Use of dexamethasone and prednisone in acute asthma exacerbations in pediatric patients

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ABSTRACT

QUESTION Children frequently present to my rural emergency department with asthma exacerbations. Should I prescribe systemic corticosteroids? If so, which systemic corticosteroid should I prescribe?

ANSWER A short course of steroids is indicated in the treatment of asthma exacerbations. Both prednisone (1 to 2 mg/kg daily for 5 days) and dexamethasone (0.3 to 0.6 mg/kg daily for 1 to 5 days) are effective in reducing hospital admissions and unscheduled return to care, with minimal side effects.

RÉSUMÉ

QUESTION Au service des urgences en milieu rural où je travaille, je vois souvent des enfants qui font un épisode d'exacerbation de l'asthme. Devrais-je leur prescrire des corticostéroïdes systémiques? Dans l'affirmative, quel corticostéroïde convient le mieux?

RÉPONSE Il est indiqué de prescrire un traitement de courte durée aux stéroïdes dans les cas d'exacerbation de l'asthme. Le prednisone (1 à 2 mg/kg par jour pendant 5 jours) et le dexaméthasone (0,3 à 0,6 mg/kg par jour pendant 1 à 5 jours) sont tous 2 efficaces pour réduire le nombre d'admissions à l'hôpital ou les visites d'urgence et ont peu d'effets secondaires.

Asthma is one of the most common presentations to adult and pediatric emergency departments (EDs), accounting for approximately 10 to 15 of every 1000 visits.[1]

There are various triggers of acute exacerbation of asthma. Bronchospasm and airway inflammation with edema and mucus production are key physiologic factors leading to clinical symptoms. β-Agonists and other bronchodilators target bronchospasm while corticosteroids reduce the inflammatory response by inhibiting the activation of inflammatory cells and by reducing mediator production, microvascular leakage, and mucus formation.[2]

Corticosteroids have been used to treat asthma for approximately 50 years. Their benefit in the ED treatment of asthma exacerbations was first demonstrated in 1986.[3] In 1990, Tal et al[4] showed a similar benefit in children.

Treatment guidelines of the Canadian Thoracic Society, Canadian Association of Emergency Physicians, British Thoracic Society, and American National Asthma Education and Prevention Program recommend the use of systemic corticosteroids for moderate to severe exacerbations of asthma and for mild exacerbations not responsive to bronchodilator therapy.[5-7] These published guidelines were developed primarily for use in acute care settings and are helpful in EDs; however, there is very little information available on the use of systemic steroids in ambulatory care settings.

Systemic corticosteroids in asthma exacerbations

The Cochrane Collaboration maintains numerous ongoing systematic reviews of randomized controlled trials of systemic steroids versus placebo in acute exacerbations of asthma in children and adults. In one Cochrane Review, patients who were treated with short courses (ie, 3 to 10 days) of steroids required significantly less care as defined by relapse to additional care within 7 to 10 days (relative risk 0.38, 95% confidence interval [CI] 0.20 to 0.74), fewer hospitalizations (relative risk 0.35, 95% CI 0.13 to 0.95), and less need of β-agonist use (-3.3 activations per day of inhaler; 95% CI -5.6 to -1.0). In addition, patient symptom scores improved with steroid therapy; however, no significant comparisons could be made owing to a lack of standardization in the use and reporting of scores between the studies. The overall incidence of side effects, such as vomiting and headache, was reported as rare, with no significant differences between the groups; this might be partly due to the limited information provided in these studies. No significant differences were identified between different routes of administration. The review concludes that a short course of systemic steroids is beneficial in moderate to severe asthma exacerbations. Mild exacerbations can be treated with β-agonist therapy and inhaled corticosteroids, with the addition of systemic steroids if a patient's symptoms do not improve.[8]

In another Cochrane Review, children and adults who were given corticosteroids within 1 hour of presentation were significantly less likely to be admitted to hospital (odds ratio 0.50, 95% CI 0.31 to 0.81; number needed to treat=8, 95% CI 5 to 21) than those not given steroids. Maximal benefit was observed within 4 to 6 hours of administration of corticosteroids. A benefit in peak expiratory flow rate with a standard mean difference at the end of therapy of 0.54 (95% CI 0.01 to 1.1) was suggested in the treated group.[9]

Systemic steroids for treating asthma

Oral prednisone and dexamethasone are the currently recommended systemic steroids for moderate to severe asthma exacerbations. Formulations such as hydrocortisone and methylprednisolone can be given parenterally. Studies have found these routes to be equally effective, with the oral route being less painful and invasive.[10,11] Prednisone is given for 5 days at a dose of 1 to 2 mg/kg daily (maximum 50 mg/d). Dexamethasone can be given for 1 to 5 days at a dose ranging from 0.3 to 0.6 mg/kg daily. Dexamethasone is a long-acting glucocorticoid with a half-life of 36 to 72 hours, and is 6 times more potent than prednisone. Prednisone is shorter acting, with a half-life of 18 to 36 hours.[12]

Recognizing the debate in choice and dose of corticosteroids, the Cochrane Database generated a protocol to investigate this issue in hospitalized patients with asthma, but a review has not yet been published.[13]

Prednisone vs dexamethasone

Few trials compare oral dexamethasone head-to-head with oral prednisone. In 2001, Qureshi et al[14] compared 2 days of dexamethasone (0.6 mg/kg daily; maximum 16 mg/d) to 5 days of prednisone (1 mg/kg daily; maximum 60 mg/d). Dexamethasone had a similar efficacy as measured by relapse rates (7.4% vs 6.9%, $P=.84$), hospitalization rates (11% vs 12%), and the persistence of symptoms at 10 days (22% vs 21%). The patients treated with dexamethasone had increased compliance (99.6% vs 96%, $P=.004$) and fewer side effects, such as vomiting (0.3% vs 3%, $P=.008$). Part of the increased compliance in the dexamethasone group was believed to be owing to patients being discharged from EDs with the medication, whereas prednisone required a prescription to be filled at a pharmacy. Although dispensing medication is feasible in some EDs, it is often not an option in the ambulatory practice setting. Furthermore, dexamethasone is given at a smaller volume and can be mixed with better-tasting syrups to allow for better palatability and therefore compliance.

