Weight Outcome in Infants with Prolonged Hyperinsulinemic Hypoglycemia Treated with Diazoxide versus those with Spontaneous Resolution

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BACKGROUND

- Physiological transition of glucose metabolism is typically completed within 48-72h of life, yet *prolonged hypoglycemia* beyond 5d of life is not uncommonly encountered, especially in infants at-risk of hypoglycemia.
- Hyperinsulinemic hypoglycemia (HH) may be a cause of *prolonged hypoglycemia*. It is characterized by high GIR >10mg/kg/min to maintain normoglycemia (3.5–5.9mmol/L). During hypoglycaemia, HH infants have inappropriate insulin & c-peptide levels, hypoketonemia and hypofattyacidemia.
- Management of HH includes feeding and dextrose infusion while awaiting spontaneous resolution (SR) or Diazoxide (DZX) therapy.
- As a K_{ATP} channel agonist, DZX blocks insulin release by keeping the K_{ATP} channel open, preventing β-cell depolarization.
- **KNOWLEDGE GAP:** Since DZX acts by suppressing insulin release, concerns arise whether weight gain in infancy will be suppressed while on DZX. Conversely, will awaiting SR result in excessive weight gain in untreated HH infants?

STUDY AIM:

To compare weight change patterns in infants with prolonged HH managed with dextrose infusion awaiting SR versus those who received DZX treatment.

METHODS

Prolonged HH infants met all the following inclusion criteria:

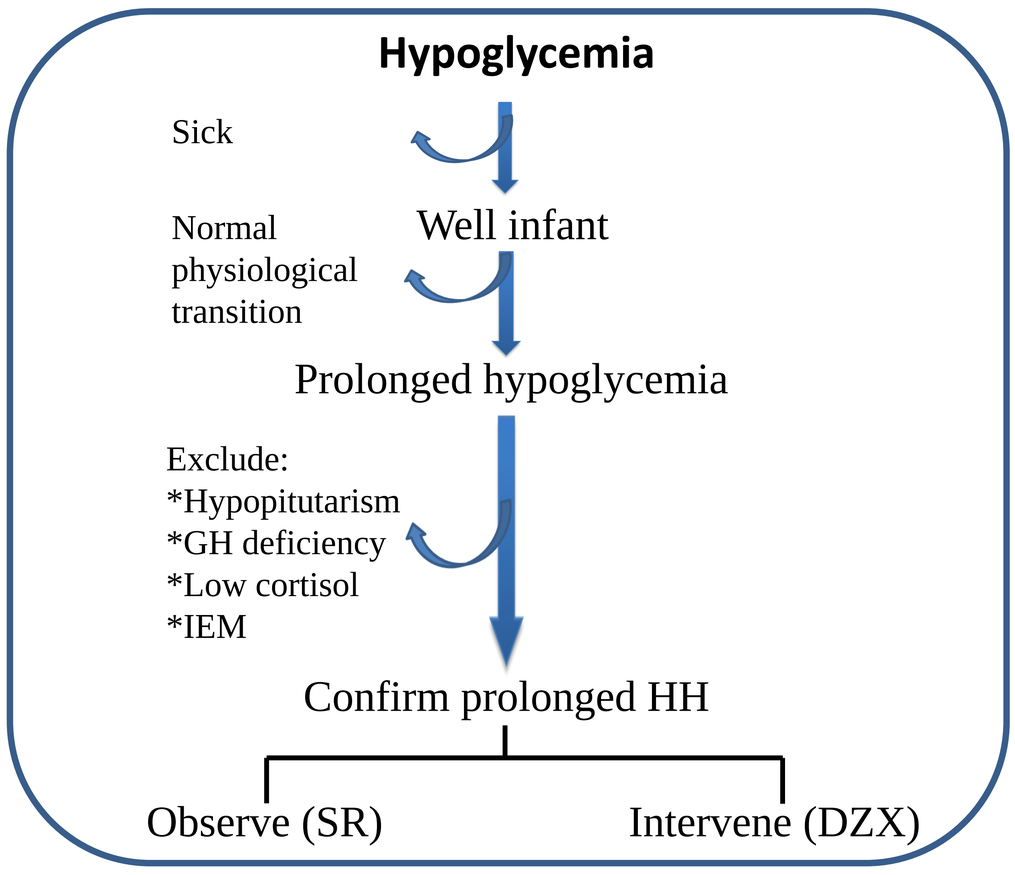
- BG <3.5mmol/L at ≥5d of life
- GIR >10 mg/kg/min to maintain blood glucose (BG) >3.4mmol/L
- Inappropriate insulin levels when BG <3mmol/L
- Hypoketonemia

