

Adrenal suppression following intralesional corticosteroids for periocular haemangiomas

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ABSTRACT

Background/aims Treatment with intralesional triamcinolone/betamethasone is recommended for infantile sight-threatening periocular haemangiomas. This study investigates the endocrine and weight changes in 15 infants undergoing therapy over 12 years. **Methods** 15 infants, median age 19 weeks (range 10–56) receiving intra/perilesional triamcinolone/betamethasone underwent serial measurement of weight, early morning serum cortisol and adrenocorticotropic hormone (ACTH) before and after injection.

Results Cortisol fell from a median (range) of 383 (112–594) to 28 (<10–506) nmol/l ($p=0.005$) and ACTH from 26 (14–134) to 9 (5–20) ng/l ($p=0.05$) from before injection to 4 weeks after treatment. Prolonged adrenal suppression occurred in 13 out of 15 cases with time to recovery being 19.5 (4–65) weeks. Failure to gain weight appropriately was observed in 14 infants but recovered once normal adrenal function was re-established.

Conclusion Prolonged adrenal suppression following triamcinolone/betamethasone injection for periocular haemangiomas is common and associated with faltering weight gain.

INTRODUCTION

Haemangiomas are the most common benign tumour of infancy, the estimated prevalence in neonates being 1–3% with 70–90% resolving spontaneously by 7 years of age. Periocular haemangiomas have a number of potential complications including amblyopia, astigmatism, strabismus, proptosis and optic atrophy. If sight-threatening complications are envisaged, intervention with corticosteroids should be considered.¹ Until recently intralesional injection with triamcinolone/betamethasone was considered the treatment of choice to induce resolution (figure 1A,B). However, propranolol may offer a new treatment modality for the future.²

Previous observations of reversible adrenal suppression and poor weight gain following triamcinolone/betamethasone therapy³ led to the instigation of a treatment protocol (see Methods section for details), whereby all children receiving such therapy had adrenal function assessed before and after treatment. Where adrenal suppression occurred, treatment with hydrocortisone was started until recovery of adrenal function. This paper describes the outcomes for a cohort of children treated under this joint care (ophthalmology and paediatric endocrinology) protocol from 1996 to 2007. The systematic documentation of adrenal function and weight in these children has confirmed the clinically significant consequences of this treatment on adrenal function and weight

gain and has implications for the management of children with sight-threatening haemangiomas. Propranolol may offer a less toxic treatment modality but has yet to undergo rigorous trials.²

METHODS

All children treated with triamcinolone/betamethasone for periocular haemangiomas in a single teaching hospital from 1996 to 2007 inclusive were identified. The dose of triamcinolone varied between 20 and 40 mg, whereas betamethasone was given in a fixed dose of 2 mg. All children received a mixture of both triamcinolone and betamethasone simultaneously.

Morning serum cortisol concentrations were measured before injection (ADVIA Centaur Cortisol; Siemens Healthcare Diagnostics, Deerfield, Illinois, USA) and 4-weekly thereafter. Children with an early morning serum cortisol concentration of <120 nmol/l (the lower limit of reference range for the assay) 4 weeks after injection were considered to have adrenal suppression and hydrocortisone treatment was instigated (10 mg/m²/day in two or three divided doses) with a 'steroid card' provided to alert other healthcare professionals. Early morning serum cortisol and adrenocorticotropic hormone (ACTH) concentrations (Immulite; Siemens Healthcare Diagnostics) were remeasured every 4–6 weeks on hydrocortisone treatment following omission of the previous evening and morning doses of hydrocortisone. Testing continued until recovery of basal adrenal function was confirmed (early morning serum cortisol concentration >120 nmol/l). Regular hydrocortisone therapy was then stopped and a Synacthen test performed to evaluate adrenal responsiveness. A normal Synacthen response was taken as a baseline cortisol concentration >120 nmol/l with a peak response >550 nmol/l and/or a doubling of the baseline value.

Weight was measured at each visit and results converted to SD scores (SDS) using 1990 British reference data. This study was considered an audit of service provision and therefore ethics consent was not considered necessary. Statistical comparisons were performed using non-parametric analysis.

