

## INSULIN

### Use

Insulin can be used to correct acute hyperkalaemia, and to reduce perceived 'hyperglycaemia' in the very preterm baby receiving IV glucose. Only small doses are needed in children with true neonatal diabetes mellitus.

### Pathophysiology

Diabetes mellitus can be caused by inadequate insulin production (type 1 diabetes), or by abnormal resistance to insulin secretion (type 2 diabetes). All such women need to optimise glucose homeostasis both during conception (aiming for a glycated haemoglobin (HbA<sub>1c</sub>) level below 7.5% to minimise the risk of congenital malformation and miscarriage) and during pregnancy and, because insulin (first isolated as a hormone from pancreatic islet  $\beta$  cells in 1922) does not cross the placenta or appear in human milk, this is the drug of choice during pregnancy. Glucose intolerance ('gestational' diabetes) often increases during pregnancy, and the use of insulin, or of a sulfonylurea drug such as glibenclamide (q.v.), reduces the risk of fetal macrosomia (usually defined as a baby weighing over 4 kg at birth) if dietary advice alone does not suffice.

Newborn babies are relatively intolerant of glucose and the response of the pancreas to an IV load is relatively sluggish. The infusion of 10% dextrose at a rate appropriate to normal fluid and calorie needs may sometimes exceed the very preterm child's ability to metabolise glucose, or turn glucose into glycogen, especially in the first week of life and it is not clear that a glucose uptake of more than 14 mg/kg per minute is actually desirable. Intolerance usually resolves rapidly if the rate of glucose infusion is reduced for 6–12 hours, but insulin can be used for a time if parenteral feeding is constrained by plasma glucose levels that are persistently above 12 mmol/l once it is clear that a sudden rise is not the first sign of sepsis or other illness. Glycosuria can be ignored unless the blood glucose level exceeds 15 mmol/l.

Arrhythmia due to sudden unexplained neonatal hyperkalaemia ( $K^+ >7.5$  mmol/l) is occasionally seen in very preterm babies especially in the first 3 days of life. Continuous infusions of glucose and insulin have been widely employed to control such hyperkalaemia, and may work quicker than a rectal cation-exchange resin (q.v.), but nebulised or IV salbutamol (q.v.) may be the treatment of choice at least initially.

### Treatment

**Parenteral nutrition:** A trial of giving 0.05 units/kg of insulin per hour continuously to <1.5 kg babies in the first week of life while monitoring subcutaneous glucose found that, while this increased calorie intake, it had no long term impact on growth, and there were more deaths in the insulin treated babies in the first 28 days of life.

**Hyperkalaemia:** Combine IV glucose with between 0.3 and 0.6 units/kg per hour of IV insulin.

**Neonatal diabetes:** This rare condition, which presents with acidosis, dehydration and hyperglycaemia (usually >20 mmol/l), but little ketosis, responds to a very low dose insulin infusion: 0.5–3.0 units/kg IV per day is usually adequate. A continuous subcutaneous infusion may be appropriate if problems persist for more than 2 weeks, but treatment can usually be tailed off within 4–6 weeks and, if evidence of type 1 diabetes does re-emerge, this can usually be held in check by giving 0.1 to 0.4 mg/kg of glibenclamide by mouth twice a day.

### Compatibility

Insulin can be added (terminally) to a line containing TPN (with or without lipid), and into a line containing dobutamine (but not dopamine), glyceryl trinitrate, midazolam, milrinone, morphine, or nitroprusside.

### Supply and administration

10 ml multidose vials of human soluble insulin containing 100 units/ml cost approximately £15 each. They are best stored at 4°C, but contain m-cresol as a preservative and can be kept for a month at room temperature. Do not freeze. Any short-acting soluble product (such as Humulin S<sup>®</sup>) can be used for IV or subcutaneous administration. These products should not be used if the fluid appears hazy or coloured. Long-acting slow-release products, containing a cloudy crystalline zinc suspension (such as Humulin Zn<sup>®</sup>), or isophane protamine (such as Humulin I<sup>®</sup>), are only suitable for subcutaneous use.

Take 0.25 ml (25 units) from the vial and dilute to 50 ml with 0.9% sodium chloride to obtain a preparation containing 0.5 unit/ml. Insulin adheres to plastic and consistent IV delivery will not be achieved for several hours unless the delivery tubing is flushed with at least 20 ml of fluid before use. Delivery is more constant if the set is also left with fluid in it for an hour before being flushed through. While such priming is less essential when treatment is first started because the initial infusion rate is likely to be determined by the response achieved, failure to prime any *replacement* set could well destabilise glucose control. The IV solution is stable and does not need to be changed daily. Pharmacies can provide an oral suspension of glibenclamide on request.

### References

See also the relevant Cochrane reviews ©

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