

PHARMACOTHERAPY

# The Effect of Administrative Cessation of the Use of Ipratropium Bromide in the Treatment of Acute Asthma Attacks in the Emergency Department

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**Background.** The anticholinergic agent ipratropium bromide has demonstrated effectiveness in the treatment of severe asthma exacerbations. **Methods.** We conducted a retrospective quasi-experiment to investigate the clinical consequences on acute asthma patients of the administrative removal of ipratropium bromide from an emergency department (ED) of a large tertiary hospital. We compared the combined negative outcome (hospitalization, length of stay in the ED, hospital readmission within 48 hours or 7 days, intubation, and death) of acute asthma patients, treated in the 12 months preceding ( $n = 394$ ; Period A) and the 12 months following ( $n = 334$ ; Period B) the policy change. Multiple imputations based on sequentially improved regressions were performed for missing data on measures of severity. **Results.** Administration of steroid medications increased from 49.8% to 61.4%;  $p = .002$  from Period A to Period B. There was no statistically significant difference in combined negative outcome between Periods A and B (41.1% and 42.9%, respectively). **Conclusions.** An administrative decision to stop the purchase of ipratropium bromide in an ED was followed by an increased use of steroids; adverse consequences did not increase in acute asthmatic patients. In the absence of ipratropium bromide in the ED, steroids may thus serve as an appropriate substitute, an observation that calls for a randomized controlled clinical trial.

**Keywords** quasi-experiment, administrative intervention, emergency department readmission

## INTRODUCTION

Studies of the use of the anticholinergic agent ipratropium demonstrate its effectiveness in the treatment of moderate to severe asthmatic exacerbations, yet less for mild cases. A Cochrane Database Review of 13 studies involving 205 participants concluded that anticholinergic agents are more effective for acute asthma than placebos (1). However, in the same review, a meta-analysis of 9 studies involving 440 patients did not show an advantage to the combination of anticholinergic agents and beta-2 agonists over the use of beta-2 agonists alone (1). In contrast, a meta-analysis of 32 randomized trials ( $n = 3611$  subjects), 26 of them double blind, concluded that early administration of inhaled anticholinergic agents in the emergency department (ED), in conjunction with beta-2 agonists, reduces hospital admissions. Greater baseline severity of asthma amplified the benefit (2). More recent studies have demonstrated the effectiveness of anticholinergic agents for severe cases of asthma (3, 4). In a recent study, the use of ipratropium bromide was found to increase the risk of cardiovascular events in chronic obstructive pulmonary disease (COPD) patients (5).

Due to the lack of clear evidence of its beneficial effect in acute asthma and the lack of clear evidence-based guidelines prior to 2009 (6, 7), ipratropium bromide was removed from the ED in the Sheba Medical Center. No substitute medications were officially introduced. The aim of this study was to investigate whether this administrative action that reduced the availability of ipratropium bromide affected the outcome of acute asthma patients and whether it had adverse clinical consequences.

## MATERIALS AND METHODS

### Study Design

This is a retrospective study investigating a nonrandomized administrative intervention. We compared the clinical outcomes of acute asthma patients treated at the ED of our medical facility during two consecutive periods of time: Period A – 12 months during which ipratropium bromide was available in the ED and Period B – 12 subsequent months during which ipratropium bromide was excluded from the drug arsenal of the ED.

### Setting

The data for this study were obtained retrospectively from the ED medical records of a large tertiary-care university-affiliated hospital. The study was approved by the Sheba Medical Center IRB committee. An exempt from obtaining informed consent was received due to the retrospective design of the study.

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### *Study Subjects*

The subjects of this study comprised all patients aged 17–35 years who were admitted to the ED of our hospital during a 24-month period with a primary diagnosis of acute asthma. The upper age limit was set at 35 years, to minimize the possibility that patients would be comorbid for COPD.

### *Intervention*

The nonrandomized administrative intervention in this study was the cessation of purchase of ipratropium bromide for use in the ED.

### *Methods of Measurement*

We retrieved and analyzed patients' medical records during the 12 months preceding (Period A) and following (Period B) institutional removal of ipratropium bromide from the ED. These two time periods represented the main independent variable of interest in the study.

### *Outcome Measures*

Outcome measures were hospitalization, length of stay in the ED (hours), ED readmission within 48 hours or 7 days, intubation, and death. All ED readmissions occurring more than 1 week after a previous hospitalization were considered separate observations. Readmissions of the same patient within 1 week were excluded from the primary analysis, under the assumption that these readmissions were in fact due to the same attack as the previous admission and the possibility that the patient may have been prematurely discharged. A combined negative outcome was defined as the presence of at least one of the following: ED readmission within 48 hours or 7 days, hospitalization, intubation, or death.

