Does an IV Bolus of Methylprednisolone Relieve Dyspnea in Asthma Exacerbations?*

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Study objectives: To assess whether IV methylprednisolone exerts a specific early effect on dyspnea in patients with an exacerbation of asthma.

Design: Randomized, placebo-controlled, double-blind crossover trial.

Setting: Medium-sized university general hospital.

Patients: Twenty-five asthma patients attending the chest clinic with spontaneous complaints of increases in dyspnea and with a Borg scale dyspnea rating ≥ 1 at rest.

Interventions: At 0 min, IV methylprednisolone (125 mg) vs saline solution; at 60 min, 5 × 500 μg terbutaline inhaled from an inhaler device.

Measurements and results: Change in dyspnea was assessed with bipolar visual analog scale (VAS) (much more short of breath, −100%; much less short of breath, +100%), FEV₁, and visual memory (using the Benton visual retention test). Eighteen subjects (mean age, 61 years) completed the study. At 5 min and 60 min, shortness of breath improved with no statistically significant difference between saline solution and methylprednisolone. The mean (SD) VAS rating at 60 min was 29% (39%) on the day that saline solution was administered and 36% (25%) on the day the steroid was administered. The FEV₁ and Benton score did not significantly change from baseline on either study day. Shortness of breath and FEV₁ improved following terbutaline administration, with no significant difference between the days on which saline solution and the steroid were administered. In the seven subjects who were randomized to receive methylprednisolone on the first day, baseline dyspnea rated on the Borg scale was significantly lower on the second day (first day: median, 3; range, 3 to 4; second day: median, 2; range, 0.5 to 3; p = 0.040).

Conclusions: We conclude that in patients with an exacerbation of asthma, an IV bolus of methylprednisolone does not reduce dyspnea more than saline solution after 5 min and 60 min.

(CHEST 2000; 118:1530–1537)

Key words: asthma exacerbation; dyspnea; methylprednisolone; visual analog scale

Abbreviations: CI = confidence interval; DR = dyspnea rating; MEF₅₀ = maximal expiratory flow at 50% of FVC; VAS = visual analog scale

Asthma guidelines recommend that patients with asthma use inhaled anti-inflammatory agents as maintenance therapy. In addition, short-acting inhaled sympathomimetics are proposed as rescue therapy in everyday life to control asthma symptoms, whereas systemic corticosteroids are left for more severe exacerbations. As steroids do not exert any favorable effect on lung function before 6 to 12 h after administration,¹ they should never be used alone. When trying to disseminate these recommendations among general practitioners, we have been regularly challenged because some doctors think that shortness of breath experienced during an asthma exacerbation can be improved shortly after an IV bolus of methylprednisolone.
injection of a steroid. In a group of 193 general practitioners attending a symposium that was organized by our school of medicine, we observed that 43 (22.3%) made no distinction between inhaled or systemic bronchodilators, on the one hand, and an IV corticosteroid, on the other hand, in their ability to quickly relieve dyspnea during an asthma exacerbation (for details see “Appendix”). When an asthma patient claims to have experienced a rapid decrease in shortness of breath after an IV bolus of a steroid, we usually argue that this is a placebo effect, as is also seen after the inhalation of saline solution, but to our knowledge, no data are available to support this hypothesis.

The present study was designed to evaluate the early effects on dyspnea of an IV bolus of 125 mg methylprednisolone vs saline solution in a group of outpatients who were symptomatic because of an asthma exacerbation. The effect on dyspnea was assessed using a previously validated bipolar visual analog scale (VAS).

### Materials and Methods

#### Subjects

The subjects were consecutively recruited by the same pulmonary physician (A.N.) from among patients who regularly attended (for at least 3 years) a medium-sized general hospital chest clinic and who had a history of episodic breathlessness and a lung function chart showing an obstructive ventilatory pattern (FEV1/FVC ratio, < 65%) varying over time, the difference between the best and the worst FEV1 values in the chart exceeding 15% predicted. Only patients spontaneously complaining of a recent increase in dyspnea were selected. Furthermore, the rating of dyspnea at rest when sitting on a chair, using the Borg scale, had to be ≥ 1 (ie, subject at least “very slightly short of breath”). Symptoms such as chest pain or purulent sputum were not present, and physical examination did not disclose any sign suggestive of an etiology other than asthma exacerbation. In all subjects, spirometry findings showed a sharp decrease in FEV1 compared to the values in the chart (Table 1).

