Interventions to improve adherence to inhaled steroids for asthma

Respiratory department

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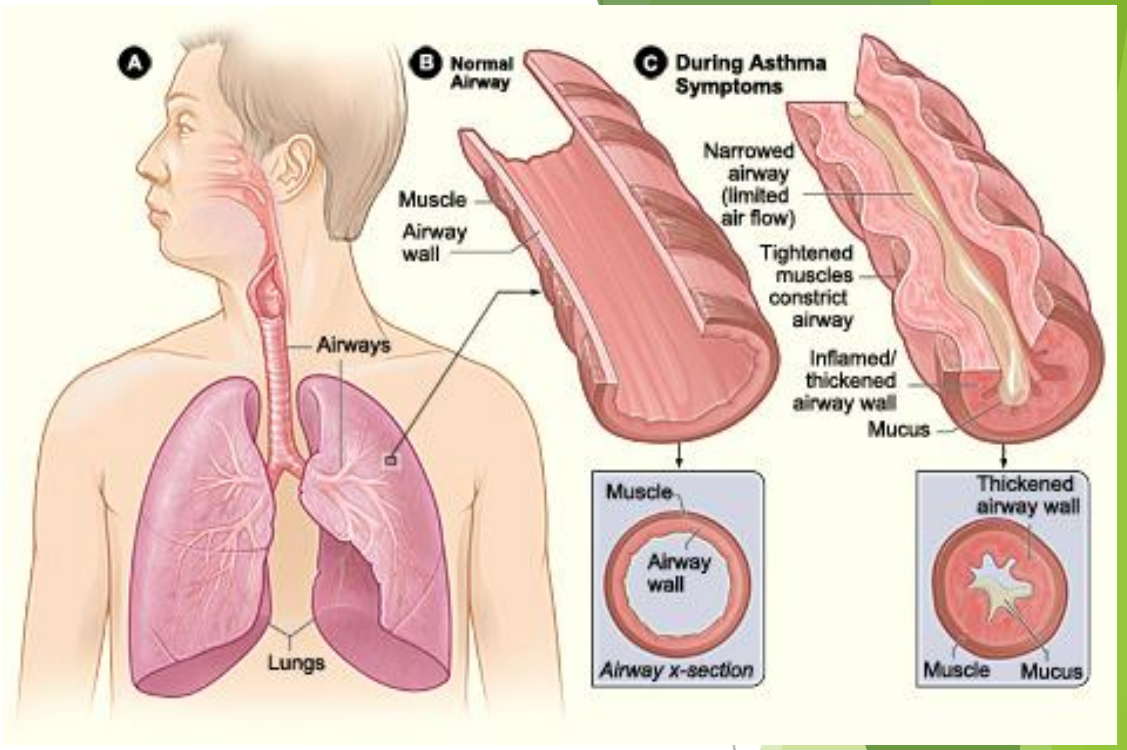

Overview

- Asthma is a chronic breathing condition that affects more than 300 million adults and children worldwide.
- Asthma can cause shortness of breath, chest tightness and cough and typically presents with wheezing.
- ICS can result in symptom improvement and reduced asthma-related morbidity and mortality. ICS commonly used today include budesonide, beclomethasone, fluticasone (propionate and furoate), mometasone and ciclesonide. They can be given alone or in combination with other preventer medications such as long-acting beta2-agonists (LABAs) or leukotriene receptor antagonists (LTRAs) (BNF).

Overview

- Adherence (WHO) :"the degree to which use of medication by the patient corresponds with the prescribed regimen".
- Reasons for non-adherence vary among individuals. Commonly cited reasons include complexity of the treatment regimen; cost; administration route; and patient beliefs about therapy, including safety, necessity and risk of dependence. Lower socioeconomic status, inclusion in a minority ethnic group and fewer years of education have also been associated with reduced adherence : the result of forgetfulness or a busy, unpredictable lifestyle, failure to appreciate the specifics of regimens or the need for adherence, a purposeful choice to reduce or discontinue ICS use for many reasons, including side effects, fear of side effects or a perception that the benefits do not outweigh the disadvantages.

Research

- Review – corchrane 2017: Interventions to improve adherence to inhaled steroids for asthma.
- Review – corchrane 2017: Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth.
- Gina 2017

Review – corchrane 2017: Interventions to improve adherence to inhaled steroids for asthma.

