ELBWIs admitted to our hospital between January 2017 and March 2023. who developed hyperglycemia after 8 days of age and who were treated with insulin or sulfonylurea were eligible.

Efficacy of enteral sulfonylurea therapy for Extremely Low Birth Weight Infants

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Abstract

Background : There are few reports on the use of enteral sulfonylurea therapy for hyperglycemia in extremely low birth weight infants (ELBWIs), and its efficacy and safety remain unclear.
Objective: To evaluate the effect of sulfonylurea on blood glucose (BG) levels in ELBWIs with hyperglycemia.
Methods: This was a retrospective single-center study. We evaluated the duration of treatment, time from treatment initiation to reaching BG levels <180 mg/dL, and the number of hypoglycemic events. A p-value of < 0.05 was considered statistically significant.
Results: Of the 26 hyperglycemic infants, 19 were treated with insulin and 7 with sulfonylurea. The treatment periods were 3 and 3 days (p = 0.36), and the time to hyperglycemia improvement was 35 and 22 h (p = 0.20), respectively. Hypoglycemia occurred in one patient in the insulin group, but no cases were reported in the sulfonylurea group.
Conclusion: Sulfonylurea can reduce BG levels in ELBWIs with hyperglycemia similar to insulin; however, further studies are required.

Introduction

The incidence of hyperglycemia in extremely low birth weight infants (ELBWIs) is high, ranging from It has been shown to be associated with various20–80%[1–2]. adverse outcomes, such as retinopathy of prematurity, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, and death. However, no evidence-based criteria exist to ensure an effective intervention for hyperglycemia or blood glucose (BG) levels in ELBWIs. Intravenous insulin is commonly administered to hyperglycemic infants; however, it increases the risk of hypoglycemia. Therefore, safe alternative drugs with efficacy comparable to or better than that of insulin are required for the treatment of hyperglycemia in ELBWIs. Sulfonylureas are oral antidiabetic agents that enhance the secretion of endogenous insulin by binding to the receptor of the ATP-sensitive potassium (KATP) channel on pancreatic β-cells. Sulfonylureas are an established treatment for infants with neonatal diabetes mellitus[3]. There have been few reports regarding use of enteral sulfonylurea for the treatment of hyperglycemia in ELBWIs[4], and the efficacy and safety of sulfonylurea in these infants are unknown. Therefore, in this study, we compared enteral sulfonylurea and intravenous insulin treatment for hyperglycemic ELBWIs.

Methods

We retrospectively evaluated the medical records of infants admitted to our hospital between January 2017 and March 2023. Infants with hyperglycemia (BG ≥ 180 mg/dL) who were administered either intravenous insulin or enteral sulfonylurea after postnatal day 8 were eligible. We excluded patients who received both insulin and sulfonylurea or were transferred to another hospital. This study was approved by the Central Ethics Board of our institution.
We collected data on the demographic and clinical characteristics of the patients, including sex, gestational age (weeks), birth weight (g), comorbidities, age at the onset of hyperglycemia after day 8, nutritional status, maximum BG levels before treatment, concomitant use of steroids or catecholamines, and death before discharge. At our hospital, we initiate intravenous insulin or enteral sulfonylurea treatment in patients with persistent BG levels above 300 mg/dL. We administered crushed glibenclamide as a sulfonylurea via an enteral tube. The prescribed dosage of sulfonylurea was 0.1–0.2 mg□kg-1□day-1 based on previous reports.
We compared the treatment duration, time to achieve normoglycemia (BG levels <180 mg/dL), and hypoglycemic events in both groups to evaluate efficacy and safety.
Continuous variables were expressed as medians and interquartile ranges, whereas categorical variables were expressed as frequencies and proportions. All analyses were performed using the EZR 1.60. A p-value of <0.05 was considered statistically significant.

Results

In total, 273 ELBWIs were born during the study period. Of these, 199 (73%) developed hyperglycemia, 19 (26%) received intravenous insulin, and seven (4%) received enteral sulfonylurea treatment.
There were no significant differences in patient characteristics **(Table 1)**. The duration of treatment and time to achieve normoglycemia (BG level <180 mg/dL) showed no statistically significant differences **(Table 2**). One patient in the insulin group developed hypoglycemia, but no hypoglycemic events occurred in the sulfonylurea group. The changes in BG levels after treatment in each group are shown in **(Figure 1)**.