#### Table 1—Characteristics of the Population Studied

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, yr</th>
<th>Smoking History</th>
<th>Atopy</th>
<th>Best FEV1, % predicted</th>
<th>Baseline FEV1, % predicted</th>
<th>Drop in FEV1, % predicted</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Saline Solution Day</td>
<td>Steroid Day</td>
<td>Saline Solution Day</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/M/71</td>
<td>PS</td>
<td>–</td>
<td>95</td>
<td>44</td>
<td>51</td>
</tr>
<tr>
<td>2/M/72</td>
<td>PS</td>
<td>–</td>
<td>37</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3/M/78</td>
<td>NS</td>
<td>–</td>
<td>100</td>
<td>73</td>
<td>27</td>
</tr>
<tr>
<td>4/F/69</td>
<td>NS</td>
<td>+</td>
<td>74</td>
<td>38</td>
<td>36</td>
</tr>
<tr>
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<td>NS</td>
<td>+</td>
<td>47</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
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<td>+</td>
<td>90</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
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<td>66</td>
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<td>36</td>
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<tr>
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<td>NS</td>
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<td>115</td>
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<td>—</td>
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<td>13</td>
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<tr>
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<td>80</td>
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<td>NS</td>
<td>+</td>
<td>84</td>
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<td>18/M/70</td>
<td>PS</td>
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<td>34</td>
<td>—</td>
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<tr>
<td>19/M/67</td>
<td>PS</td>
<td>+</td>
<td>47</td>
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<td>29</td>
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<tr>
<td>20/F/58</td>
<td>PS</td>
<td>–</td>
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<tr>
<td>21/M/34</td>
<td>NS</td>
<td>+</td>
<td>73</td>
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<td>—</td>
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<td>NS</td>
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<td>62</td>
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<td>24</td>
</tr>
<tr>
<td>23/F/69</td>
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<td>101</td>
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<td>NS</td>
<td>+</td>
<td>75</td>
<td>36</td>
<td>39</td>
</tr>
<tr>
<td>25/F/69</td>
<td>NS</td>
<td>+</td>
<td>102</td>
<td>63</td>
<td>39</td>
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</tr>
<tr>
<td>SD 12</td>
<td>23</td>
<td></td>
<td>18</td>
<td>20</td>
<td>10</td>
</tr>
</tbody>
</table>

*M = male; F = female; NS = never smoker; PS = past smoker.

1In each subject, the best FEV1 value is derived from the lung function chart; this analysis is based on an average of 10 measurements (range, 6 to 18) made over a time span of 3 years.

2Best value minus baseline.

3Subject did not agree to participate.

4Subject was excluded for being unable to use the dyspnea scales.

5Subject was excluded because she experienced a spontaneous improvement in dyspnea (Borg scale DR, 0).
Study Design

All subjects gave informed consent, and the study protocol was approved by the ethics committee of the Centre Hospitalier Universitaire Brugmann. The study was performed on two consecutive afternoons, with the delay between recruitment at the chest clinic and the first study day ranging from 1 to 3 days. In between, no change in therapy was made. A double-blind, randomized, crossover design was used. All sessions started at 2 PM, and all subjects were asked to abstain, as much as possible, from using inhaled short-acting sympathomimetics after 9 AM, from using inhaled anticholinergics after 7 AM, and from using inhaled long-acting sympathomimetics after the preceding evening. Treatment with inhaled steroids and/or oral theophylline was not withheld. On arrival, each subject comfortably rested on a chair for 5 min, and a baseline rating for dyspnea was obtained on the Borg scale. Subsequently, visual memory was assessed and baseline spirometry was performed. At this time (time 0) the IV injection (125 mg methylprednisolone or saline solution) was made. Ratings for dyspnea (ie, primary outcome measure) and spirometry (ie, secondary outcome measure) were obtained after 5 min (time 5) and 60 min (time 60), at which time visual memory again was assessed. At this stage, each subject was given 5 × 500 μg terbutaline, inhaled via an inhaler device (Turbohaler; AstraZeneca; London, UK). Ratings for dyspnea and spirometry were obtained again 5 min later (time 65) and 30 min later (time 90). Side effects were not monitored, but spontaneous comments about the IV injection and the inhalation were recorded.

