Opioid-induced endocrinopathy in a toddler with chronic codeine intoxication

S. Van Aken, S. Vanderstraaten, K. De Waele, M. Cools, M. Craen, J. De Schepper.

Department of Pediatric and adolescent Endocrinology , University Hospital Ghent, Belgium

Background

Several studies in adults have provided evidence for opioid-induced hypofunction of the hypothalamo-pituitary-adrenal & GH-IGF-1 axis after chronic (oral and intrathecal) administration (1,2,3).

Opioids act primarily at the pituitary level and also have effects on the peripheral glands, such as the adrenals (4).

This so-called opioid endocrinopathy has not been reported in children.

Objective and hypothesis

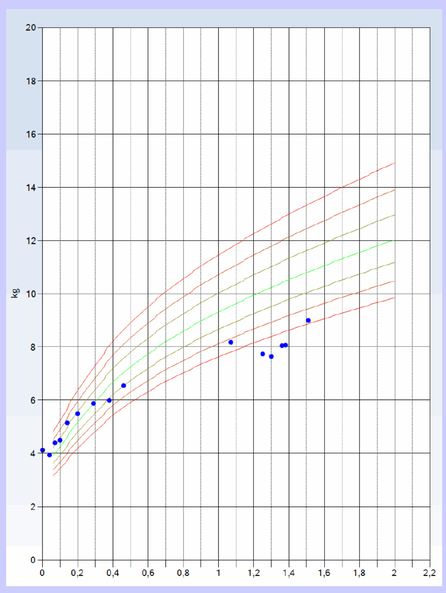
We report the occurrence of delayed growth with low serum IGF-1 levels and recurrent hypoglycemia due to central hypocorticism in a toddler after a presumably intentional chronic codeine administration by her parents.

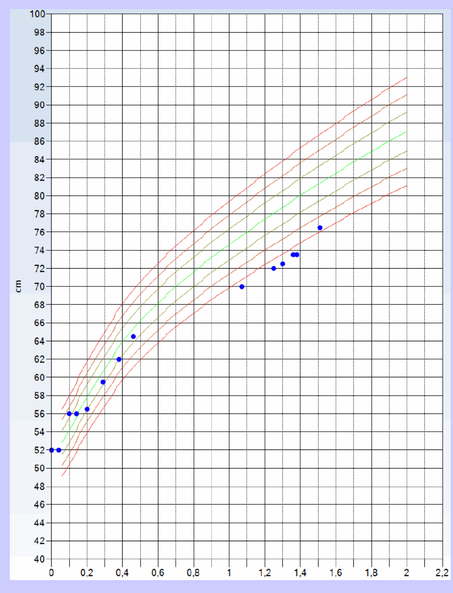
Method

In a healthy 12 months old girl, admitted for coma related to a benzodiazepine and codeine intoxication, a symptomatic hypoglycemia (glucose < 45 mg/dl) , responding to glucose administration, was documented when excessive sleepiness reoccurred at the third day of hospitalization.

Subsequent glucose monitoring showed several asymptomatic hypoglycemic episodes during the next day.

Poor growth and previous episodes of excessive sleepiness were evidenced during the 4 months preceding the hospitalization.





Results

A critical sample analysis documented a ACTH level of 10 pg/mL and a cortisol of 1.7 µg/dL, which increased up to 13.9 µg/dL after a low dose ACTH test. Basal serum PRL and TSH were normal , but IGF-1 was low (26 µg/L) and DHEAS not measurable.

A normal pituitary and hypothalamus were seen on MR imaging of the brain.

After the instauration of hydrocortisone therapy, glucose levels remained normal and hydrocortisone was stopped after 6 weeks.

Critical sample

ACTH : 10 pg/mL (<46)

Cortisol : 1.7 µg/dL (5.15 - 23.6 morning)

Low dose ACTH test

Cortisol 0’ : 4.18 µg/dL

Cortisol 10’ : 11.2 µg/dL

Cortisol 20’ : 13.07 µg/dL

Cortisol 30’ : 13.99 µg/dL

Basal hormonology

TSH : 1.6 mU/L (0.70-6.0)

FT4 : 1.3 ng/dL (1.0-1.8)

Prolactin : 3.62 µg/L (6-30)

GH : 4.6 µg/L (<8)

IGF-1 : 26 (Z-Score: -3.61) ng/mL (66-328)

DHEAS : <5 µg/dL (0.47-19.4)

Four weeks after stopping therapy, a normal basal cortisol , but a weak response to ACTH was documented.

A normal GH and cortisol response at glucagon testing was found after 6 weeks.

Glucagon stimulation test

Glucose		GH	insulin	Cortisol
0’	0.69 g/L	2.85 µg/L	1.9 mU/L	10.06 µg/dL
30’	1.21 g/L		82 mU/L	
60’	0.95 g/L		13 mU/L	
90’	0.51 g/L	11.2 µg/L		9.67 µg/dL
120’	0.44 g/L	3.50 µg/L		16.18 µg/dL
150’	0.5 g/L	1.65 µg/L		16.93 µg/dL
180’	0.51 g/L	2.01 µg/L		12.86 µg/dL

At the age of 2 years 11 months, her height (-1.4 SD) and weight (-0.4 SD) are normal. Her neuromotor development is normal.

Conclusion

In contrast with hyperglycemia seen in toddlers with acute codeine intoxication, recurrent hypoglycemia due to a transient central hypocorticism can be observed in chronic codeine ingestion. Genetic differences in opioid receptor binding and metabolizing properties might be responsible for the induction and recovery of the endocrine dysfunction after opioid administration in children

References

1.Effect of oral morphine and naloxone on pituitary-adrenal response in man induced by human corticotropin-releasing hormone.B. Allolio;Acta Endocrinol apr 1987,114(4):509-514

2.Secondary adrenal failure and secondary amenorrhoea following hydromorphone treatment.K. Müssig;Clinical Endocrinology 2007,66:602-605

3.Endocrine consequences of long-term intrathecal administration of opioids; R. Abs; JCEM 2000 ,85 (6):2215-2222

4.The effects of opioids and opioid analogs on animal and human endocrine systems. C. Vuong; Endocrine Reviews feb 2010, 31(1):98-132