- 39 RCTs from two months to two years (median six months) in high-income countries.

- Adherence education versus control (20 studies); electronic trackers or reminders versus control (11 studies); simplified drug regimens versus usual drug regimens (4 studies); and school-based directly observed therapy (3 studies). Two studies are described separately.

Adherence education compared with controls

Patient or population: asthma
Setting: community
Intervention: adherence education
Comparison: control group (no education)

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Risk with controls	Risk with adherence education				
% Adherence WMD of follow-up 71.7 weeks (all studies)	**Objective measures**	Mean adherence in the control group was **46.7%**	Mean adherence with adherence education was **20.13% higher** (7.52 higher to 32.74 higher)	-	280 (5 RCTs)	⊕⊕◯◯ **LOW**[a,b,c]	Only studies in which adherence was measured with an electronic monitor
	All measures	Mean adherence in the control group was **57.1%**	Mean adherence with adherence education was **11.59% higher** (3.72 higher to 19.46 higher)	-	1693 (10 RCTs)	⊕⊕◯◯ **LOW**[a,b,c]	
Exacerbations requiring OCS (people with 1 or more) WMD of follow-up 30.8 weeks		**149 per 1000**	**242 per 1000** (148 to 370)	OR 1.82 (0.99 to 3.36)	349 (3 RCTs)	⊕⊕◯◯ **LOW**[a,d]	
Asthma control (ACQ) WMD of follow-up 28.5 weeks		Mean ACQ score was **1.52**	Mean score with adherence education was **0.03 better** (0.49 better to 0.43 worse)	-	455 (4 RCTs)	⊕⊕⊕◯ **MODERATE**[a,e]	Lower score indicates better control. Scale 0 to 6. MCID 0.5

Adherence education compared with controls

Asthma control (ACT) WMD of follow-up 29.5 weeks	Mean ACT score was **18.88**	Mean score with adherence education was **0.30 better** (1.43 better to 0.82 worse)	-	333 (3 RCTs)	⊕⊕⊕◯ **MODERATE**[a,e]	Higher score indicates better control. Scale 5 to 25. MCID 3
Unsheduled visits to a healthcare provider (people with 1 or more) WMD of follow-up 67.2 weeks	**159 per 1000**	**83 per 1000** (35 to 184)	OR 0.48 (0.19 to 1.19)	688 (4 RCTs)	⊕◯◯◯ **VERY LOW**[a,b,d,f]	Includes visits to ED, GP, hospital for any cause
Absenteeism WMD of follow-up 63.3 weeks	We did not perform an analysis of absences because the data were heavily skewed		-	109 (2 RCTs)	Not graded	
Quality of life (AQLQ) WMD of follow-up 27.4 weeks	Mean AQLQ score was **5**	Mean score with adherence education was **0.01 better** (0.20 worse to 0.23 better)	-	734 (6 RCTs)	⊕⊕⊕◯ **MODERATE**[a,e]	Higher score indicates better QOL. Scale 1 to 7. MCID 0.5

* **The risk in the intervention group** (and its 95% confidence interval) is based on assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

ACQ: Asthma Control Questionnaire; ACT: Asthma Control Test; AQLQ: Asthma Quality of Life Questionnaire; CI: confidence interval; ED: emergency department; GP: general practitioner; MCID: minimal clinically important difference; OCS: oral corticosteroid; OR: odds ratio; QOL: quality of life; RCT: randomised controlled trial; WMD: weighted mean duration

Electronic trackers or reminders (± feedback) compared with controls

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
		Risk with controls	Risk with electronic trackers or reminders (± feedback)				
% Adherence WMD of follow-up 47.6 weeks	**Objective measures only**	Mean adherence in the control group was **53.27%**	Mean adherence was **19.86% higher** (14.47 higher to 25.26 higher)	-	555 (6 RCTs)	⊕⊕⊕◯ **MODERATE**[a]	Only studies in which adherence was measured with an electronic monitor
	All measures	Mean adherence in the control group was **56.06%**	Mean adherence with trackers was **18.41% higher** (11.82 higher to 25.00 higher)	-	762 (8 RCTs)	⊕⊕◯◯ **LOW**[a,b]	
Exacerbations requiring OCS (people with at least 1) WMD of follow-up 48.6 weeks		**218 per 1000**	**169 per 1000** (94 to 280)	OR 0.72 (0.37 to 1.39)	3063 (4 RCTs)	⊕◯◯◯ VERY **LOW**[a,b,c]	
Asthma control (ACQ) WMD of follow-up 43.0 weeks		Mean ACQ score in the control group was **0.89**	Mean score with trackers or reminders was **0.24 better** (0.29 worse to 0.78 better)	-	109 (2 RCTs)	⊕⊕◯◯ **LOW**[a,c]	Lower score indicates better control. Scale 0 to 6. MCID 0.5