Methylprednisolone

The solutions used in the present study were made up and coded independently in the hospital pharmacy, using a randomization table. The galenical form we used was a ready-to-use lipidal solution of 125 mg methylprednisolone that was indistinguishable from saline solution (Promedrol; Pharmacia & Upjohn; Piscataway, NJ). The code remained located in the hospital pharmacy during the whole study.

Dyspnea Rating

To refer to dyspnea, we always used the item “shortness of breath” when talking with the patients since it is the most frequently chosen and the most reproducible descriptor in patients with asthma. The subjects were given neutral information about the IV agent. They were told they would receive on each of the two study days an IV agent that could modify the sensation of shortness of breath. Questions about which IV agent would be used were not answered. At the time of terbutaline inhalation, the subjects were told they would inhale a bronchodilator agent that was expected to improve lung function. We rated baseline dyspnea at the time of inclusion, as well as before starting with the study protocol on each study day, using a modified Borg scale. The scale is a 20-cm vertical line labeled with numbers from 0 to 10 with descriptors ranging from “not short of breath at all” to “extremely short of breath.” The Borg scale dyspnea rating (DR) aimed to rate the intensity of shortness of breath at the very moment the scale was shown to the subject. On each study day, we used a bipolar VAS to rate the change in dyspnea from baseline. The scale is a 40-cm horizontal line that has the midpoint that was labeled “no change,” and the left end labeled “very much shorter of breath,” and the right end labeled “very much less short of breath.” The VAS DR, expressed as a percentage (range, −100% to +100%), aimed to assess the change in shortness of breath from baseline at the very moment the scale was shown to the subject. Throughout the study, we carefully recommended to the subjects that they rate only shortness of breath and ignore other sensations such as cough, nasal irritation, or throat irritation.

Lung Function

A portable spiograph (Microspirom; Chest; Tokyo, Japan) was used. In all subjects, two to three technically acceptable maneuvers were obtained for the baseline evaluation as well as at each step following the IV injection or the terbutaline inhalation. The variable retained for analysis was the FEV1, with the highest FEV1 value obtained being the one reported. The FVC and the maximal expiratory flow at 50% of FVC (MEF50) (measured, as recommended at 50% of the baseline FVC value) also were analyzed; however, as FVC and MEF50 data yielded no additional information compared to that obtained from FEV1, data, only the latter are reported.

Visual Memory

Visual memory was assessed using the Benton visual retention test. The test is based on a design reproduction, using 10 cards each showing one to three geometric figures. A 10-s exposure of the card to the subject is followed by the removal of the card and the drawing of its contents by the subject. Subjects’ scores are derived from a standardized scoring procedure supplied with the test (score range, 0 to 10). In subjects aged 55 to 65 years, the expected scores range from 4 (poor visual memory level) to 8 (high level). The test includes two parallel series of 10 cards; the first series was used for a baseline assessment, at time zero, and the second was used for a repeated assessment, at time 60 min.

Statistical Analysis

Samples statistics were reported as mean (SD) or median (range). Confidence intervals (CIs) were calculated when appropriate. Values from paired samples were compared using Student’s t test or the Wilcoxon test when the variable was not normally distributed (Borg scale DR). Correlations were evaluated using Pearson linear regression or Spearman rank correlation when the variable was not normal. An analysis of variance with time and drug as the repeated measures (time at five levels and the drug at two levels) was performed to assess the time effect and the effect of methylprednisolone or saline solution on VAS DR and FEV1. Planned comparisons were performed subsequently for comparing specific times. The study was designed to give a 90% chance of detecting a 25% change in dyspnea with a 5% probability of a type I error. Taking into account a 25% between-subject coefficient of variation for the change in dyspnea recorded on the bipolar VAS following saline solution inhalations in a population with asthma, the sample size estimation indicated that at least 13 subjects were required.

