



# The Effectiveness of Sirolimus in a Newborn with Hyperinsulinemic Hypoglycemia

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## Introduction:

Hyperinsulinemic Hypoglycemia (HH) is a rare genetic disease and the treatment of HH in cases with unresponsiveness to medical therapy is subtotal pancreatectomy. In a recent study, the authors showed that sirolimus could be an alternative treatment in these patients<sup>1</sup>. We aimed to evaluate the effectiveness of sirolimus in a newborn with HH.

## Case:

A 10 day-old neonate presented with hyperinsulinemic hypoglycemia (glucose: 26 mg/dl, insulin: 55 mIU/ml). She was born at term with a birth weight of 3300 gr. Hypoglycemia had persisted despite

- IV glucose perfusion 20 mg/kg/min
- Diazoxide 15 mg/kg/d
- Octreotide 40 mcg/kg/d (postnatal 14<sup>th</sup> day)
- Glucagon infusion 0.01 mg/kg/h (postnatal 21<sup>st</sup> day)
- Sirolimus 0.5 mg/m<sup>2</sup>/d

**Table 1:** The follow-up of the patient after sirolimus treatment

	5. day	11. day	16. day	19. day	24. day	30. day	34. day	44. day	77. day
Sirolimus level (4.5-28 µg/l)	3,1	20	10	4,6	10,9	8	7,7	9,9	11,9
Sirolimus dose (mg/m <sup>2</sup> /d)	0,5	1	1	1	1,6	1,6	2,3	3	2,4
Octreotide dose (µg/kg/d)	40	40	40	40	stop	40	40	40	25
Glucagon (µg/kg/h)	10	5	stop						
GPR (mg/kg/min)	18	10	6	12,5	5	10	stop		
Diazoxide dose (mg/kg/d)	15	5	stop						

**Table 2:** The laboratory findings of the patient during AGE

	Sirolimus stop ↓ 0. day	Sirolimus restart ↓ 3. day	Sirolimus stop ↓ 5. day	7. day
WBC (4-10 <sup>3</sup> /ml)	28.400	12.450	7300	
CRP (0-10 mg/L)	1.3	2.8	2.1	
AST (0-40 U/L)	298	68	144	51
ALT (0-40 U/L)	302	140	171	61

A novel homozygous ABBC8 mutation (p.H59P) was detected. She had also congenital hypothyroidism and received L-thyroxine. When she was 10 months old, sirolimus was discontinued due to high liver enzyme levels (Table 2). She is currently 11 months old and uses only octreotide (8 mcg/kg/d). After 4 hours fasting, glucose: 132 mg/dl insulin: 11.3 uIU/ml

**Conclusion:** Sirolimus could be beneficial in patients with unresponsiveness to diazoxide and octreotide treatment. However, should be vigilant in terms of its side effects.

1. Senniappan S, et al. Sirolimus therapy in infants with severe hyperinsulinemic hypoglycemia. N Engl J Med. 2014 Mar 20;370(12):1131-7

