

laboratory results become available.⁴ The use of pleural fluid levels of ADA provides a rapid and accurate method of suggesting a diagnosis of tuberculosis, especially in high prevalence areas, thereby expediting the initial decision making process and management of the patient. It is important to recognise, however, that pleural fluid levels of ADA may be high in other conditions, and particularly when the cause is a pyogenic infection.

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Posterior subcapsular cataract and inhaled corticosteroid therapy

Faisal Abuekteish, J N P Kirkpatrick, George Russell

Abstract

Background - Although posterior subcapsular cataract complicates both systemic and topical corticosteroid therapy, the literature on the effects of inhaled corticosteroids is conflicting.

Methods - One hundred and forty children and young adults on inhaled corticosteroids were examined by slit lamp ophthalmoscopy after pupillary dilatation; 103 had received one or more short courses (≤ 7 days) of oral corticosteroids in the management of acute asthmatic attacks and four had also received one or more prolonged courses (≥ 4 weeks) of alternate day oral corticosteroid therapy.

Results - Bilateral posterior subcapsular cataract was identified in one girl who had received several prolonged courses of oral corticosteroids, but was not identified in any other patient.

Conclusions - There is no evidence to support the contention that inhaled corticosteroid therapy on its own, or in association with short courses of oral corticosteroid therapy, might cause cataracts. Although children receiving long term systemic corticosteroid therapy should be screened for cataracts, this is unnecessary in children on inhaled corticosteroids alone.

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Keywords: childhood asthma, posterior subcapsular cataract, corticosteroids.

The association between systemic corticosteroid therapy and the development of posterior subcapsular cataract, first described by Black *et al* in adults in 1960,¹ has also been reported in children receiving systemic corticosteroids for asthma. There are also reports

Department of
Medical Paediatrics,
Royal Aberdeen
Children's Hospital,
Foresterhill, Aberdeen
AB9 2ZG, UK
F Abuekteish
G Russell

Department of
Ophthalmology,
University of
Aberdeen,
Foresterhill, Aberdeen
AB9 2ZG, UK
J N P Kirkpatrick

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Dr G Russell.

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Table 1 Ages of 140 patients on inhaled corticosteroid therapy and duration of treatment at time of examination

Age (years)	
≤5	10
6-10	36
11-15	66
16-20	18
21-25	1
26-30	7
>30	2
Mean (SD)	12.2 (5.9)
Duration of treatment (years)	
≤4	70
5-8	49
9-12	14
13-16	2
17-20	4
21-24	1
Mean (SD)	6.7 (4.3)

suggesting a link between inhaled corticosteroids and posterior subcapsular cataract formation, but these are difficult to interpret, partly because most fail to define the population from which the cases are drawn, but mainly because of uncertainty regarding previous use of systemic corticosteroid therapy. However, Simons *et al*² found no evidence of posterior subcapsular cataract in 95 young asthmatic patients on inhaled corticosteroids, nor did

Tinkelman *et al*³ in a multicentre study in which 102 children received beclomethasone. We report the prevalence of posterior subcapsular cataract in 140 young asthmatic patients on inhaled corticosteroids, four of whom had also received prolonged courses of oral steroids.

Methods

One hundred and fourteen children and adolescents attending the asthma clinic at the Royal Aberdeen Children's Hospital and 28 adult asthmatic subjects selected from a list of former patients who were known to have received inhaled corticosteroids for >5 years were invited to have their eyes examined; there was one refusal in each group, leaving a study population of 140, of whom 81 were male and 59 were female. A detailed history of current and previous oral and inhaled corticosteroid therapy was obtained. All patients underwent an ophthalmic examination which included slit lamp biomicroscopy and direct ophthalmoscopy following pupillary dilation with tropicamide 0.5%. Ethical approval was obtained from the University of Aberdeen and Grampian Health Board.

Table 2 Daily doses of inhaled corticosteroids at time of examination

Dose (µg)	Beclomethasone		Budesonide		Both		Total	
	n	%	n	%	n	%	n	%
≤200	7	15.2	5	7.5	0	0	12	8.5
201-400	15	32.6	7	10.4	7	25.9	29	20.6
401-800	16	34.8	36	53.7	16	59.3	68	48.2
801-1600	7	15.2	18	26.9	4	14.8	29	20.6
>1600	1	2.2	1	1.5	0	0	2	1.4
Total	46		67		27		140	
Mean (SD) daily dose (µg)	499 (365)		657 (355)		590 (252)		592 (346)	

Although most patients had received the same drug since treatment was started, some had had both beclomethasone and budesonide at different times and these are shown separately.

