Glucagon therapy in preterm infants with hyperinsulinemic hypoglycaemia

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Introduction

The treatment of preterms with hyperinsulinemic hypoglycaemia is a well-known challenge. One of the difficulties of the therapy is the excessive application of intravenous fluids to compensate high carbohydrate needs. There are various drug alternatives such as glucagon, diazoxide or somatostatin analogues apart from intravenous glucose application.

Hypothesis: Intravenous or continuous subcutaneous glucagon therapy are suitable alternatives to stabilise blood sugar levels without causing complications in preterm infants.

Methods

A two-centre retrospective data analysis was initiated. Data of patients with the diagnosis of prematurity and hyperinsulinemic hypoglycaemia with glucagon therapy between 2008 and 2019 were analysed.

Results

Medical records from 762 preterm patients were evaluated. 9 preterms were treated with glucagon aside from intravenous glucose therapy.

Continuous treatment was applied either intravenously or subcutaneously (off-label). Start of therapy was between day 3 and 25 after birth.

Amount of carbohydrate intake scaled between 9 and 24.4 g/kg/d. All 10 patients showed a rapid stabilization of blood sugar levels in the first 48 hours of glucagon therapy. Median increase of blood sugar levels ranged between 9 and 140%.

Treatment lasted between 4 and 39 days with a glucagon dose range of 12.9 to 34 µg/kg/h. 2 patients were treated intravenously.

3 patients were treated intravenously and through time subcutaneously. 4 other patients were treated intravenously or subcutaneously with glucagon, additional oral diazoxide and/or subcutaneous octreotide.

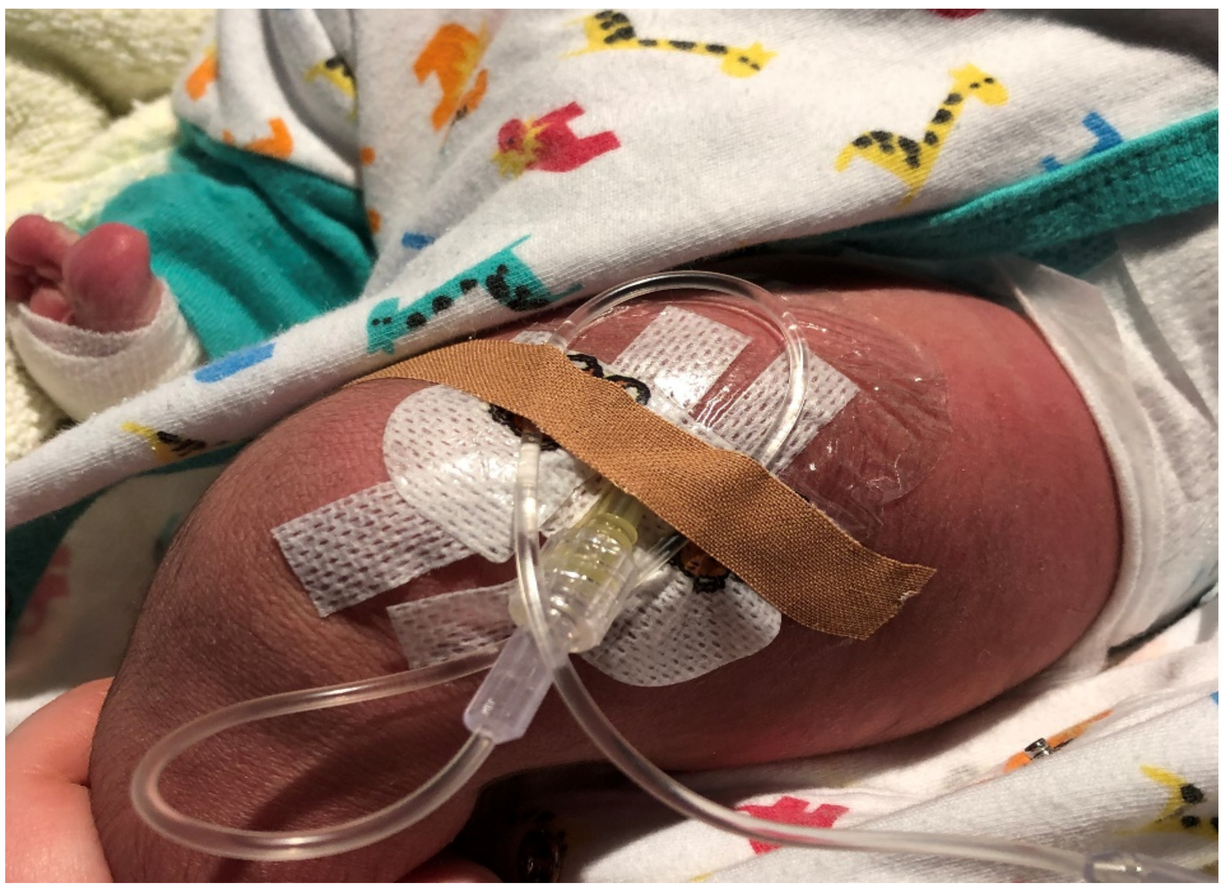
Due to low solubility of glucagon high infusion rates and periodic exchange of the subcutaneous catheter were necessary to prevent catheter obstruction.