RESULTS

Patients

The characteristics of the 25 patients asked to participate in the study are shown in Table 1. Maintenance therapy in these subjects included inhaled steroids (n = 22), short-acting (n = 9) or long-acting (n = 9) inhaled sympathomimetics, inhaled anticholinergics (n = 7), and oral theophylline...
All the patients inhaled short-acting sympathomimetics as rescue medication. Twenty-one subjects agreed to participate and were randomized. On the first study day, three subjects were excluded because of an inability to use the dyspnea scales (n = 2) or because of a spontaneous improvement in dyspnea, with a baseline Borg scale DR at 0 (n = 1). Eighteen patients (10 men, 8 women; mean age, 61 years [13 years]) completed the study, and all the results that follow involve these 18 subjects. Eleven subjects received the saline solution/steroid sequence, while 7 subjects received the reverse sequence. All subjects claimed they had succeeded in abstaining from inhaled bronchodilators, but this could not be assessed objectively. There was no protocol deviation. The median Borg scale DR at the time of recruitment was 3 (range, 1 to 4). The mean mini-mental state was 28.9 (1.0). As shown in Table 1, the drop in FEV1, defined as the best FEV1 performed when the patient was in stable condition minus the baseline FEV1 performed during the study, exceeded 10% of predicted in all subjects on both study days. It was >20% of predicted in 14 subjects and >30% predicted in 7 (steroid day) to 9 (placebo day) subjects.

Baseline Values: Placebo Day vs Steroid Day

All the subjects, except one, had a baseline Borg scale DR that was higher on at least one of the study days than at the time of recruitment. The median baseline Borg scale DR was 3 (range, 0.5 to 7) on the saline solution day, and 3.5 (range, 1.5 to 7) on the steroid day (difference not statistically significant). The relationship (Fig 1) of the baseline Borg scale DR did not reach significance with either baseline FEV1 (r = -0.27 [saline solution day];

![Figure 1](image1.png)

Figure 1. Baseline dyspnea (Borg scale DR) plotted against baseline FEV1 (left) or drop in FEV1 (best from the chart minus baseline, right) in 18 patients undergoing an exacerbation of asthma. ● = measurements made on the saline solution day; ○ = measurements made on the steroid day.

![Figure 2](image2.png)

Figure 2. Baseline FEV1 and dyspnea (Borg scale DR) on the first vs the second study day in 11 subjects randomized to receive saline solution on the first day (left) and in 7 subjects randomized to receive methylprednisolone on the first day (right).
In the 11 subjects randomized to receive saline solution on the first day, the median baseline Borg scale DRs were 4 (range, 2 to 7) and 4 (range, 1.5 to 7), respectively, on the first and the second day. The corresponding mean baseline FEV\(_1\) values were 42\% (19\%) of predicted for the first day and 43\% (21\%) of predicted for the second day. The differences were not statistically significant. Individual data are shown in Figure 2.

In the seven subjects who were randomized to receive methylprednisolone on the first day, the baseline Borg scale DR was significantly (p = 0.040) lower on the second day than on the first day (median, 2 [range, 0.5 to 3] vs median, 3 [range, 3 to 4]). The mean baseline FEV\(_1\) was 36\% (19\%) of predicted on the first day and 39\% (16\%) of predicted on the second day (difference was not statistically significant). Individual data are shown in Figure 2. The changes in baseline Borg scale DR from the first to the second day were unrelated to those in FEV\(_1\) (Spearman rank correlation, -0.13) or to those in the Benton score (Spearman rank correlation, -0.24).

**Effects of Methylprednisolone vs Saline Solution**

The effect of the IV injection of saline solution or methylprednisolone on dyspnea, assessed using the VAS DR, is shown in Table 2 and Figure 3. Five and 60 min after IV injection, an improvement in shortness of breath occurred after either methylprednisolone or saline solution injection, with no statistically significant difference between them. Inhaled terbutaline produced a further decrease in dyspnea on both study days. Comparing the mean VAS DR at times 65 and 90 with the mean VAS DR at times 5 and 60, respectively, led to a mean difference of 19\% (significantly different from zero, p = 0.001; 95\% CI, 10 to 27\%) on the saline solution day and 15\% (significantly different from zero, p = 0.048; 95\% CI, 0 to 30\%) on the steroid day.

No significant change in FEV\(_1\) from baseline was observed at either 5 min or 60 min (Table 2). Comparing the mean FEV\(_1\) levels at 65 min and 90 min with the mean levels at 0 min, 5 min, and 60 min led to a mean difference of 0.18 L or 7\% of predicted (95\% CI, 0.07 to 0.28 L) on the saline solution day and 0.12 L or 5\% of predicted (95\% CI, 0.02 to 0.25 L) on the steroid day.

