Rapid Effects of Inhaled Corticosteroids in Acute Asthma

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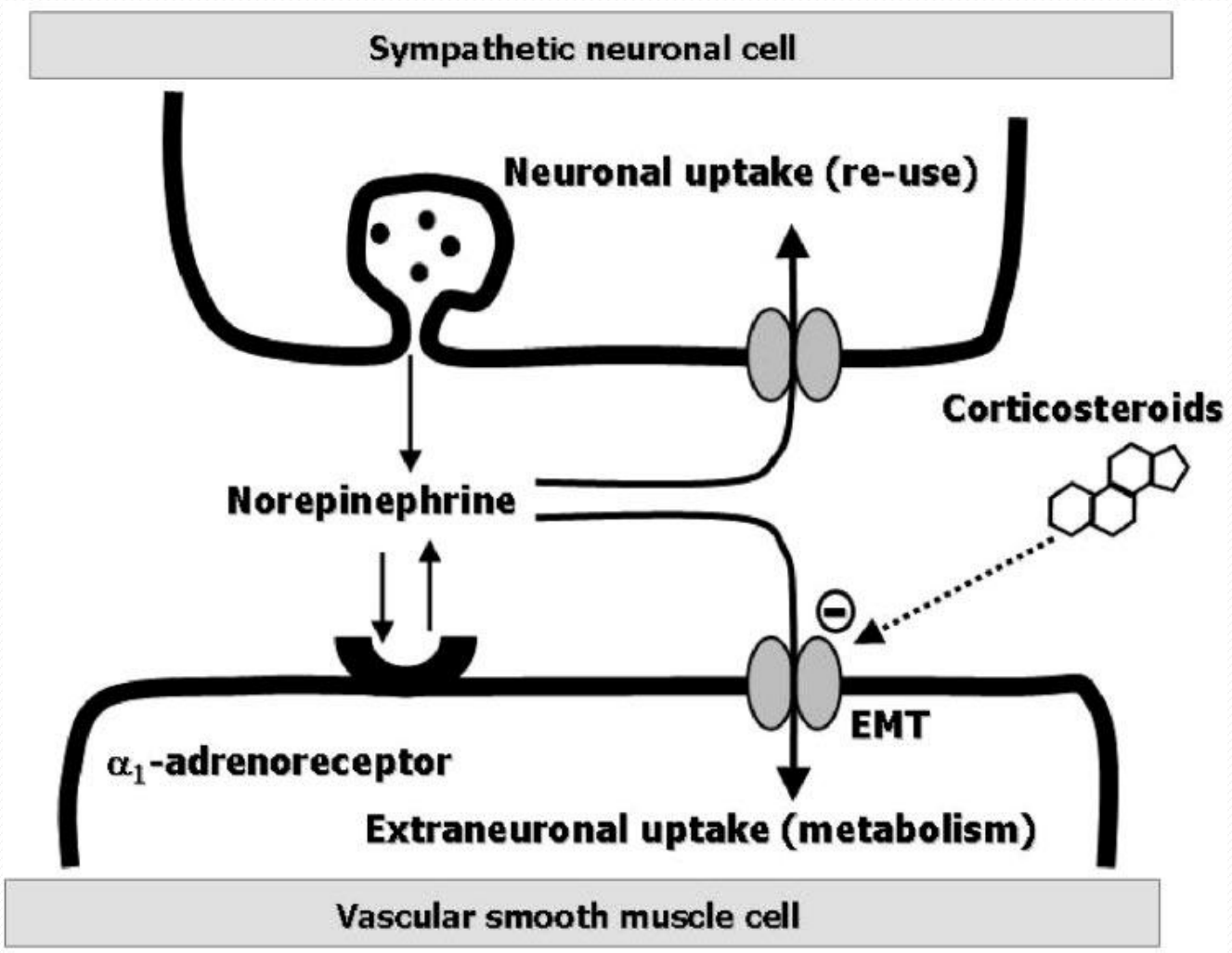
Background: Current reviews on the use of inhaled corticosteroids (ICS) for acute asthma underestimated their early clinical impact

Objective: The analysis of the best evidence available on the early (1 to 4 h) clinical impact of ICS for patients with acute asthma in the emergency department (ED).


Sympathetic neuronal cell
Neuronal uptake (re-use)
Corticosteroids
Norepinephrine
EMT
α_1-adrenoreceptor
Extraneuronal uptake (metabolism)
Vascular smooth muscle cell

METHODS

Included studies met the following criteria:

(1) Target population: children (6 months - 17 years old) and adults (≥ 18 years old) with acute exacerrbations of asthma ,all study participants had a clinical diagnosis of acute asthma

(2) Design: randomized controlled trials conducted in an ED

(3)Intervention: ICS compared / placebo or SCS

(4)Primary – outcomes : admission and ED discharge rates.