Electronic trackers or reminders (± feedback) compared with controls

Asthma control (ACT) WMD of follow-up 34.0 weeks	Mean ACT score in the control group was **20.04**	Mean score with trackers or reminders was **0.74 better** (0.20 worse to 1.69 better)	-	596 (4 RCTs)	⊕⊕◯◯ **LOW**[a,b,d]	Higher score indicates better control. Scale 5 to 25. MCID 3
Unscheduled healthcare visits to a healthcare provider (ED) WMD of follow-up 50.0 weeks	**84 per 1000**	**95 per 1000** (75 to 119)	OR 1.14 (0.88 to 1.47)	2918 (2 RCTs)	⊕⊕⊕◯ **MODERATE**[c]	Two studies (n = 2865) also reported hospitalisations. OR 0.97 (0.53 to 1.78)
Absenteeism (people with at least 1 absence) Follow-up 26 weeks	**327 per 1000**	**409 per 1000** (285 to 546)	OR 1.42 (0.82 to 2.47)	220 (1 RCT)	⊕⊕◯◯ **LOW**[c,e]	
Quality of life (AQLQ) WMD of follow-up 36.8 weeks	Mean AQLQ score in the control group was **5.15**	Mean score with trackers or reminders was **0.03 worse** (0.13 better to 0.20 worse)	-	369 (4 RCTs)	⊕⊕⊕◯ **MODERATE**[a,d]	Higher score indicated better QOL. Scale 1 to 7. MCID 0.5

Simplified compared with usual regimens for asthma

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual regimens	Risk with simplified regimens				
% Adherence (objective measures) WMD of follow-up 12.9 weeks	Mean adherence in the control group was **86.73%**	Mean adherence with simplified regimens was **4.02%** higher (1.88 higher to 6.16 higher)	-	1310 (3 RCTs)	⊕⊕⊕◯ **MODERATE**[a]	Only studies in which adherence was measured with an electronic monitor
Exacerbations requiring OCS People with 1 or more Follow-up 12 weeks	**125 per 1000**	**250 per 1000** (24 to 823)	OR 2.33 (0.17 to 32.58)	16 (1 RCT)	⊕⊕◯◯ **LOW**[b]	
Asthma control (ACQ) Follow-up 24 weeks	Mean ACQ score in the control group was **0.89**	Mean score with simplified regimens was **0.03 better** (0.34 better to 0.28 worse)	-	103 (1 RCT)	⊕⊕⊕◯ **MODERATE**[c]	Lower score indicates better control. Scale 0 to 6. MCID 0.5
Unscheduled visits Follow-up 12 weeks	**63 per 1000**	**72 per 1000** (46 to 113)	OR 1.17 (0.72 to 1.90)	1037 (1 RCT)	⊕⊕◯◯ **LOW**[a,d]	
Absence from work/ school Follow-up 12 weeks	**19 per 1000**	**18 per 1000** (7 to 43)	OR 0.93 (0.37 to 2.30)	1037 (1 RCT)	⊕⊕◯◯ **LOW**[a,d]	

Simplified compared with usual regimens for asthma

Change in quality of life (ITG-ASF) Follow-up 12 weeks	Mean change in quality of life in the control group was **14**	Mean change with simplified regimens was **6 points better** (0.76 worse to 12.76 better)	-	1037 (1 RCT)	⊕⊕◯◯ **LOW**[a,e]	Higher score indicates better QOL. Range 0 to 100. MCID not known
All adverse events Follow-up 12 weeks	**175 per 1000**	**139 per 1000** (106 to 181)	OR 0.76 (0.56 to 1.04)	1233 (1 RCT)	⊕⊕◯◯ **LOW**[a,f]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
ACQ: Asthma Control Questionnaire; CI: confidence interval; ITG-ASF: Integrated Therapeutics Group - Asthma Short Form; MCID: minimal clinically important difference; OCS: oral corticosteroid; OR: odds ratio; QOL: quality of life; RCT: randomised controlled trial; WMD: weighted mean duration