On the saline solution day, the score for visual memory on the Benton test was 4.4 (2.0) at baseline and 4.6 (2.2) at time 60. The corresponding scores on the steroid day were 5.2 (2.2) and 4.8 (1.8). No difference was statistically significant. The correlations between VAS DR at time 60 and the parallel changes in the Benton score for visual memory were not statistically significant (saline solution day, r = -0.38; steroid day, r = 0.07).

**Table 2—Acute Effect of Methylprednisolone vs Saline Solution on Dyspnea and FEV\(_1\) in 18 Subjects With Asthma Exacerbations*\n
<table>
<thead>
<tr>
<th>Time, min</th>
<th>Saline Solution Day</th>
<th>Steroid Day</th>
<th>Saline Solution Day</th>
<th>Steroid Day</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>—</td>
<td>—</td>
<td>41 (18)</td>
<td>40 (20)</td>
</tr>
<tr>
<td>5</td>
<td>+24 (25)</td>
<td>+16 (14)</td>
<td>42 (18)</td>
<td>40 (20)</td>
</tr>
<tr>
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<td>+29 (39)</td>
<td>+36 (25)</td>
<td>39 (19)</td>
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</tr>
<tr>
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<td>+41 (34)</td>
<td>47 (21)</td>
<td>45 (20)</td>
</tr>
<tr>
<td>90</td>
<td>+44 (44)</td>
<td>+42 (42)</td>
<td>48 (19)</td>
<td>45 (20)</td>
</tr>
</tbody>
</table>

*Values given as mean (SD).

\( r = -0.24 \) [steroid day]) or with the drop in FEV\(_1\) (for best value minus baseline value, see Table 1) \( (r = 0.31 \) on both study days).
Patients’ Comments

One subject complained about a painful IV injection (steroid day), and another developed skin erythema following IV injection (saline solution day). Complaints following inhaled terbutaline administration included tremor (n = 3), palpitations (n = 2), and nervousness (n = 2) on the two study days. One subject mentioned headache in the hours following the study (steroid day), and another mentioned insomnia on the night following the study (steroid day). No serious effect was observed, and the study code was not broken.

Discussion

In the present study, we have found in 18 patients with symptomatic asthma that an IV bolus moderately reduced dyspnea after 5 and 60 min. However, no change in FEV₁ occurred within 60 min, methylprednisolone had no more effect than saline solution, and it enhanced neither the intensity nor the perception of the bronchodilation induced by terbutaline inhaled 60 min after the IV injection. These findings are consistent with a placebo effect.

It may be questioned whether our subjects were really asthmatic. First, in 4 of 18 subjects, the best FEV₁ from the chart was < 50% of predicted, a pattern that is consistent with chronic severe obstruction. Second, the amount of terbutaline-induced bronchodilation was very modest in this study, although the 2,500-μg dose of terbutaline inhaled from the inhaler device was reported to be effective in acute asthma exacerbation. Such a small bronchodilation may look surprising in patients with asthma. However, the magnitude of the acute response to a given dose of a bronchodilator is known to vary over time in the same individuals. On the basis of the large variability in FEV₁ over time, which was a selection criterion for this study, we consider that our subjects really had asthma. The patients we studied presented at the chest clinic with moderate exacerbation that was judged not to need an immediate increase in treatment; however, they were undoubtedly in a phase of aggravation of bronchial obstruction, with a FEV₁ on the study days lower than their best FEV₁ by 30% of predicted on average. In this setting, we think that the small response to terbutaline that we observed during the study reflected the severity of the subjects’ conditions at the time that they were studied. In particular, marked airway inflammation is known to cause a reversible decrease in bronchodilator responsiveness at the time of exacerbation. The relevance of this study depends on whether the chosen variables were appropriate. We used a Borg scale to rate baseline dyspnea and a bipolar VAS to rate the changes in dyspnea induced by the IV injection and/or by inhaled terbutaline. Indeed, the Borg scale is not well-suited to assess an acute change, as there is little room on the scale to rate any improvement in subjects with baseline dyspnea of low intensity. However, the bipolar VAS is specifically devised for interval estimation and has been validated in our laboratory to assess changes in dyspnea following acute interventions. To assess lung function, we used spirometry and focused on the FEV₁. Several groups have shown that airway resistance, respiratory motor drive, and hyperinflation play a role in the sensation of dyspnea experienced by asthmatics. However, the same and other investigators have found that there is a close relationship among patients with asthma between the changes in dyspnea and the parallel changes in FEV₁. In this study, FEV₁ did not change from baseline within 60 min on either study day. The absence of effect of IV methylprednisolone on lung function after 60 min was not unexpected. In a group of eight patients with asthma, Klaustermeyer and Hale reported a mean increase in MEF₅₀ of 0.29 L/s 2 h after methylprednisolone, 125 mg IV, administration. In a similar group of eight patients with asthma, Ellul-Micallef reported a mean increase in peak expiratory flow of 23% of baseline 1 h after hydrocortisone, 200 mg IV, administration. However, these studies are of limited relevance in view of the small numbers of subjects and the modest, although statistically significant, changes reported. Most studies involving large numbers of subjects concluded that 6 to 12 h are required before steroids exert their effect on lung function. The only effect of IV steroids that has been shown to occur within 60 min is restoration of β₂ mimetic responsiveness. In the present study, however, the amount of bronchodilation induced by terbutaline 60 min after the IV injection was very similar on both study days.

