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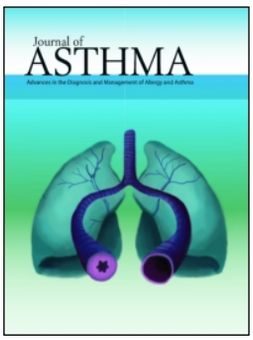

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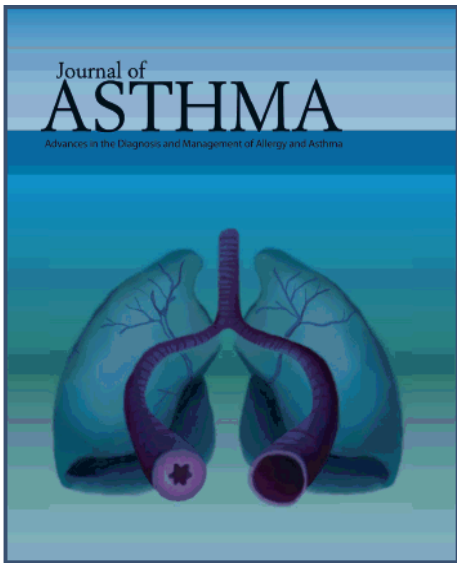

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Abstract

Introduction: Worldwide asthma guidelines recommend short courses of oral prednisolone in children with acute exacerbations generating high prescription numbers. There is a paucity of evidence to inform the optimal dose and course duration. This has led to a variation in the recommendations for prednisolone prescribing. Our objective was to assess prednisolone prescribing practice for children with acute asthma in a representative sample of UK prescribers.

Methods: We developed an online questionnaire asking prescribers the prednisolone dosage, course duration and formulation used, whether they discussed oral prednisolone side effects with the family and at what child's age they changed from prescribing soluble to non-soluble formulations. This was sent to 1006 UK prescribers including Paediatric Respiratory Consultants, doctors in training, asthma nurses and General Practitioners.

Results: 200 complete responses were received (response rate 20%). The majority of surveyed prescribers follow the British National Formulary for Children recommendations on dosage rather than those included in the British Thoracic Society and the Scottish Intercollegiate Guidelines Network. Despite this, we highlighted a four-fold variation in prednisolone dosages for acute asthma. The majority of prescribers chose three days as the course duration. High use of soluble formulations was highlighted.

Conclusions: There is wide variation in the dose of prednisolone prescribed for children with acute asthma in the UK. This reflects a relative lack of evidence which needs addressing.

Title: A review of prednisolone prescribing for children with acute asthma in the UK

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DECLARATION OF INTERESTS

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

A REVIEW OF PREDNISOLONE PRESCRIBING FOR CHILDREN WITH ACUTE ASTHMA IN THE UK

ABSTRACT

Introduction

Worldwide asthma guidelines recommend short courses of oral prednisolone in children with acute exacerbations generating high prescription numbers. There is a paucity of evidence to inform the optimal dose and course duration. This has led to a variation in the recommendations for prednisolone prescribing. Our objective was to assess prednisolone prescribing practice for children with acute asthma in a representative sample of UK prescribers.

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We developed an online questionnaire asking prescribers the prednisolone dosage, course duration and formulation used, whether they discussed oral prednisolone side effects with the family and at what child's age they changed from prescribing soluble to non-soluble formulations. This was sent to 1006 UK prescribers including Paediatric Respiratory Consultants, doctors in training, asthma nurses and General Practitioners.

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There is wide variation in the dose of prednisolone prescribed for children with acute asthma in the UK. This reflects a relative lack of evidence which needs addressing.