Table 3 Estimated lifetime dose of inhaled corticosteroids

Lifetime dose (µg/m ²)	Beclomethasone		Budesonide		Both		Total	
	n	%	n	%	n	%	n	%
≤200	13	28	1522		0	0	2820	
201-400	9	20	1218		0	0	2115	
401-800	8	17	1319		622		2719	
801-1600	9	20	1522		1348		3726	
1601-3200	5	11	1015		726		2215	
3201-6400	2	4	2	3	1	4	5	4
Total	46		67		27		140	
Mean dose	869 mg/m ²		8179 mg/m ²		1368 mg/m ²		4464 mg/m ²	

"Both" refers to patients who had received both beclomethasone and budesonide at different times.

Table 4 Clinical details of four children who had received long term alternate day oral corticosteroid in addition to inhaled corticosteroids

	Case 1	Case 2	Case 3	Index case
Age (years)	15.8	14.5	13.3	12.8
Sex	F	M	F	F
Duration of asthma (years)	13.8	1.0	11.3	10.8
Duration of treatment with inhaled corticosteroid (years)	5.0	0.9	9.8	4.5
Estimated daily dose of inhaled corticosteroid (µg/m ²)	1091	1250	492	1267
Estimated cumulative dose of inhaled corticosteroid (mg/m ²)	1991	411	1760	2081
Number of short courses of oral corticosteroid in past year	5	10	4	4
Duration of alternate day oral corticosteroid treatment (months)	6	7	18	5

Results

One hundred and forty asthmatic patients on inhaled corticosteroids were studied between August 1992 and June 1993. Details of their ages and of the dose, cumulative dose, and duration of inhaled corticosteroid therapy are presented in tables 1-3. In addition, 103 patients had received a mean (SD) of 2.24 (1.91) (range 1-10) short courses (≤7 days) of oral prednisolone for acute asthma. Details of the four patients who had also received one or more prolonged courses (≥4 weeks) of alternate day oral corticosteroid therapy for intractable chronic asthma are given in table 4.

Bilateral posterior subcapsular cataracts were identified in one patient who had received frequent courses, both short and long, of oral prednisolone; her history is presented in detail below. No other cataract was found in any other patient in this study.

CASE REPORT

The patient was 13 years old at the time of ophthalmic examination. Her father had asthma and her maternal grandfather had age-related cataracts. There was no other family history of note. She had suffered from asthma since the age of two and, from the age of six, the severity of her asthma had gradually increased. She was treated with a wide variety of medications which included sodium cromoglycate, β₂ agonists (including inhaled salmeterol and controlled release oral salbutamol), ipratropium bromide, sustained release oral theophylline, inhaled budesonide and beclomethasone through various inhalation devices, oral prednisolone and, because of psychological disturbance in relation to prednisolone therapy, betamethasone. She had

required frequent admission to hospital for exacerbations of asthma, invariably receiving oral steroids, and numerous other exacerbations had been dealt with by her general practitioner using nebulised β_2 agonists, short courses of oral corticosteroids being required about four times a year. In May 1992 she was started on oral prednisolone 20 mg on alternate days and, at the time of the examination five months later, she was still on prednisolone 15 mg on alternate days and budesonide 600 μ g twice daily, as well as various bronchodilator inhalers and nebuliser solutions.

Discussion

Inhaled corticosteroid therapy is recommended for the prophylaxis of asthma in those children in whom treatment with cromoglycate has failed.⁴ However, despite the efficacy of inhaled corticosteroids, oral corticosteroids must still be used in the management of severe acute asthma⁴ and occasionally long term oral therapy has to be prescribed for problematic cases. It is therefore difficult to identify a substantial number of children whose corticosteroid therapy has been given exclusively by the inhaled route with the result that, whereas the association between posterior subcapsular cataract formation and prolonged systemic corticosteroid therapy has been well documented in asthmatic adults⁵ and children,^{6,7} the relationship with inhaled corticosteroids is much less clear.

Various dose-related systemic side effects have been observed with inhaled corticosteroids⁸ and it would not be surprising if such therapy were also associated with posterior subcapsular cataract formation. However, despite the use of relatively high doses of inhaled corticosteroids in the present series, and the exposure of the majority of our patients to short courses of oral corticosteroid therapy for acute attacks, we found posterior subcapsular cataract only in association with the prolonged administration of oral corticosteroids. There

were no apparent differences between the child with posterior subcapsular cataract and the other children on long term oral corticosteroids to explain why she developed cataract; cases 1 and 3 had had similar cumulative doses of inhaled corticosteroids and more prolonged treatment with alternate day oral corticosteroids, supporting the proposal that there is a personal predisposition to cataractogenesis,⁹ possibly based on a genetic factor.¹⁰

Taking the findings of the present study in conjunction with those of Simons *et al*² and Tinkelman *et al*,³ the failure to identify posterior subcapsular cataract in a total of 333 (136 + 95 + 102) patients on inhaled corticosteroids implies that the risk of developing this complication is extremely low, and we agree with Simons *et al*² in concluding that the routine ophthalmological screening of patients on inhaled corticosteroids is not warranted on present evidence.

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