Some other features of the design of our study need a critical evaluation. Because a double-blind procedure could not be guaranteed with the commercially available galenical form (lyophilized powder), a methylprednisolone solution that was characterized by its limpidity was used. The dose of methylprednisolone was fixed at a sufficiently high level (125 mg) to avoid the possibility that a negative result could be ascribed to the use of too low a dose. Indeed, although the optimal dosage of glucocorticoid treatment in asthma exacerbation is still disputed, the 125-mg dose lies within current dose recommendations and practices. Finally, a crossover design may not be optimal for a comparison between a steroid agent and placebo. To account for any carryover effect of methylprednisolone in the
seven subjects randomized to receive the active agent on the first study day, we analyzed this subgroup separately and found that baseline dyspnea significantly decreased from the first to the second day. This decrease may be due to several factors. In asthmatic children, steroid therapy has been shown to affect cognitive performance, including visual memory assessed with the Benton visual retention test, as soon as 6 h after oral ingestion. In our study, however, reduced dyspnea, as rated on the Borg scale, is very unlikely to result from a nonspecific effect on cognitive function, since changes in Borg scale DRs and changes in Benton scores were unrelated. The parallel change in FEV\textsubscript{1} (ie, from the first to the second day) was very small (mean, 0.08 L [3% of predicted]); as the changes in Borg scale DR were unrelated with those in FEV\textsubscript{1}, the reduction in dyspnea cannot be ascribed to an improvement in FEV\textsubscript{1}. The most attractive explanation is that shortness of breath improved as a consequence of steroid-reduced inflammation within the airways. There is some experimental support to the concept that dyspnea and inflammation may be linked in patients with asthma. It has been shown, for example, that in asthma patients with normal baseline FEV\textsubscript{1}, dyspnea is higher when a given degree of bronchoconstriction is induced by some agent (eg, by hypertonic saline solution), which is known to induce inflammatory mechanisms, rather than by methacholine.

In conclusion, this placebo-controlled study shows that in patients with asthma who attended the chest clinic and who had increased dyspnea and decreased FEV\textsubscript{1}, IV methylprednisolone, at a dose of 125 mg, has no more effect on dyspnea than saline solution, within a time course of 60 min. Doctors should be aware that an IV bolus has a placebo effect on dyspnea in patients experiencing an exacerbation of asthma, but they should no longer think that the administration of an IV corticosteroid has any early specific effect on shortness of breath in such patients.

ACKNOWLEDGMENT: The authors thank F. Martinez Vadillo for secretarial assistance.

APPENDIX

General practitioners attending a symposium about asthma organized by the Université Libre de Bruxelles were asked the following question: “Which treatment for asthma exacerbation has no more rapid effect on dyspnea than a placebo: nebulized sympathomimetic, subcutaneous adrenaline, IV theophylline, IV corticosteroid, or none of these.” Only one choice was allowed. This question was intended to evaluate the understanding of general practitioners of a concept widely present in international guidelines about asthma (namely, the distinction between bronchodilator agents and anti-inflammatory agents), so that the expected answer was “IV corticosteroid.” Of 193 doctors, 147 chose the expected answer, while 14 chose IV theophylline, 6 chose nebulized sympathomimetic, 4 chose subcutaneous adrenaline, and 19 answered that all four agents have more rapid effects than placebo. Three did not answer.

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