Table 1. Patient characteristics

	Insulin group n=19	sulfonylurea group n=7	P-Value
Gestational age (wk)	24 [22-24]	23 [23-24]	0.93
Birth weight (g)	557 [498-608]	525 [483-569]	0.65
Day onset of hyperglycemia (day)	8 [8-10]	10 [9-12]	0.08
Date of enteral feeding ≧100 ml/kg/day (day)	16 [14-23]	15 [13-18]	0.37
Maximum BG levels before treatment (mg/dL)	358 [308-410]	368 [319-409]	0.56
Day of initial treatment	14 [12-34]	26 [20-27]	0.13
Steroid	13 (68)	7 (100)	0.15
Cathecolamine	11 (58)	2 (29)	0.38
Intraventricular hemorrhage	6 (32)	1 (14)	0.63
sepsis	4 (21)	0	0.55
Necrotizing enterocolitis	2 (11)	0	1
Severe ROP	0	1 (14)	0.27
Death before discharge	2(11)	1 (14)	1

Table 2. details of treatment

	Insulin group n=19	sulfonylurea group n=7	P-Value
Initial dose	0.09 mg/kg/day [0.09-0.10]	0.7 U/kg/day [0.4-1.3]	
Duration of treatment (days)	3 [2-9]	3 [3-6]	0.75
Time to achieve BG levels <180 mg/dL (hr)	22 [14-58]	35 [26-104]	0.20
Hypoglycemic events during treatment	1 (5)	0	1

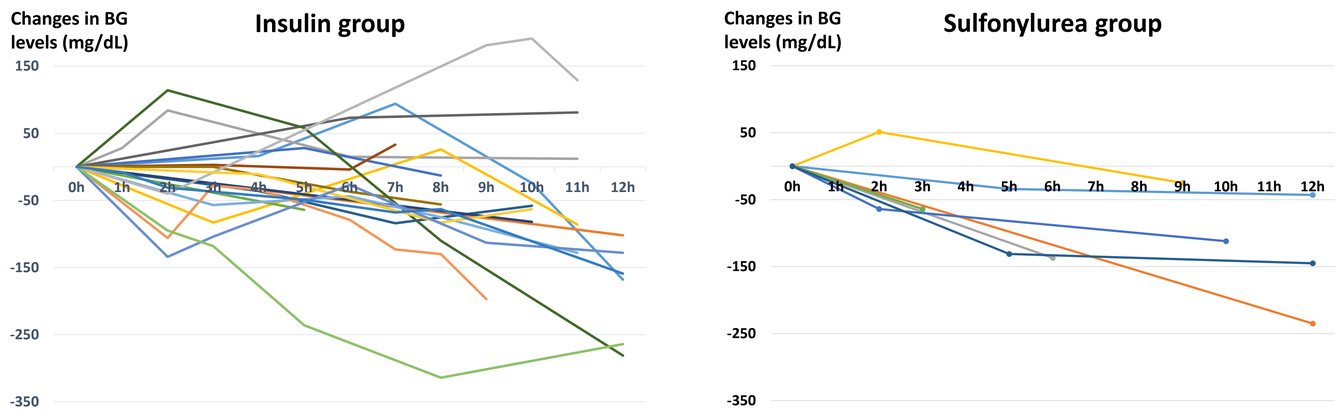

Fig 1. Changes in BG levels after the start of treatment
This figure shows that the insulin group has a greater range of blood glucose variability; however, there is no difference in the treatment duration required to achieve euglycemia between the insulin and sulfonylurea groups..

Discussion

This study shows that enteral sulfonylurea treatment can lower BG levels, similar to insulin, with no hypoglycemic events occurring during treatment. In a previous study, sulfonylureas normalized BG levels within a few days in ELBWIs with hyperglycemia without serious adverse events. In our study, the median treatment period for the sulfonyl group was 3 days, consistent with previous results[4]. Although no difference was found in the time taken to achieve normoglycemia, it appears that the insulin group had greater BG variability during treatment than the sulfonylurea group. This is thought to be due to the difficulty in regulating insulin doses in ELBWIs, including the need for multiple dilutions, time required insulin delivery in the body, and possibility of insulin absorption on the catheter.

This study has several limitations. First, it was a retrospective study with a small number of cases. Second, the dosage of sulfonylurea and insulin and the timing of BG measurements were determined at the discretion of each clinician. Third, neonatal diabetes could not be excluded, which may have led to an overestimation of the effects of sulfonylurea.
This is the first report comparing insulin and sulfonylurea treatments in ELBWIs with hyperglycemia. In conclusion, enteral sulfonylurea treatment was as effective as intravenous insulin treatment, and no hypoglycemic events were observed in the sulfonylurea group. Further studies are required to investigate the efficacy and safety of enteral sulfonylurea treatment, its risk for

References

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