Mitotane (op'DDD) restores growth and puberty in nine children with Cushing's disease

Titre	Mitotane (op'DDD) restores growth and puberty in nine children with Cushing's disease
Type de publication	Article de revue
Auteur	Motte, Emmanuelle [1], Rothenbuhler, Anya [2], Gaillard, Stephan [3], Lahlou, Najiba [4], Teinturier, Cécile [5], Coutant, Régis [6], Linglart, Agnès [7]
Editeur	BioScientifica
Type	Article scientifique dans une revue à comité de lecture
Année	2018
Langue	Anglais
Date	Décembre 2018
Numéro	12
Pagination	1280-1287
Volume	7
Titre de la revue	Endocrine Connections
ISSN	2049-3614
Résumé en anglais	To investigate whether low-dose mitotane (up to 2 g/day) could be a temporary therapeutic alternative to transsphenoidal surgery (TSS) in pediatric Cushing's disease (CD). Twenty-eight patients with CD aged 12.2 years (± 2.2) were referred to our center. We compared nine patients treated with mitotane alone for at least 6 months to 13 patients cured after surgery. Primary outcomes were changes in growth velocity, BMI and pubertal development. The following results were obtained: (1) Mitotane improved growth velocity z-scores (−3.8 (±0.3) vs −0.2 (±0.6)), BMI z-scores (2.1 (±0.5) vs 1.2 (±0.5) s.d.) and pubertal development. After 1 year on mitotane, the mean BMI z-score was not significantly different in both groups of patients. (2) Control of cortisol secretion was delayed and inconsistent with mitotane used as monotherapy. (3) Side effects were similar to those previously reported, reversible and dose dependent: unspecific digestive symptoms, concentration or memory problems, physical exhaustion, adrenal insufficiency and hepatitis. (4) In one patient, progressive growth of a pituitary adenoma was observed over 40 months of mitotane treatment, allowing selective adenomectomy by TSS. In conclusions, low-dose mitotane can restore growth velocity and pubertal development and decrease BMI in children with CD, even without optimal control of cortisol secretion. It may promote pituitary tumor growth thus facilitating second-line TSS. However, given its possibly life-threatening side effects (transient adrenal insufficiency and hepatitis), and in the absence of any reliable follow-up procedures, this therapy may be difficult to manage and should always be initiated and monitored by specialized teams.
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DOI	10.1530/EC-18-0215 [9]

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