### *Primary Data Analysis*

We collected data from the medical records of the ED regarding signs and symptoms of the asthma attack: heart rate (beats per minute), presence of rales (yes/no), wheezes (yes/no), prolonged expirium (yes/no), the use of respiratory muscles (yes/no), and oxygen saturation measurement (%). Viral etiology of the attack was evaluated by information on a current febrile disease provided by the patient to the attending ED physician. General severity of the asthma disease was assessed by information on previous hospitalizations and intensive care unit (ICU) admissions provided by the patient to the attending ED physician. Treatment administered in the ED and asthma medications used at home were recorded as well. Length of stay in the ED was calculated from the time of entry to the time of departure from the ED. The attending physician was determined according to the signature on the ED medical chart. Potential confounders included age and sex, severity of the asthma attack upon arrival to the ED (according to signs and symptoms), and professional status of the attending physician. Attending physicians working in the ED during the study period were classified according to their discipline and level

of training: emergency physician specialists, internal medicine or other specialists, and residents.

Heart rate, O<sub>2</sub> saturation, and length of stay at the ED were continuous variables, and the others were categorical.

### *Statistical Analysis*

In univariate comparisons between the two time periods, we used the chi-square test and Fisher's exact test for categorical independent variables and the Student's *t*-test for continuous independent variables. Reported *p*-values are two tailed. Plus-minus values are mean  $\pm$  standard deviation.

The probability of the combined negative outcome was estimated using logistic regression (procedure LOGISTIC of SAS 9.1.3, SAS/STAT software, Version 9.2 of the SAS System for Unix). The main factor of interest was the period variable. We assessed, in addition, the predictive value on the combined negative outcome, of sex, age, and clinical signs, while adjusting for the effect of the institutional cessation of ipratropium bromide. There were missing values for the following explanatory variables: pulse rate (originally available for  $n = 697$ ), O<sub>2</sub> saturation ( $n = 563$ ), rales ( $n = 704$ ), wheezes ( $n = 712$ ), prolonged expirium ( $n = 673$ ), and the use of respiratory muscles ( $n = 582$ ). The structure of the pattern of missing values was not monotone, preventing the use of a standard SAS procedure MI for multiple imputations. Therefore, we used an alternative method of multiple imputation based on sequentially improved regressions, which is a variant of fully conditional specification approach (8).

To calculate the sample size and power of the study, we assumed the rate of combined negative outcomes to be 40% for Period A and not more than 42% for Period B; a 50% rate would indicate a significant increase. We then calculated that 450 patients during each period would yield two-sided significance of 0.05 and power of 0.8.

## RESULTS

There were 976 entries of acute asthma attack in our ED during the study period. After excluding 47 readmissions of the same patient within 1 week, and patients below age 17 or above age 36, 394 entries remained during Period A and 334 during Period B. Of the 47 readmissions, 19 (5%) occurred in Period A and 28 (8%) in Period B. Demographic and clinical characteristics of the patients were similar during the two study periods, including age and gender distribution, morbidity parameters, the classification of attending physicians, the proportion with febrile disease, and the use of previous medications for asthma, including home use of steroids (Table 1).

Of note, 31 patients (9.9%) received ipratropium bromide during Period B, despite the hospital policy to exclude it from acute treatment. We did not find statistically significant differences between patients treated with and without ipratropium bromide during

TABLE 1.—Baseline characteristics by period of admission to the emergency department—before and after cessation of ipratropium bromide use of 728 acute asthma patients.