Hyponatraemia or thrombocytopenia as known side effects of glucagon therapy were not detected.

One patient treated subcutaneously showed a cutaneous abscess. Uncomplicated relief puncture showed a good curative treatment.

Conclusions

In our cohort, glucagon therapy was rarely initiated. Based on the rare experiences glucagon seems to be an adequate medication for rapid stabilisation of low blood sugar levels for hyperinsulinemic hypoglycaemic preterms. It can be used to bridge the time until diazoxide, as a potential long term medication, shows effectiveness. Intravenous or subcutaneous application of the dose spectrum mentioned shows good effects and tolerance. Continuous peripheral intravenous and subcutaneous application of glucagon seem to be advantageous methods to prevent hyperhydration and edema through excessive intravenous glucose application. Through subcutaneous therapy a continuous glucagon application is guaranteed even if peripheral glucose treatment is interrupted.
Off-Label subcutaneous glucagon therapy should be used more often leading to the establishment of standards for glucagon therapy in preterm.



References

- Mehta, A. et al., 1987. Effect of diazoxide or glucagon on hepatic glucose production rate during extreme neonatal hypoglycaemia. *Archives of disease in childhood*, 62(9), pp.924–30.
- Miralles, R.E. et al., 2002. Experience with intravenous glucagon infusions as a treatment for resistant neonatal hypoglycemia. *Archives of pediatrics & adolescent medicine*, 156(10), pp.999–1004.
- Belik, J., Musey, J. & Trussell, R.A., 2001. Continuous infusion of glucagon induces severe hyponatremia and thrombocytopenia in a premature neonate. *Pediatrics*,107(3), pp.595–7. Sunehag, A., Gustafsson, J. & Ewald, U., 1994. Very Immature Infants (≤ 30 Wk) Respond to Glucose Infusion with Incomplete Suppression of Glucose Production. *Pediatric Research*, 36(4), pp.550–555.
- Wald, M. et al., 2002. Glucagon therapy as a possible cause of erythema necrolyticum migrans in two neonates with persistent hyperinsulinaemic hypoglycaemia. *European Journal of Pediatrics*, 161(11), pp.600–603.
- Charsha, D.S., McKinley, P.S. & Whitfield, J.M.,2003. Glucagon infusion for treatment of hypoglycemia: Efficacy and safety in sick, preterm infants. *Pediatrics*,111(1), pp.220–1.
- Jackson, L. et al., 2003. An inadequate glycaemic response to glucagon is linked to insulin resistance in preterm infants? *Archives of disease in childhood. Fetal and neonatal edition*, 88(1), pp.F62-6.
- Mohnike, K. et al., 2008. Long-term non-surgical therapy of severe persistent congenital hyperinsulinism with glucagon. *Hormone research*,70(1), pp.59–64.

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