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to the estimate of effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of effect but may be substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a] Downgraded once primarily owing to lack of blinding and some concerns regarding attrition bias, selective reporting and selection bias (-1 risk of bias)

School-based ICS therapy compared with home therapy for asthma

Settings: school
Intervention: ICS given at school
Comparison: ICS given at home

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	School-based ICS therapy				
Unscheduled visits 1 or more hospitalisations for any cause WMD of follow-up 35.8 weeks	**49 per 1000**	**29 per 1000** (8 to 96)	OR 0.58 (0.16 to 2.05)	279 (2 RCTs)	⊕⊕◯◯ **LOW**[a,b]	
Quality of life (PACQLQ) 1 to 7; higher is better WMD of follow-up 35.8 weeks	Mean PAQLQ score in the control group was **6.31**	Mean score in the intervention groups was **0.25 higher** (0.01 to 0.49 higher)	-	279 (2 RCTs)	⊕⊕⊕◯ **MODERATE**[a]	
Adverse events Follow-up 30 weeks	No events observed in either arm		-	99 (1 RCT)	Not graded	

*The basis for the **assumed risk** (e.g. median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)
CI: confidence interval; ICS: inhaled corticosteroid; OR: odds ratio; PAQLQ: Paediatric Asthma Quality of Life Questionnaire; RCT: randomised controlled trial; WMD: weighted mean difference

- All pooled results for adherence education, electronic trackers or reminders and simplified regimens showed better adherence than controls:
  - Adherence education showed a benefit of 20 percentage points over control (95% confidence interval (CI) 7.52 to 32.74; five studies; low-quality evidence)
  - Electronic trackers or reminders led to better adherence of 19 percentage points (95% CI 14.47 to 25.26; six studies; moderate-quality evidence)
  - Simplified regimens led to better adherence of 4 percentage points (95% CI 1.88 to 6.16; three studies; moderate-quality evidence).

Inhaled corticosteroids in children with persistent asthma: effects on growth

- 25 trials involving 8471 (5128 ICS-treated and 3343 control) children with mild to moderate persistent asthma.
- Compared with placebo or non-steroidal drugs, ICS produced a statistically significant reduction in linear growth velocity (14 trials with 5717 participants, MD -0.48 cm/y, 95% CI -0.65 to -0.30, moderate quality evidence) and in the change from baseline in height (15 trials with 3275 participants; MD -0.61 cm/y, 95% CI -0.83 to -0.38, moderate quality evidence) during a one-year treatment period.

Gina 2017

- ICS may reduce growth velocity in first 1- 2 years of treatment, but this is not progressive or cumulative.
- Long-term effects of asthma treatment show that only 0.7% decrease in adulthood.
- Poor control of asthma is the cause of the child's lack of development.

Uptodate 2016

- In children, both ICS therapy and untreated asthma itself have been associated with deceleration of growth velocity. The effects are most pronounced with severe asthma. Inhaled GC cause growth deceleration when assessed by very sensitive measures of growth velocity. However, asthmatic children continue to grow over a long period of time, and their ultimate adult height is approximately 1.2 cm less than without ICS.
- To minimize the risk of adverse effects from ICS, we advise use of the lowest dose that maintains asthma control, attention to compliance, and regular evaluation for co-existent conditions and triggers that can exacerbate asthma symptoms. In addition, spacers should be used with metered dose inhalers to optimize delivery to the lung, especially in adults receiving ≥800 mcg daily and children receiving ≥400 mcg daily through a MDI device. (See 'Measures to minimize systemic side effects' above.)

References

- Interventions to improve adherence to inhaled steroids for asthma, Normansell R, Kew KM, Stovold E, Corchrane 2017 .
- Inhaled corticosteroids in children with persistent asthma: dose-response effects on growth, Pruteanu AI, Chauhan BF, Zhang L, Prietsch SOM,Ducharme FM, Corchrane 2017.
- Gina 2017.
- Major side effects of inhaled glucocorticoids, uptodate Apr 01, 2016.