had a massive aspiration of feeds that resulted in cardio-pulmonary arrest. With resuscitation, and following three weeks of mechanical ventilation, he only partially recovered consciousness and was left with spastic quadriplegia and frequent seizures. Following this cerebral insult, it was noticed that his blood pressure (systolic and diastolic) which was initially normal, became persistently high, being above the 95th centile for his age.[1] His serial renal profile, serum electrolytes, blood glucose and liver function tests were within normal limits from admission. Abdominal ultrasound showed normal sized kidneys for the age and his arterial blood gas results were satisfactory while he was being mechanically ventilated.

The child has one sibling aged 18 months; both parents are well and there is no family history of diabetes mellitus.

The patient's hypertension was treated with nifedipine at an initial dose of 1mg/kg/day every four hours. For the seizures, he received phenobarbitone which was the only additional medication that was used. Milk and drugs were fed through a nasogastric tube. On the second day of nifedipine therapy, his blood glucose level which was initially normal, rose to levels ranging from 12-14 mmol/l (220-240mg/dl) and his urine tested positive for glucose but there were no ketones. As there was no significant improvement in his blood pressure levels within the first three days of therapy, the dose of nifedipine was increased to 2mg/kg/day every four hours. With this doubling of nifedipine dose, his serial blood glucose level was in the range of 8-13 mmol/l (142-234 mg/dl) but no improvement was observed in the blood pressure for another four days.

Since the seven-day course of nifedipine still did not ameliorate the hypertension, it was replaced with hydralazine. On this new drug, he became normotensive and the blood sugar level reverted to a normal range (4-7mmol/l or 72-126 mg/dl) within 48 hours; the normotensive/euglycaemic state was sustained thereafter. Meanwhile, his seizures had been effectively controlled within 24 hours of commencing phenobarbitone therapy.

During the course of treatment with nifedipine, and for the first two weeks on hydralazine, the patient was being fed with *Similac* milk formula (*Ross Products Division of Abbot Laboratories, Columbus, Ohio*) as the only source of calories. The daily fluid intake was maintained at 100ml/kg and he did not receive intravenous infusion. The patient's blood pressure was checked two hourly, and the blood glucose was estimated 12-hourly in the hospital laboratory. Inadvertently, no accurate record was kept of his daily urine output, but at no stage did he show signs of dehydration or require additional fluids. There were no facilities to estimate serum insulin and C-peptide levels. As at the time of reporting, the infant was still hospitalized because of his sustained semi-comatose state. He continued to receive phenobarbitone and hydralazine and remained euglycaemic.

Discussion

The onset of hyperglycaemia from the second day of therapy with nifedipine and the rapid return to euglycaemic state following its discontinuation/replacement, strongly suggests that the hyperglycaemia was induced by the nifedipine. One way of confirming the hyperglycaemic effect of nifedipine in this child would have been to re-challenge him with the drug after achieving a euglycaemic state, but this approach would most probably have been unethical. Nifedipine-induced hyperglycaemia is well documented in animal studies,[4,5] and there are reports of similar experience in non-diabetic human adults.[7,8] Heyman *et al* demonstrated a 30 percent increase in the daily insulin requirement of a 60-year old diabetic following nifedipine administration.[9] In contrast, Collens *et al* who studied the effects of nicardipine and nifedipine on 20 adult non-insulin dependent diabetics over a four-week period, discovered that these two dihydropyridines produced no significant effect on their glucose tolerance, plasma insulin and haemoglobin A1 levels.[6] To our knowledge, hyperglycaemia as a side effect of nifedipine in infancy and childhood has not yet been reported hence this appears to be the first of such documentation.

The exact mechanism by which nifedipine induces hyperglycaemia is controversial. It is postulated that the diabetogenic effect associated with nifedipine is mediated by a suppressed islets beta cell function.[9] Dihydropyridines function by decreasing calcium efflux out of the cells and inhibiting insulin release, thus inducing hyperglycaemia. Others speculate that its effect is extra-pancreatic and is attributed to interference with peripheral glucose utilization.[5,8]

In our patient, the hyperglycaemia occurred with a dose of 1mg/kg/day within 48 hours of initiating treatment and increasing the dose to 2mg/kg/day did not cause any further increase in the blood glucose levels. From this observation, it appears that the hyperglycaemic effect of nifedipine in infants may not be dose-related.

We are unable to explain why our patient's hypertension did not respond to nifedipine. Perhaps the stress of being extremely ill and in a semicomatose state might have contributed. Inadvertently, no record was kept of the child's urine output, hence it was not possible to determine if the hyperglycaemic state had induced an osmotic diuresis. However, the fact that the patient maintained a satisfactory state of hydration during the medication would suggest that if there had been diuresis, it was probably minimal. Nevertheless, the fact that such high blood glucose levels could cause polyuria with dehydration poses a risk to small infants. Since nifedipine is currently being recommended for both children and infants, including neonates,[1,2] and in view of the possibility of developing hyperglycaemia, it is pertinent to caution physicians on its use on outpatient basis in infants.

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