RESULTS

Fifteen infants (three boys, 12 girls) received treatment between 1996 and 2007. The median age at injection was 19 (range 10–56) weeks. Seven infants received a second dose of triamcinolone/betamethasone due to inadequate resolution of the haemangioma at varying intervals.

Short report



Figure 1 (A) Patient before and (B) after treatment with an intralesional triamcinolone/betamethasone mixture.

Thirteen of 15 patients sustained adrenal suppression 4 weeks following triamcinolone administration (cortisol <120 nmol/l). There was a fall in serum cortisol concentration from a median (range) of 383 (112–594) nmol/l before treatment (n=13) to 28 (<10–506) nmol/l ($p<0.005$) 4 weeks after injection (n=15). Likewise, the median (range) ACTH concentration fell from 26 (14–134) ng/l (n=10) to 9 (5–20) ng/l (n=11) ($p<0.05$) over the same period. The time from first injection of triamcinolone/betamethasone to basal adrenal recovery/resolution for all 15 infants varied markedly from 4 to 65 weeks (median (IQR) 19.5 (8–42) weeks) but was significantly longer in the seven infants requiring a second injection (median (range) time to adrenal recovery for infants receiving one or two triamcinolone/betamethasone injections, respectively, 8 (4–35) and 41 (15–65) weeks; $p=0.017$). Figure 2 shows the time to recovery of adrenal function for all 15 infants. Synacthen tests performed after a normal basal cortisol were all normal.

Failure to gain weight appropriately following the steroid injection was demonstrated in 14 of 15 children. A significant fall in weight SDS was observed 4 and 8 weeks after the steroid injection (median (range) weight SDS at injection, 4 weeks and 8 weeks, respectively, -0.08 (-2.27 to 2.16), -0.67 (-2.60 to 1.55) and -0.82 (-3.09 to 1.65); $p<0.05$). However, by the time of basal cortisol recovery and normal Synacthen response, there was no significant difference in the weight SDS compared to before triamcinolone treatment (-0.63 (-3.72 to 1.65)

and 0.15 (-3.72 to 1.33), respectively) demonstrating catch-up growth. Furthermore, the effect of triamcinolone/betamethasone on adrenal suppression and/or weight gain did not appear to be dose-dependent. Although some infants receiving two injections took longer to recover adrenal function, there was no significant association between the total dose of triamcinolone/betamethasone received and time to recovery.

DISCUSSION

This retrospective analysis of systematic monitoring of adrenal function demonstrates prolonged adrenal suppression in 13 of 15 patients undergoing intralesional injection of a triamcinolone/betamethasone mixture and demonstrates this to be a common and potentially serious side-effect with two children sustaining adrenal suppression for more than a year.

Previously, Goyal *et al*⁸ speculated that the initial release of glucocorticoids into the circulation led to acute adrenal suppression. The clinical concern is that continued systemic absorption of steroids from the injection site would then decline at an unknown rate until a point when circulating glucocorticoids would be insufficient to prevent an adrenal crisis occurring during intercurrent illness given co-existent iatrogenic adrenal failure. It is not easy clinically to judge when circulating triamcinolone concentrations are insufficient to prevent an adrenal crisis or when full recovery of the hypothalamic-pituitary-adrenal axis has occurred.