INTRODUCTION

Short courses of oral prednisolone are beneficial in children with an acute exacerbation of asthma. They reduce the severity and duration of symptoms, the need for hospitalisation, the amount of short acting beta-agonists required and the likelihood of relapse.(1) Despite this, the two most widely used UK guidelines recommend different dosing regimens. The British Guideline on the Management of Asthma produced by the British Thoracic Society and the Scottish Intercollegiate Guidelines Network (BTS/SIGN) recommends a three day course of prednisolone at a daily dose of 10mg for <2 year olds, 20mg for 2-5 year olds and 30-40mg for >5 year olds.(2) The British National Formulary for Children (BNFC) recommends prednisolone 1-2 mg/kg for 3 days for <12 year olds (max 40mg) and 40-50mg daily for at least 5 days for 12-18 year olds.(3) These differences reflect a lack of evidence to inform practice on the optimum dose, duration of treatment or type of formulation that should be used. This lack of evidence and the need for further research has been highlighted in a Cochrane Systematic Review.(1) In that review it was stated "we were surprised at the limited number and small samples sizes of available trials upon which recommendations were based". It also stated the need for "a high quality multi-centre randomised controlled trial examining different route, doses and durations of systemic corticosteroid therapy". The present study aimed to conduct a national survey to assess the prescribing practices of various UK professional groups for children with acute exacerbations of asthma to determine doses and durations of prednisolone therapy actually given to the children.

METHODS

A 10 point online questionnaire was developed using the Qualtrics System. It asked prescribers the prednisolone dosage, course duration and formulation used, whether they discussed oral side effects of prednisolone and the timing of the dose with the family as well as at what age of the child they changed from prescribing soluble to non-soluble formulations. The final question asked if they routinely prescribed prednisolone courses for children of different ages with viral induced wheeze. See Appendix 1. A link to the online questionnaire was distributed by e-mail to 379 Paediatric Respiratory Consultants via the British Paediatric Respiratory Society, to 160 Asthma Nurses via the National Paediatric Respiratory Nurses Group, to 242 general paediatric and paediatric respiratory trainees and to 225 local General Practitioners (GPs). Statistical analysis was undertaken using SPSS (IBM). The Chi-Square Test was used to assess if one professional group was more likely than the others to give a particular answer. This was a survey of current practice and not research. It was discussed with our own Research and Development Department and the National Research and Ethics Service who both agreed that ethical approval was not required.

RESULTS

Responses were received from 210 prescribers but 10 were excluded because of incomplete data. Overall response rate was 20%. Of the valid 200 responses, 63 were from Paediatric Consultants (response rate 17%), 58 from Paediatric Trainees (response rate 24%), 46 from GPs (response rate 20%) and 33 from asthma nurse prescribers (response rate 21%). In total, 174 (87%) used a mg/kg dosage which varied between 0.5mg/kg to 2mg/kg. 153 (77%) used a dosage within the range recommended in the BNFc (1-2 mg/kg). See Table 1. Of those using a mg/kg dosage, 105 (60%) stated they used a maximum dose (40mg in all cases). Consultants were more likely to prescribe 2mg/kg than the other groups. (Chi-square = 32.1, $p < 0.001$). Only 16 (8%) prescribers reported using the BTS/SIGN guideline. Ten (5%) prescribers did not use a mg/kg dose or the BTS/SIGN guideline. They all used specified doses based on age but the doses or the age bands were different to those in the BTS/SIGN guideline.

172 (86%) chose a course duration of 3 days. None stated they used a five day course for 12-18 year olds as recommended in the BNFC. In viral-induced wheeze (VIW), 44 (22%) prescribers routinely prescribed prednisolone for children aged 1-2 years old and 70 (35%) did so for children aged 2-3 years old. There was no significant difference between the prescribing groups in their answer to the VIW questions. Only 30 (15%) prescribers advised early discontinuation of the prednisolone course if the child recovered quickly. One hundred and ten prescribers (55%) advised children to take prednisolone with food. The potential side effects of prednisolone were discussed with the family by 112 (56%) prescribers. Which side effects were discussed varied widely. See Figure 1. The mean (SD) age at which prescribers changed from soluble to non-soluble tablet formulations was 9.9 (4.5) years.

