

# Different Potent Glucocorticoids, Different Routes of Exposure but The Same Result: Iatrogenic Cushing's syndrome and Adrenal Insufficiency

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## Introduction

Cushing's syndrome (CS) is very rare in childhood and the most common cause is the high doses of synthetic glucocorticoids administered to children for treatment or misuse of it. Potent glucocorticoids (GC) cause iatrogenic CS (ICS) due to suppress hypothalamo-hypophyseal-adrenal (HPA) axis and later even adrenal insufficiency (AI). The aim of this study is to review the clinical and laboratory findings of patients with ICS and to review other side effect.

## Methods

In this retrospective study, all of data is obtained from patients' medical records. The 14 (9 girls, 5 boys) aged between 0.19 and 11.89 years, were enrolled to the study. All patients had been given a high dose of moderate to high potent glucocorticoids by oral and / or skin. The mother of case 12 had used an ointment to prevent diaper dermatitis from birth on which she thought to have contained panthenol. The manufacturer stated that there was no glucocorticoid in the cream. The possibility of AI was investigated by low-dose ACTH test. Hydrocortisone was started in patients with adrenal failure. A 24-hour urine sample and a morning fasting blood sample of the Case 12 were obtained before treatment was initiated. Blood steroid analyze was performed. Also, urine steroid profile was performed at University of Birmingham College of Medical and Dental Sciences.

## Results

A clinical summary of the patients is given in Table. The duration of exposure ranged from 1 to 72 months. Ten patients had been given topical GC such as clobetasol-propionate, diflucortolone-valerate, metilprednisolon-aceponate and betamethasone exposure, rest of them had been administered oral exposure such as metilprednisolon and prednisolone. One infant (Case 12) used a cream for diaper dermatitis that was claimed to be because of panthenol. Infant's blood and urine steroid analysis revealed all the endogenous steroids were suppressed (Figure). At the admission of the 14, 11 had AI and two infants had hypercalcemia and nephrocalcinosis. Of 11 patients, ultrasonography revealed five patients have hepatosteatosi. The HPA axis returned to normal at a median of 60(160) days.

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Age, years	12	0.21	9	0.56	0.41	2.45	1.08	11.56	11.89	10.88	0.46	0.19	11.4	6
Sex	F	M	F	F	F	M	M	F	M	F	F	F	M	F
Complaint	CS suspicion in a patient treated for ITP	Puffiness on the face and abdomen	Maculopapular rash	Genital hair	Rapid gain weight	Hair on the face	Widespread hypertrichosis	Gain weight	Gain weight	Gain weight	Pubic hair, ichthyosis	Gain weight	Gain weight	Gain weight
Corticosteroid (CS) product	MPZ	Prednisolone	MPZ	Diflucortolone Valerate 0.3% and isoconazole nitrate	Diflucortolone Valerate 0.3% and isoconazole nitrate	Clobetasol Propionate 0.05%	Clobetasol Propionate 0.05%	Clobetasol Propionate 0.05%	Clobetasol Propionate 0.05% and MPZ	MPZ	MPZ, dexamethasone, betamethasone Valerate	Coresatin®	MPZ	Clobetasol Propionate 0.05%
Duration,	24 months	1.6 months	1 months	Since birth	Since birth	7 months	2 months	3 years	6 years	2 years	1 month	2 months	1 month	3 moths
CS potency/ HC equivalent dose, mg/m <sup>2</sup> /d	5 times/ 180	4 times/148	5 times/165	100-150 times/ Unpredictable	100-150 times/ Unpredictable	Up to 600times/ Unpredictable	Up to 600times/ Unpredictable	Up to 600times/ Unpredictable	Up to 600times/ Unpredictable	5 times	5 times/30 times/25 times	Unknown	5 times	Up to 600times/ Unpredictable
CS application route	oral	oral	oral	skin	skin	skin	skin	skin	skin	oral	skin	skin	oral	skin
Weight SD	0.04	0.08	2.75	0.74	5.23	-1.25	-1.93	2.43	2.27	4.06	-2.1	2.26	2.12	1.79
Height SD	-3.35	-1.33	0.6	0.03	-0.22	-1.47	-1.21	-1.24	1.37	0.58	-1.7	1.45	-0.03	-0.01
BMI SD	1.98	1.57	2.9	0.91	6.21	-0.3	-1.63	3.12	2.08	3.74	-1.44	1.58	2.47	2.22
Physical Examination	Buffalo hump, moon face, central obesity, purple striae	Moon face, central obesity, facial acne, oral and diaper candidiasis	Moon face, central obesity, widespread maculopapular rash in the whole body	Diffuse fine hair in the genital and sacral region	Moon face, central obesity, prominent skin folds	Moon face, central obesity, widespread hypertrichosis	Moon face	Moon face, buffalo hump, central obesity, purple striae	Moon face, central obesity, widespread white-yellow plaques in the whole body	Moon face, central obesity, purple striae	Moon face, hepatomegaly, fine hair at mons pubis	Moon face, central obesity, prominent skin folds	Moon face, Buffalo hump, central obesity, purple striae	Moon face, central obesity
Basal Cortisol, µg/dL	3.73	2.1	0.6	4.52	<1	<1	7.85	3.76	6.87	<1.0	<1.0	<1.0	11.7	12.4
Basal ACTH, pg/mL	<5	7.48	15.3	19	<5	19.5	37	19	16.9	9.1	<5	<5	35.2	56
Stimulated Cortisol, µg/dL	ND	5.4	6.21	16.3	ND	3	9.44	4.57	12.6	6	<1.0	1.1	18.1	21.2
Abdominal USG	Splenomegaly	Bilateral nephrocalcinosis	Hepatosteatosi s grade 2	Normal	NA	Normal	NA	Hepatosteatosi s, hepatosplenomegaly	Hepatosteatosi s	Hepatosteatosi s	Normal	Hepatosteatosi s grade 1, nephrocalcinosis at right kidney	Hepatosteatosi s grade 2, hepatomegaly	NA
Normalization time of the HPA axis, day	40	None	150	51	Unknown	60	Unknown	Unknown	780	1110	30	66	HPA axis was normal	HPA axis was normal
Therapy	Splenectomy for ITP; metformin for hyperglycemia	HC started as 20mg/m <sup>2</sup> /d and FC 0.1 mg/d for adrenal atrophy; furosemide and pamidronate for hypercalcemia	HC started as 20mg/m <sup>2</sup> /d	None	Parents refused to all investigations and therapy	HC started as 20mg/m <sup>2</sup> /d	HC started as 20mg/m <sup>2</sup> /d	HC started as 20mg/m <sup>2</sup> /d	PR equivalent to 20mg/m <sup>2</sup> /d hydrocortisone	HC started as 20mg/m <sup>2</sup> /d	HC started as 20mg/m <sup>2</sup> /d	HC started as 20mg/m <sup>2</sup> /d	None	None

## Conclusion:

In this series, 70% of the patients with life-threatening AI and two patients with hypercalcemia were detected. These results pointed out potent GCs cause serious side effects especially in infants. Physicians should be aware of the possible misuse of GCs and products that have the possibility of containing synthetic glucocorticoids since parents are not informed of the use of these drugs side effects.

