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Adverse Effects Associated with Diazoxide Use in Neonates

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Background

Diazoxide is the first-line treatment used to manage infants with hyperinsulinemic hypoglycemia (HIH).[1]

From 1997 to 2016, the percentage of infants diagnosed with hypoglycemia and treated with diazoxide increased significantly.[2]

This has prompted heightened concern regarding the possible side effects of diazoxide in this population. Circulatory complications such as fluid retention and, in severe cases pulmonary hypertension, have been reported following treatment with diazoxide. In a few cases, reopening of the PDA has also been reported.[2-4] Blood dyscrasias, including neutropenia and thrombocytopenia, have also been reported.[3,5-6]

One study reports transient gastrointestinal reactions after initiation of diazoxide.[7] Additional data regarding GI disturbance and feeding difficulty in neonates receiving diazoxide is lacking.

Objective

To evaluate the type and frequency of adverse effects associated with diazoxide used for treatment of hyperinsulinemic hypoglycemia (HIH) in neonates.

Methods

- An IRB-approved retrospective case control study of all neonates admitted to the NICU treated with diazoxide for hypoglycemia after a diagnosis of HIH between January 1, 2015 and September 1, 2019.
- Subjects were younger than six months of age at treatment initiation with diazoxide.
- Data regarding general patient characteristics and diazoxide dosing was collected.
- Data including findings on echocardiogram, electrolyte values, blood counts, episodes of emesis, oral intake, and intake via NG/OG tube was collected at time before and after treatment initiation with diazoxide to allow for comparison.
- Descriptive analysis was done with means (standard deviations) and percentages reported as appropriate.
- Paired t-test or repeated measures Anova were performed for comparison of continuous or discrete measures before and after the administration of diazoxide
- McNemar test was performed for categorical measures.

Results

- A total of 25 patients (64% males) met inclusion criteria.

Circulatory complications

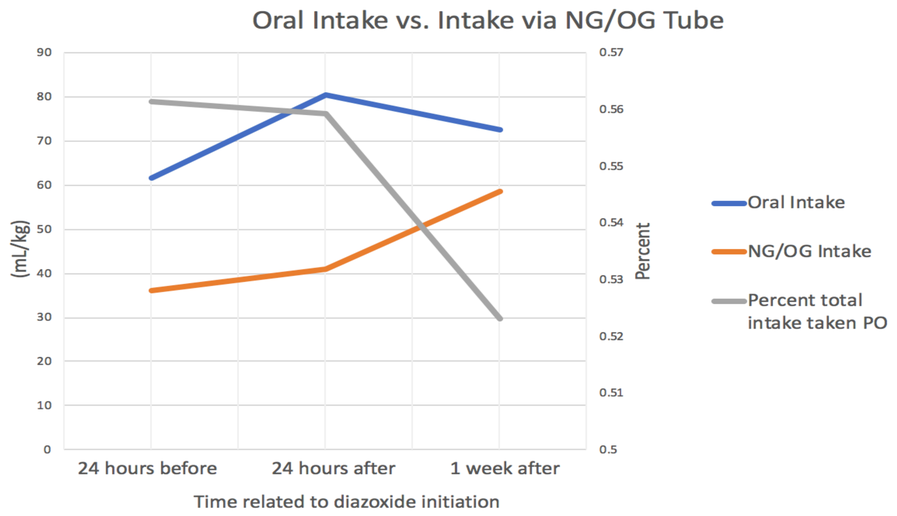
- One patient (4%) had pulmonary hypertension (PHN) documented on echocardiogram before diazoxide initiation, 5 patients (20%) were diagnosed with PHN after diazoxide initiation.
- Nine patients (36%) required increased diuretic dose after diazoxide initiation.
- There were 5 cases (20%) of reopening of the PDA, defined as a new finding of PDA on echocardiogram after diazoxide treatment initiation.

Blood cell dyscrasias

- Mean platelet count was higher and neutrophil count lower 1 week after diazoxide initiation compared to before; however neither was statistically significant.

Feeding difficulties

- Mean number of episodes of emesis in the three days after diazoxide initiation was significantly higher than the three days before (1.24 and 0.28 respectively, p=0.006).
- There was a trend for decrease in oral intake and increase in intake via NG/OG tube after diazoxide initiation.



Demographics

	Mean +/- SD
Gestational age at birth (weeks)	35.65 +/- 3.99
Birth weight (grams)	2112.12 +/- 954.17
Weight at diazoxide initiation (grams)	2375.76 +/- 827.71
Gestational age at diazoxide initiation (weeks)	37.61 +/- 2.88
Postnatal age at diazoxide initiation (days)	13.76 +/- 12.41
Duration of diazoxide therapy (days)	19.56 +/- 15.92
Diazoxide initial dose (mL/kg/day)	10.94 +/- 2.24
Diazoxide max dose (mL/kg/day)	12.14 +/- 2.729

Adverse Effects

Condition	Prior to diazoxide initiation	After diazoxide initiation	p-value
Pulmonary hypertension (mean frequency, %)	4.0%	20.0%	0.13
Platelet count (mean +/- SD, cells/μL)	149.13 +/- 100.497	212.93 +/- 108.197	0.13
Neutrophil count (mean +/- SD, cells/μL)	4.99 +/- 2.785	3.93 +/- 2.363	0.19
Emesis (mean +/- SD, count)	0.280 +/- 0.68	1.24 +/- 1.48	0.006*

Conclusions

- Cardiovascular complications, such as new onset pulmonary hypertension and re-opening of the PDA were observed after initiation of diazoxide treatment.
- There were significant gastrointestinal complications seen after diazoxide initiation, such as increase in emesis events and lack of improvement in oral intake.
- There were no significant side effects in relationship to blood cell dyscrasias seen in this sample.
- As diazoxide appears to be used more liberally, larger studies are needed to further evaluate the extent and severity of side effects seen with this medication.

References

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