|                                                                                     | Period A<br><i>n</i> (%) | Period B<br><i>n</i> (%) | Chi-square<br>test <i>p</i> |
|-------------------------------------------------------------------------------------|--------------------------|--------------------------|-----------------------------|
| Number of patients                                                                  | 394                      | 334                      |                             |
| Age (years); mean $\pm$ SD                                                          | 23.9 $\pm$ 5.0           | 23.7 $\pm$ 5.0           | .6 <sup>a</sup>             |
| Gender <i>n</i> (%)                                                                 |                          |                          |                             |
| Male                                                                                | 188 (47.7)               | 167 (50.0)               | .5                          |
| Female                                                                              | 206 (52.3)               | 167 (50.0)               |                             |
| Febrile disease                                                                     | 86 (21.8)                | 82 (24.6)                | .4                          |
| Number of previous hospitalizations (%)                                             | 100 (25.4)               | 83 (24.9)                | .9                          |
| Number of previous ICU admissions (%)                                               | 12 (3.0)                 | 13 (3.9)                 | .5                          |
| Number of patients who performed steroid/amino/theophylline inhalations at home (%) | 278 (70.6)               | 246 (73.7)               | .4                          |
| Number of patients who used steroids at home (%)                                    | 98 (24.9)                | 103 (30.8)               | .07                         |
| Amino/theophylline administered at home (%)                                         | 26 (6.6)                 | 33 (9.9)                 | .11                         |
| Pulse (beats per minute) <sup>a</sup> ; mean $\pm$ SD                               | 102.1 $\pm$ 19.7         | 101.6 $\pm$ 19.7         | .8 <sup>b</sup>             |
| Oxygen saturation (%) <sup>a</sup> ; mean $\pm$ SD                                  | 94.4 $\pm$ 8.2           | 95.1 $\pm$ 4.2           | .14 <sup>b</sup>            |
| Use of respiratory muscles                                                          | 32 (9.4)                 | 26 (10.8)                | .6                          |
| Prolonged expirium                                                                  | 267 (70.6)               | 254 (86.1)               | <.0001                      |
| Wheezes                                                                             | 318 (82)                 | 269 (83)                 | .7                          |
| Rhales                                                                              | 47 (12.3)                | 35 (10.9)                | .6                          |
| Ipratropium administered in the emergency department                                | 238 (60.4)               | 31 (9.3)                 | <.0001                      |
| Steroids administered in the emergency department, by type                          |                          |                          |                             |
| Inhaled                                                                             | 13 (3.4)                 | 5 (1.5)                  | .12                         |
| IV hydrocortisone                                                                   | 129 (33.4)               | 164 (49.3)               | <.0001                      |
| Per os                                                                              | 57 (14.7)                | 41 (12.3)                | .4                          |
| Total                                                                               | 196 (49.8)               | 205 (61.4)               | .002                        |
| Physician type                                                                      |                          |                          |                             |
| ED specialist                                                                       | 75 (20.3)                | 67 (21.6)                | .3                          |
| Other specialist                                                                    | 57 (15.4)                | 33 (10.6)                |                             |
| Resident                                                                            | 221 (59.9)               | 199 (64.2)               |                             |
| Unknown                                                                             | 16 (4.3)                 | 11 (3.5)                 |                             |

Note: <sup>a</sup>Mean values after imputation for missing data; <sup>b</sup>by *t*-test.

Period A (Table 2), except that the number who reported steroid/theophylline/aminophylline inhalations at home, and the degree of severity of the asthmatic attack, as measured by oxygen saturation and presence of wheezes, was greater among those treated with ipratropium bromide. Note that the rate of any steroid use at home, prior to emergency room visit, was similar between those treated and not treated with ipratropium (Table 2).

Administration of steroid medications in the ED increased from 49.8% in Period A to 61.4% in Period B; *p* = .002. Specifically, an increase was observed in the administration of intravenous (IV) hydrocortisone steroid and not of inhaled or per os steroid (Table 1). The frequency of use of treatments other than steroids for acute asthma did not change following the administrative cessation of ipratropium bromide in the ED. During both the study periods, beta-2 agonists and xanthins were

TABLE 2.—Patients characteristics and outcome by ipratropium bromide treatment during period prior to policy change (Period A).

|                                                           | Ipratropium<br>+ <i>n</i> = 238 | Ipratropium<br>- <i>n</i> = 156 | <i>p</i>           |
|-----------------------------------------------------------|---------------------------------|---------------------------------|--------------------|
| Age (years), mean $\pm$ SD                                | 24.0 $\pm$ 4.9                  | 23.8 $\pm$ 5.0                  | .7 <sup>a</sup>    |
| Gender, <i>n</i> (%)                                      |                                 |                                 |                    |
| Male                                                      | 121 (50.8)                      | 67 (42.9)                       | .13 <sup>b</sup>   |
| Female                                                    | 117 (49.2)                      | 89 (57.1)                       |                    |
| Febrile disease, <i>n</i> (%)                             | 52 (21.9)                       | 34 (21.8)                       | .99 <sup>b</sup>   |
| Previous hospitalizations, <i>n</i> (%)                   | 65 (27.3)                       | 35 (22.4)                       | .3 <sup>b</sup>    |
| Previous ICU admissions, <i>n</i> (%)                     | 10 (4.2)                        | 2 (1.3)                         | .14 <sup>c</sup>   |
| Inhalations at home, <i>n</i> (%)                         | 180 (75.6)                      | 98 (62.8)                       | .006 <sup>b</sup>  |
| Steroids use at home, <i>n</i> (%)                        | 62 (26.1)                       | 36 (23.1)                       | .5 <sup>b</sup>    |
| Amino/theophylline use at home, <i>n</i> (%)              | 18 (7.6)                        | 8 (5.1)                         | .3 <sup>b</sup>    |
| Pulse rate <sup>d</sup> (beats per minute), mean $\pm$ SD | 102.5 $\pm$ 19.2                | 101.4 $\pm$ 20.5                | .6 <sup>a</sup>    |
| O <sub>2</sub> saturation <sup>d</sup> (%), mean $\pm$ SD | 93.5 $\pm$ 10.1                 | 95.9 $\pm$ 2.8                  | .0007 <sup>a</sup> |
| Use of respiratory muscles, <i>n</i> (%)                  | 23 (11.1)                       | 9 (6.7)                         | .17 <sup>b</sup>   |
| Prolonged expirium, <i>n</i> (%)                          | 173 (75.2)                      | 94 (63.5)                       | .015 <sup>b</sup>  |
| Wheezes, <i>n</i> (%)                                     | 207 (88.1)                      | 111 (72.5)                      | .0001 <sup>b</sup> |
| Rhales, <i>n</i> (%)                                      | 23 (10)                         | 24 (15.8)                       | .09 <sup>b</sup>   |
| Discharge, <i>n</i> (%)                                   |                                 |                                 |                    |
| Home                                                      | 144 (60.5)                      | 104 (67.5)                      | .2 <sup>b</sup>    |
| Hospitalize                                               | 94 (39.5)                       | 50 (32.5)                       |                    |
| Readmission to ED, <i>n</i> (%)                           |                                 |                                 |                    |
| Within 48 hours                                           | 4 (1.7)                         | 1 (0.6)                         | .5 <sup>c</sup>    |
| After >48 hours–1 week                                    | 10 (4.2)                        | 4 (2.6)                         |                    |
| Combined negative outcome                                 | 107 (45.0)                      | 54 (35.1)                       | .05 <sup>b</sup>   |