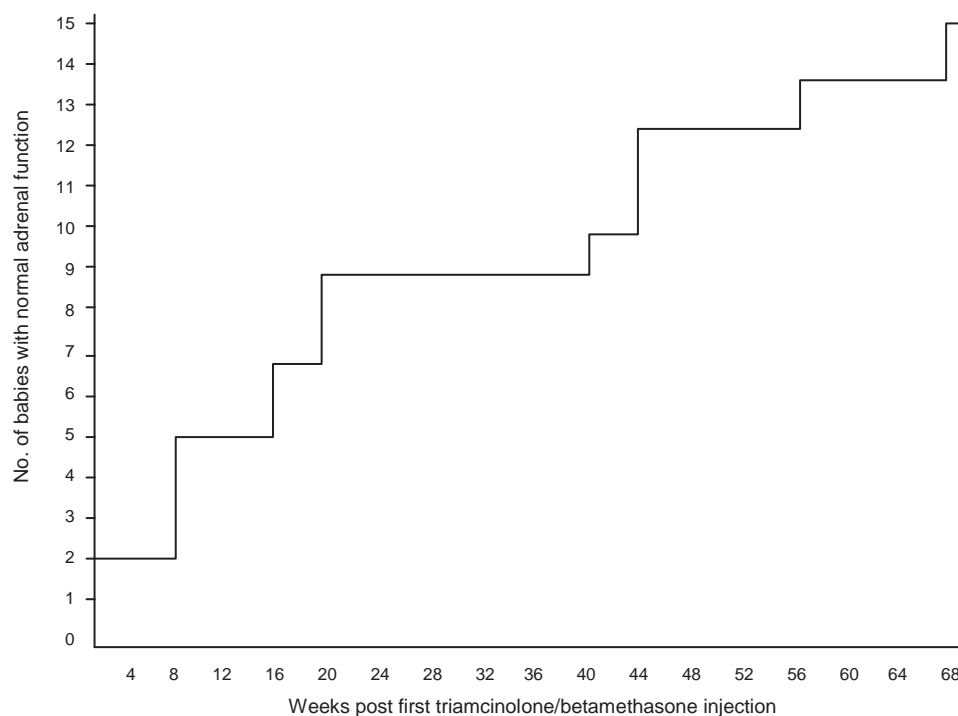


Figure 2 Normal adrenal function curve demonstrating the time frame from injection of triamcinolone/betamethasone to recovery of adrenal function (basal cortisol >120 nmol/l) for all 15 infants.

Our case series has also demonstrated a significant slowing in weight gain following triamcinolone/betamethasone injection. This clinical picture is not consistent with the well-known Cushingoid phenotype associated with high-dose glucocorticoid intake. As well as increasing adiposity, glucocorticoids inhibit protein synthesis and stimulate protein degradation, important factors in the development of muscle atrophy, a characteristic feature of Cushing's syndrome.⁴ One possible explanation for the phenotype observed in this study is that the protein catabolic effects of the exogenous steroid outweigh the increase in fat mass that co-exists in the presence of iatrogenic Cushing's syndrome. Supportive evidence for this explanation is provided by detailed body composition changes in one patient which showed a reduction in fat-free mass and an increase in fat mass during the first 50 days following triamcinolone/betamethasone administration.³

There is growing evidence that propranolol, a non-selective β -blocker, may offer an alternative treatment to corticosteroids.²⁻⁵ Currently this is an off-label indication and parents have to be well informed and give their assent. Propranolol has a well documented side-effect profile from its use in cardiovascular disease, although evidence for its effectiveness in treating haemangiomas only comes from case reports. Although this novel therapy should be exposed to more rigorous study, anecdotal evidence suggests that it is already creeping into clinical practice and it seems likely that this treatment modality will supercede corticosteroid therapy.

In conclusion, our retrospective study yields some important findings and provides some guidance for managing infants receiving intralesional triamcinolone/betamethasone for periorbital haemangiomas. The potentially life-threatening nature of an adrenal crisis necessitates the development of a dialogue and sharing of care between staff working in ophthalmology and endocrinology departments. Although propranolol may supercede the use of corticosteroid therapy for periorbital haemangiomas, continued vigilance will be required for adverse effects.

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Competing interest None.

Patient consent Obtained.

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REFERENCES

1. **Ranchod TM**, Frieden IJ, Fredrick DR. Corticosteroid treatment of periorbital haemangioma of infancy: a review of the evidence. *Br J Ophthalmol* 2005;**89**:1134–8.
2. **Zimmermann AP**, Wiegand S, Werner JA, *et al*. Propranolol therapy for infantile haemangiomas: review of the literature. *Int J Pediatr Otorhinolaryngol* 2010;**74**:338–42.
3. **Goyal R**, Watts P, Lane CM, *et al*. Adrenal suppression and failure to thrive after steroid injections for periorbital hemangioma. *Ophthalmology* 2004;**111**:389–95.
4. **Hasselgren PO**. Glucocorticoids and muscle catabolism. *Curr Opin Clin Nutr Metab Care* 1999;**2**:201–5.
5. **Léauté-Labrèze C**, Dumas de la Roque E, Hubiche T, *et al*. Propranolol for severe hemangiomas of infancy. *N Engl J Med* 2008;**358**:2649–51.



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