DISCUSSION

The BTS/SIGN guideline(2) and the BNFC(3) are the most likely sources a UK clinician would use when prescribing a short course of prednisolone for a child with acute asthma or wheezing. Both were developed using an evidence-based methodology and are regularly updated. The differences in the recommended dosages are a reflection of the lack of evidence identified in a Cochrane Review.(1) This survey has highlighted that the majority of prescribers follow BNFC guidance on prednisolone dosage. A minority follow the BTS/SIGN Guideline and 16% do not follow either. Despite the majority following the BNFC Guideline (1-2mg/kg), as some prescribed 0.5mg/kg we demonstrated a four-fold difference (0.5mg/kg to 2mg/kg) in the dosage of prednisolone prescribed. This variation is of concern given that prescribers are encouraged to prescribe medicines at their lowest effective dose. We believe that the wide variation in the prescribing of prednisolone for children with acute asthma reflects the lack of evidence from trials which is supported by the Cochrane Review.(1) In contrast to differences in dosage, there was little variation in the duration of the prescribed course: the vast majority of prescribers used three days. Very few, however, recommended increasing this to five days in the 12-18 age range as stated in the BNFC.

Clinicians continue to prescribe soluble prednisolone until children are almost 10 years of age. This occurs despite children disliking its unpleasant bitter aftertaste which could prevent them completing the full course.(4) There is also a significant cost implication. According to the BNFC, one 5mg soluble prednisolone tablet costs £1.43 compared to £0.05 for one 5mg non-soluble, non-enteric coated tablet.(3) Although this individual cost saving is small, the quantity of prednisolone prescribed worldwide means that changing from soluble to non-soluble tablets at an earlier age would have a large financial impact. The high use of soluble prednisolone may reflect a lack of awareness regarding its unpleasant taste or an assumption that children cannot swallow tablets. It is common practice in paediatric cystic fibrosis clinics for dieticians to successfully train children from 18 months upwards to swallow capsules and tablets and there is no reason why this could not be

applied to children with asthma and / or wheezing. There is also evidence that young children actually prefer tablets to liquid formulations.(4)

Nearly 20 years ago, a clinical study compared outcomes for children with acute asthma treated with 0.5mg/kg, 1mg/kg or 2mg/kg of prednisolone.(5) No differences were found between the groups in any of the measured outcomes. The behavioural side effects of anxiety and aggression are twice as common in children receiving 2mg/kg of prednisolone compared to 1mg/kg.(6) There is also an association between repeated short courses of oral prednisolone and growth impairment.(7) It is assumed that prescribers want to use the minimum effective dose to minimise the likelihood of these dose dependent side effects. There is therefore a need for well-constructed clinical studies to determine the optimal dose of prednisolone associated with maximal efficacy and minimal side effects for children with exacerbations of asthma. Until such studies take place, it is likely that children with acute asthma will continue to be exposed to the risk of side effects associated with unnecessarily high doses of oral prednisolone.

SUMMARY

This survey has demonstrated that the majority of respondents follow the guidance in the BNFC but there is still wide variation in the dose of prednisolone prescribed for children with acute asthma. In addition, soluble prednisolone is frequently prescribed for children old enough to swallow non-soluble tablets. More studies are required to determine the optimal dose of oral prednisolone for children with acute asthma. These studies may also be able to demonstrate potential benefits with regards to improved adherence and reduced costs associated with changing from soluble to non-soluble tablet formulations in children below the age of ten years. It would be also be useful if surveys similar to ours were undertaken in other countries to clarify if the issues identified in the UK are similar elsewhere.

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FIGURE LEGENDS

Figure 1 : Word cloud of the side effects discussed with the patient or parent.

The size of each word is proportional to how frequently it was mentioned by respondents.

Table 1: Prednisolone dosages prescribed by different professional groups.

Dose	Consultants	GPs	Doctors in Training	Nurses	All
0.5 mg/kg	2 (3%)	8 (17%)	8 (14%)	3 (9%)	21 (11%)
1 mg/kg	22 (35%)	27 (59%)	38 (66%)	10 (30%)	97 (49%)
1-2 mg/kg	8 (13%)	4 (9%)	3 (5%)	4 (12%)	19 (10%)
2 mg/kg	26 (41%)	3 (7%)	4 (7%)	4 (12%)	37 (19%)
BTS/SIGN Guideline	3 (5%)	2 (4%)	2 (4%)	9 (27%)	16 (8%)
Other	2 (3%)	2 (4%)	3 (5%)	3 (9%)	10 (5%)
TOTAL	**63 (32%)**	**46 (23%)**	**58 (29%)**	**33 (17%)**	**200 (100%)**

Percentages rounded to nearest whole number.