When dexamethasone (0.6 mg/kg daily) was compared with a higher dose of prednisone (2 mg/kg daily), no statistically significant differences were found in relapse rates (16% vs 8%, $P=.27$) or in the incidence of vomiting in pediatric patients with asthma exacerbations (10% vs 18%, $P=.24$).[15] However, this study was limited owing to a small sample size and a change in hospital protocol in midstudy.

Because dexamethasone has a long half-life, Altamimi et al[16] attempted to determine if a single dose of dexamethasone (0.6 mg/kg) was equal to 5 days of prednisolone (2 mg/kg daily). The single dose of dexamethasone demonstrated no difference in any of the following: hospital admission rates (13.4% dexamethasone vs 14.9% prednisolone), additional β-agonist therapy, return to baseline of patient self-assessment scores (5.21 days vs 5.22 days, respectively, mean difference -0.01; 95% CI -0.70 to 0.68), and mean pulmonary index scores (0.4 vs 0.3, mean difference 0.1; 95% CI -0.25 to 0.45) in children 2 to 16 years of age with mild to moderate asthma.[16]

In summary, these studies showed that slight differences exist in vomiting and compliance favouring dexamethasone; however, more studies are needed to further investigate these effects. To date, studies support using either prednisone or dexamethasone.

Safety

One of the greatest challenges in using systemic corticosteroids is physicians', parents', and patients' concern regarding potential side effects.[17] Short bursts of prednisone at a dose of 1 to 2 mg/kg daily for 5 days showed no effect on bone density, height, and adrenal function at 30 days, but transient decreases were noted in bone deposition and adrenal function.[17] Cochrane Reviews fail to identify significant increases in side effects such as nausea, tremor, and headache when compared with placebo, while other potential side effects such as hypertension, hyperglycemia, and behavioural disturbances have not been sufficiently reported.

Conclusion

Short courses of systemic corticosteroids are indicated in the treatment of moderate and severe asthma exacerbations as well as mild exacerbations unresponsive to increased doses of β-agonist therapy and inhaled corticosteroids. Prednisone (1 to 2 mg/kg daily for 5 days) and dexamethasone (0.3 to 0.6 mg/kg daily for 1 to 5 days) are appropriate choices, with some evidence suggesting that dexamethasone might be better tolerated and requires shorter duration of therapy. Side effects of short corticosteroid treatments appear minimal and clinically insignificant. More studies are needed to ascertain the optimal dose, duration, and choice of systemic steroids, especially in the ambulatory care setting.

Competing interests
None declared

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Revista presei medicale

Men who stay trim less apt to get prostate cancer

Men who put on a significant number of pounds after their 20s face a higher risk of prostate cancer than those who remain close to their youthful weight – but the effects vary by race, a new study indicates.

Researchers found that among nearly 84,000 middle-aged and older U.S. men followed for about a decade, white and African-American men who had gained weight since the age of 21 had a higher risk of developing prostate cancer.

Compared with white men who gained fewer than 10 pounds, those who gained more had twice the risk of being diagnosed with advanced or aggressive prostate cancer.

Among black men, the risks began increasing after a 25-pound weight gain – though the link was seen only with early-stage and less-aggressive prostate tumors, and not advanced cancer.

In contrast, men of Japanese descent actually saw their prostate cancer decline with weight gain.

These differences may have something to do with racial and ethnic differences in the way people tend to put on fat as they age, Dr. Brenda Y. Hernandez of the University of Hawaii in Honolulu and her colleagues report in the journal Cancer Epidemiology, Biomarkers and Prevention.

Regardless, the researchers say, the findings do not change the general advice that people try to maintain a normal weight throughout life.

"These results do not warrant a change in the current public health messages about obesity," Dr. Elizabeth A. Platz, another researcher on the work and an associate professor of epidemiology at Johns Hopkins University in Baltimore, said in a written statement.

"Men of normal weight in all racial/ethnic groups should be encouraged to avoid weight gain," she said, "and men who are overweight and obese should be encouraged to lose weight for good health in general."

The study included 83,879 men between the ages of 45 and 75 living in California or Hawaii. Over an average follow-up of 10 years, 5,554 were diagnosed with prostate cancer.

There was only weak evidence that men who were heavier at the start of the study had a higher risk of the disease than thinner men. Weight gain since young adulthood, on the other hand, showed a stronger link – at least in white and black men.

The findings appear to be the first to find ethnic differences in the relationship between body size and prostate cancer, according to the researchers.

It's possible, they say, that differences in body fat distribution help explain the findings. White men, for example, have been found to have more visceral fat – deep fat surrounding the abdominal organs – than African-American men, even with total body fat taken into account.

Excess body fat may, in theory, raise prostate cancer risk by altering levels of various hormones, including testosterone and insulin, or through other metabolic effects. It's thought that visceral fat, in comparison to body fat elsewhere, is more likely to spur such physiological changes.

More studies, the researchers conclude, are needed to see how and why weight gain may have varying effects in men of different races and ethnicities.

Source: *REUTERS/HEALTH* – New York