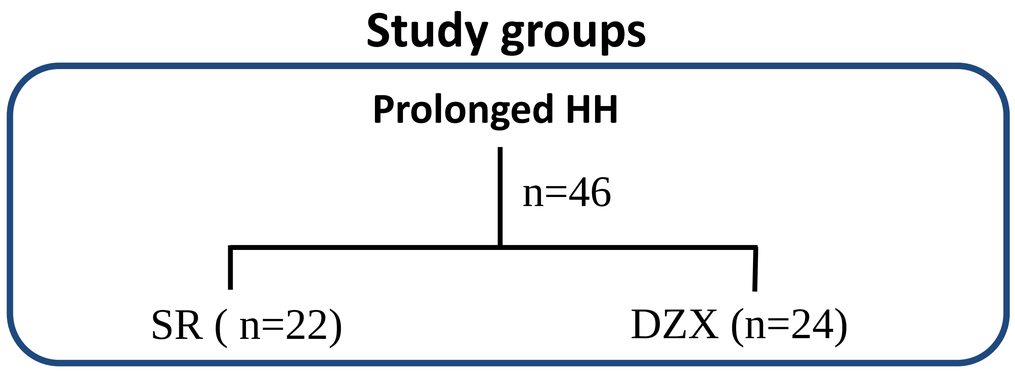
We excluded infants with sepsis, polycythemia, IEMs, hypocortisolism and growth hormone deficiency.

Resolution of HH in SR infants was confirmed by normal home glucose for 2 weeks following discharge and DZX infants passed fasting studies on completion of treatment.

Data on demographics, birth weight, gestational age, treatment modality and duration, and follow-up body weight were collected.

Birth weight z-scores were determined using Fenton 2013 tables and follow-up body weight z-scores were derived from WHO Multicenter Growth Reference Study 2006 standards. Changes in weight z-score were analyzed. The study was approved by the Institutional Review Board.





Clinical characteristics

	SR (n=22)	DZX (n=24)
Sex (Male/Female)	13 / 9	16 / 8
Preterm/Term	9 / 13	11 / 13
Mean gestational age (weeks)	36.2	36.8
SGA/non-SGA	11 / 11	17 / 7
Birth weight (g)	2647 ± 927	2133 ± 626
Birth weight SDS	**-0.56 ± 1.50**	**-1.36 ± 1.02**
Corrected age at FU (months)	3.0	3.8
Weight at FU (g)	4539 ± 1545	4673 ± 1707
Weight SDS at follow up	**-0.83 ± 1.19**	**-1.5 ± 1.11**
Median LOS (days (range))	16 (7 - 41)	18 (10 - 50)

Weight change comparison

	SR SDS change	DZX SDS change	p
All infants (n=46)	-0.27	-0.14	0.69
SGA infants (n=28)	0.00	+0.29	0.36

CONCLUSION

1. The use of DZX therapy did not suppress weight gain and resulted in weight gain patterns similar to those of SR infants.

2. Awaiting spontaneous resolution did not result in excessive weight gain compared to DZX treated infants.

3. The use of low dose diazoxide (3mg/kg/day) did not prevent catch up weight gain in DZX treated SGA infants.

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