¿Qué hay que saber para enfrentar la hiperglicemia en el prematuro extremo?

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Magnitud del problema

- **Frecuencia**: 60 a 80% de <1000 gr
- **Causas**:
  - Exceso de aporte de glucosa
  - Exceso de aporte de lípidos
  - Stress
  - Drogas
  - Aumento de producción de glucosa
  - Incapacidad de usar la glucosa a nivel tisular
    - Poca masa muscular
    - Resistencia insulínica a nivel hepático

Decaro, M. & Vain, N. Hyperglycaemia in preterm neonates: what to know, what to do. *Early human development* **87 Suppl 1,**S19–22 (2011).

Table 1. Risks for Hyperglycemia in Newborn Infants

- Preterm birth
- Intrauterine growth restriction (IUGR)
- Increased stress hormones
  - –Increased catecholamine infusions and plasma concentrations
  - –Increased glucocorticoid concentrations (from use of antenatal steroids, postnatal glucocorticoid administration, and stress)
  - –Increased glucagon concentrations
- Early and high rates of intravenous (IV) lipid infusion
- Higher-than-needed rates of IV glucose infusion
- Insufficient pancreatic insulin secretion (preterm and IUGR)
- Absence of enteral feedings, leading to diminished "incretin" secretion and action, limiting their potential to promote insulin secretion

Rozance, P. & Hay, W. Neonatal Hyperglycemia. *NeoReviews* **11,** e632–e639 (2010).

¿y? ¿cuál es el problema?

- Hiperosmolaridad
- Diuresis osmótica
- Deshidratación
- Desbalances electrolíticos
- Acidosis

Pero… no hay evidencia

- Estudios sólo en adultos y pediatría
- Enfermedad de base como causa de hiperglicemia
- ¿Qué nivel de glicemia es capaz de producir diuresis osmótica?
  - Depende del umbral (250 a 340 mg/dl)

Hey E. Hyperglycaemia and the very preterm baby. *Seminars in Fetal and Neonatal Medicine*. 2005;10(4):377-387.

¿Cuándo hay hiperglicemia?

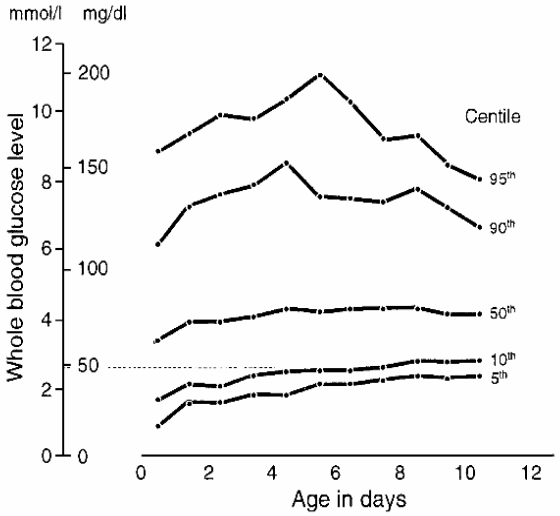

Figure 1 Laboratory estimates of whole blood glucose in a prospective study of all the babies of <32 weeks' gestation born in 1990–1991 to mothers normally resident in the north of England. Samples were collected for the study at a fixed pre-specified time each morning. Birth before 32 weeks' gestation accounted for almost 1% (781/81,784) of the region's live births. Data relating to the 176 babies who died within 28 days of birth have been excluded (1 mmol/L=18 mg/dL glucose).

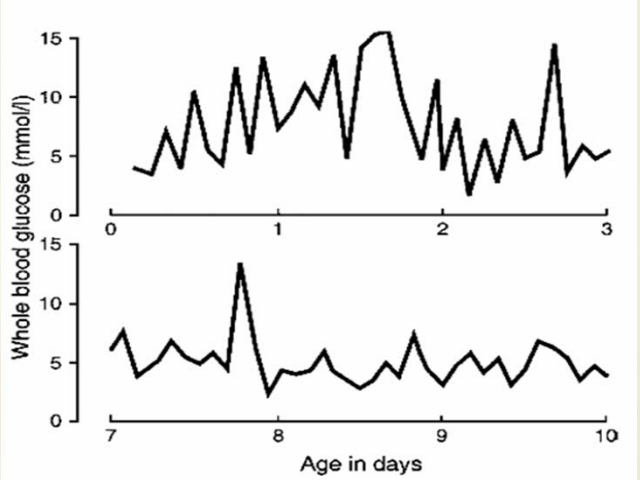

Figure 2 Whole blood glucose measurements in a 870 g baby of 26 weeks' gestation measured once every 2 h in the first 10 days of life. The baby received 5 mg/kg of glucose a minute intravenously as 10% dextrose for 24 h, rising to 7 mg/kg by 3 days, and half this amount during days 7–9. Oral feeds were introduced after 3 days. The baby was taking 2 mL/kg of breast milk an hour by 6 days (and twice this amount by 9 days). Urine passed 43 h after birth contained >1% glucose. The hyperglycaemic episode on the 8th day of life occurred when a bolus of intravenous flucloxacillin was flushed through the intravenous giving set.

