Efficacy of oral corticosteroids for preschool wheeze: a meta-analysis of individual participant data from seven randomised controlled trials

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Introduction

Our systematic review of the effects of oral corticosteroids (OCS) on preschool wheeze found inconclusive effects due to high heterogeneity between RCTs. We conducted an Individual Participant Data (IPD) meta-analysis from RCTs to evaluate the efficacy of OCS for preschool wheeze treatment.

Methods

This systematic review was followed by the Preferred Reporting Items for Systematic Review and individual participant data meta-analysis protocol. This protocol was registered on PROSPERO (CRD42020193958)

Databases: PubMed, Ovid EMBASE, CINAHLplus, Cochrane CENTRAL, Clinical Trials.gov, EudraCT, EU Clinical Trials Register and the WHO International Clinical Trials Registry Platform (ICTRP) + Gray literature (Edinburgh Research Archive (ERA), Web of Science Core Collection and Open Grey (WSCCO), Electronic Theses Online Service (EthOS) and ProQuest Dissertations and Theses Global (PQDT))

Eligibility criteria: All types of studies published between 1994 and 2020 reporting the efficacy of OCS treatment for preschool wheeze

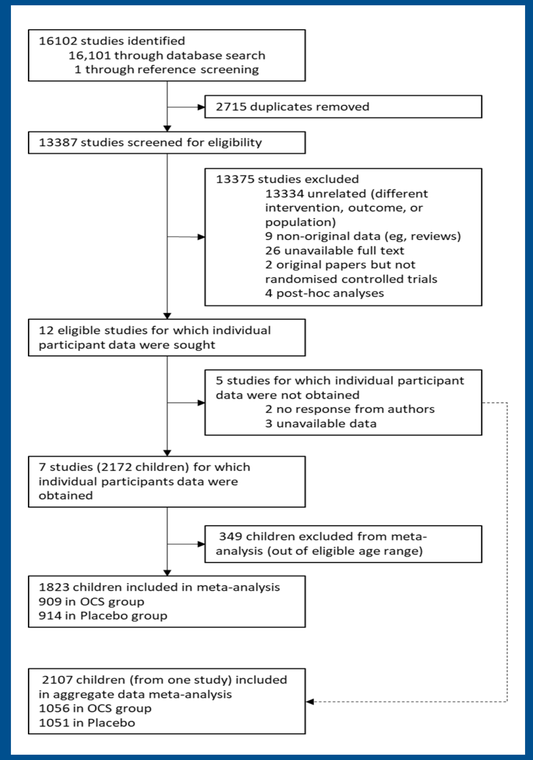
Screening and selection of studies

Search strategy	Definition
Population	Children aged 12-71 months with acute wheeze
Intervention	OCS used to treat acute wheeze according to international or national guidelines
Comparator	Placebo group that did not receive OCS
Outcome	Mainly, a wide range of measures were explored
Study design	Randomised controlled trials (RCTs) , quasi-RCTs, cohort studies, case-control studies (but not cross-sectional studies)

Data analysis: A two-stage meta-analysis, intention-to-treat approach

In the first stage: multivariable regression models adjusting for age, history of allergy, parental allergies or asthma.

In the second stage: random-effects model meta-analysis, Restricted Maximum Likelihood with the Hartung-Knapp-Sidik-Jonkman method



Main Finding

OCS could be beneficial for short-term outcomes for acute wheeze in preschool children, especially those with moderate-to-severe wheeze and risk factors. However, OCS did not appear to have long-term benefits.

Results

	Groups (n/N or mean[SD])		Number of studies included (total patients)	Combined odds ratio (OR†) or mean difference (MD‡) (95% CI)	I^2 (%)	Tau^2
	OCS (n=909)	Placebo (n=914)				
Change in WSS in 4 hours	N=282	N=246				
Full adjusted*	-1.94 (2.15)	-1.63 (2.02)	2 (n=528)	-0.31 [-0.37 to -0.24] ‡	0.0	<0.001
Change in WSS in 12 hours	N=232	N=240				
Full adjusted*	-2.52 (2.35)	-2.43 (2.46)	3 (n=472)	-0.02 [-0.17 to 0.14] ‡	0.0	<0.001
Length of stay (hrs)	N=731	N=721				
Full adjusted*	18.0 (26.0)	21.9 (28.0)	5 (n=1452)	-3.18 [-4.43 to -1.93] ‡	0.0	<0.001
Revisit to GP/ED	N=779	N=819				
Full adjusted*	189/779	185/819	7 (n=1598)	1.11 [0.86 to 1.43] †	0.0	<0.001
Rehospitalisation	N=701	N=705				
Full adjusted*	51/701	49/705	5 (n=1406)	0.94 [0.38 to 2.32] †	36.2	0.21
Additional steroids	N=724	N=756				
Full adjusted*	40/724	59/756	7 (n=1480)	0.71 [0.39 to 1.28] †	0.0	0.05
Time back to normal (days)	N=451	N=469				
Full adjusted*	4.56 (3.92)	5.04 (4.13)	5 (n=920)	-0.64 [-1.76 to 0.49] ‡	58.9	0.31
Doses of SABA in 7 days	N=210	N=236				
Full adjusted*	19.05 (28.42)	22.44 (38.15)	2 (n=446)	0.34 [-7.09 to 7.76] ‡	0.0	<0.001
Doses of SABA in 14 days	N=136	N=153				
Full adjusted*	31.02 (47.12)	39.26 (62.30)	2 (n=289)	-4.75 [-6.71 to -2.79] ‡	0.0	<0.001

- OCS was associated with the improvement in wheezing severity score at 4 hours, not 12 hours and a significant reduction in length of hospital stay (hrs)
- Sensitivity analysis including studies not providing IPD did not change the results.
- Subgroup analyses showed evidence of significantly improved outcomes in children with moderate-to-severe wheeze and previous wheezing/asthma.

Conflict of interest

All authors have nothing to disclose.

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