Secondary-outcomes (from 1-4h)

+spirometric measures (PEF , FEV_1)

+clinical symptoms

+heart and respiratory rates

+oxygen saturation

+side effects

Results:

-fifty initial articles and 17 of these randomized, double-blind, placebo-controlled studies (470 adults and 663 children)

+8 studies compared ICSs /placebo

+3 studies compared ICSs + SCSs/SCSs

+6 studies compared ICSs / SCSs

-ICS doses used in the trials ranged from **400 µg to 2 mg** dispensed by inhaler or nebulizer : budesonide (8 studies) fluticasone (3) , beclomethasone (3), flunisolide (2), dexamethasone (1)

-"***Multiple-dose***" *protocols administered* ***≥ 3 doses of ICS at ≤ 30 minute intervals*** ("single-dose" ≤2 doses at ≤30-minute intervals or ≥1 dose at >30-minute intervals.)

-Patients treated with ICS also displayed a faster **clinical improvement** compared with placebo or SCS , **early ED discharge** (OR, 4.70; 95% CI, 2.97 to 7.42; p = 0.0001).

-The advantage of ICS was also demonstrated **in spirometric and clinical measures** < 60 min.

-These benefits were obtained only when patients received ***multiple doses of ICS + β agonists*** *compared with placebo or SCS.*

Admission rate

-**A greater reduction** was observed when all trials that used **multiple doses ICS** were pooled(OR, 0.30; 95% CI, 0.16 to 0.55; I2 0%), especially when ICS were compared with placebo.

Discharge Rate

-Six studies (545 patients) examined the discharge rates after 2 to 3 h of treatment, a significantly greater proportion of ICS-treated patients were discharged from the ED compared with either placebo or with SCS

-**Patients who received multiple doses of ICS had 4.7 times greater** odds to be discharged (95% CI, 2.97 to 7.42).

SPIROMETRY

-The seven trials that reported PEF a significant improvement in PEF/ ICS treatment

-There was a dose response relation -ship ; the greater benefit when patients were treated with multiple doses of ICS.

-Patients treated with ICS showed pooled WMD in PEF of 25, 35, and 46L/min at 60, 120, and 180 min .

-Similar results were obtained for FEV1 , Pooled WMDs in FEV1 were 0.12 , 0.16 , 0.24 L at 60, 120, and 180 min, respectively.

-There was a significant improvements in FEV1 / ICS treatment compared with placebo were found at 120 min and 180 to 240 min (WMD, 0.2 L; 95% CI, 0.0 to 0.3; I2 0%; and WMD, 0.3 L; 95% CI, 0.1 to 0.5; I2 0%, respectively).

Other Outcomes

-Eight trials reported a significant reduction of clinical scores after ICS treatment / placebo and SCS.

-This reduction was dose related (WMD, 0.40; 95% CI, 0.60 to 0.20; p 0.0001, I2 12%; and WMD, 0.51; 95% CI, 0.71 to 0.31; p 0.0001;I2 40%, at 60 ,120, 180 min)

-Finally, all studies reported that there were no serious side effects.

CONCLUSIONS

-These studies suggest that ICS treatment provides early beneficial effects (**1–2 hours**) when they were used in **multiple-dose** amounts administered in time intervals of ≤30 minutes (multiple doses of ICS + β-agonists)

Implications for practice and research

-This review clearly supports the use of ICS for the treatment of children and adults with asthma exacerbations

-Nongenomic early effect of ICS / with acute asthma exacerbation may be significant in the treatment of most severe case

-The use of ICS (through an MDI and spacer or nebulization) every 10 to 30 min and > 3 doses could be recommended.

-Although there was an important variation between studies, the evidence suggests that the minimum effective nebulized doses for fluticasone and budesonide would be 500 microg and 800 microg every 30 min

-These doses would have to be administered during a minimum of 90 min, although more prolonged periods of administration could generate a greater benefit.

-Nevertheless, more future studies< 5 ages, future studies will have to clarify the relationship between

+the dose administered

+acute asthma severity

+response to treatment

-**Inhaled glucocorticosteroids can be effective as oral glucocorticosteroids** at preventing relapses

-Patients discharged from the ED on prednisone + ICS have a lower rate of relapse than those on prednisone alone

-A high - dose of ICS - **2,4 mg budesonide daily in four divided doses- achieves a relapse rate similar to 40mg prednisone daily**

THANK YOU FOR YOUR ATTENTION AND LISTENING