Hey E. Hyperglycaemia and the very preterm baby. *Seminars in Fetal and Neonatal Medicine.* 2005;10(4):377-387.

Definición

- Definición estadística: 180 a 200 mg/dl
- Definición "de trabajo"
  - El nivel en que aparece glucosuria y riesgo de diuresis osmótica

Insulina

- Hipótesis:
  - Mejora la utilización de glucosa
  - Promueve mejor crecimiento
  - Disminuye HIV
  - Aumenta IGF-1: impacto en retinopatía

- Beardsall, K. *et al.* Early Insulin Therapy in Very-Low-Birth-Weight Infants. *N Engl J Med* (2008). doi:10.1056/NEJMoa0803725
  - Estudio NIRTURE

- Alsweiler, J., Harding, J. & Bloomfield, F. Tight glycemic control with insulin in hyperglycemic preterm babies: a randomized controlled trial. *Pediatrics* **129,**639–47 (2012).

- CONCLUSIONS: Tight glycemic control with insulin in hyperglycemic preterm infants increases weight gain and head growth, but at the expense of reduced linear growth and increased risk of hypoglycemia. The balance of risks and benefits of insulin treatment in hyperglycemic preterm neonates remains uncertain.

- El estudio NIRTURE fue suspendido al encontrar mayor incidencia de daño parenquimatoso cerebral en el grupo de estudio y mayor incidencia de hipoglicemia sintomática

¿Qué hacemos, entonces?

Table 4. **Summary of Recommendations for Prevention and Management of Neonatal Hyperglycemia**

- Improved physiologic control
- Early and increased parenteral nutrition with amino acids
- Early initiation of enteral feedings
- Limited intravenous glucose infusion rates during hyperglycemia to what is required for achieving normal glucose concentrations
- Limited intravenous lipid infusions during hyperglycemia
- Reservation of insulin therapy only for severe hyperglycemia with associated clinical signs and complications.

Rozance, P. & Hay, W. Neonatal Hyperglycemia. *NeoReviews* **11,** e632–e639 (2010).

¿Hiperglicemia permisiva?

- Estudio retrospectivo 260 RNPT<1000g seguidos hasta los dos años

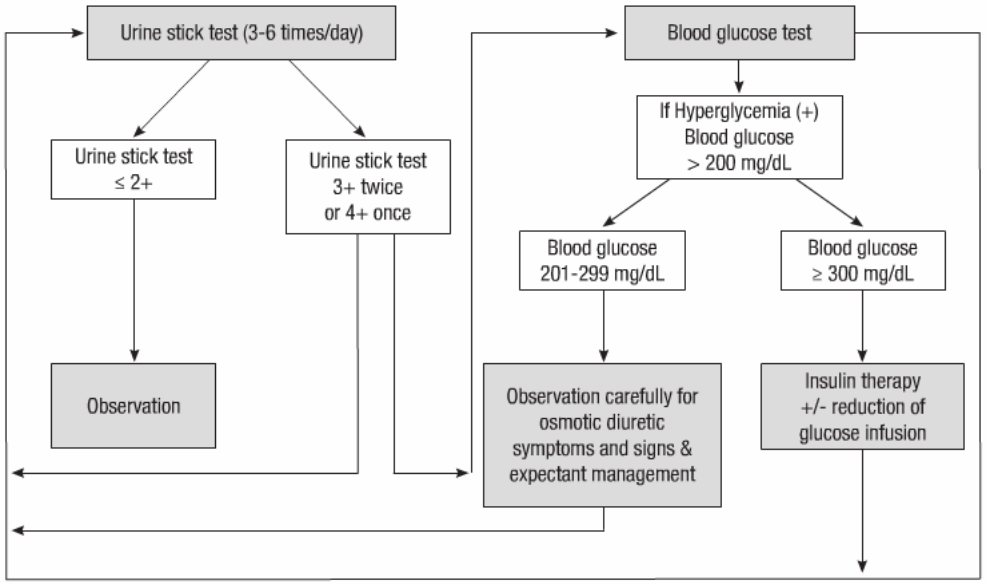

Fig. 1. Strategy for the management of neonatal hyperglycemia in extremely-low-birth-weight infants during the first 14 days of life.

Yoo, H. *et al.* Permissive Hyperglycemia in Extremely Low Birth Weight Infants. *J. Korean Med. Sci.* **28,** (2013).

Conclusiones

- Permissive hyperglycemia up to < 300 mg/dL without insulin treatment during the first 14 days of life is not associated with osmotic diuresis or increased mortality or morbidities, suggesting that it is not detrimental in ELBWIs.

Yoo, H. *et al.* Permissive Hyperglycemia in Extremely Low Birth Weight Infants. *J. Korean Med. Sci.* **28,** (2013).

Muchas gracias