Notes: Ipratropium +, patients receiving ipratropium bromide during Period A; Ipratropium -, patients not receiving ipratropium bromide during Period A.

<sup>a</sup>By *t*-test; <sup>b</sup>by chi-square test; <sup>c</sup>by Fisher's exact test; <sup>d</sup>Mean value after imputation for missing data.

TABLE 3.—Outcome measures of 728 acute asthma patients by period.

| Outcome measure                              | Period A<br><i>n</i> = 394 | Period B<br><i>n</i> = 334 | <i>p</i>         |
|----------------------------------------------|----------------------------|----------------------------|------------------|
| Readmission to ER, <i>n</i> (%)              |                            |                            |                  |
| <48 hours                                    | 5 (1.3)                    | 15 (4.5)                   | .03 <sup>a</sup> |
| >48 hours–1 week                             | 14 (3.6)                   | 13 (3.9)                   |                  |
| Hospitalize, <i>n</i> (%)                    | 144 (36.7)                 | 120 (36.3)                 | .9 <sup>a</sup>  |
| Length of stay in ED (hours) (mean $\pm$ SD) | 2.3 $\pm$ 2.4              | 2.2 $\pm$ 2.2              | .7 <sup>b</sup>  |
| Intubation, <i>n</i> (%)                     | 2 (0.5)                    | 3 (0.9)                    | .7 <sup>c</sup>  |
| Combined negative outcome, <i>n</i> (%)      | 161 (41.1)                 | 142 (42.9)                 | .6 <sup>a</sup>  |
| Death, <i>n</i> (%)                          | 2 (0.5)                    | 1 (0.3)                    | .99 <sup>c</sup> |

<sup>a</sup>By Chi-square test; <sup>b</sup>by *t*-test; <sup>c</sup>by Fisher's exact test.

the treatments most frequently administered. Emergency room readmission within 48 hours was higher during Period B than Period A: 15 (4.6%) compared to 5 (1.3%), *p* = .03. Differences between Periods A and B were not found in any of the other outcome measures (Table 3).

During Period A, ipratropium bromide use predicted readmission to the emergency room within 1 week, odds ratio = 1.8, 95% CI (1.0–3.3); *p* = .05 (not shown). However, in a logistic regression model that controlled for the severity of the asthma attack and for demographic factors (Table 4), ipratropium bromide cessation, denoted

TABLE 4.—Predictors for combined negative outcome (readmission to emergency room, death, intubation, or hospitalization).

| Predictor                  | Reference category | Prevalence (%) <sup>a</sup> | OR   | 95% CI     | <i>p</i> |
|----------------------------|--------------------|-----------------------------|------|------------|----------|
| Male                       | Female             | 49                          | 1.01 | 0.72–1.41  | .97      |
| Age (years)                |                    |                             |      |            |          |
| 31–35                      | 17–30              | 16                          | 2.03 | 1.30–3.16  | .001     |
| Pulse (beats per minute)   |                    |                             |      |            |          |
| 91–119                     | 45–90              | 48                          | 1.94 | 1.31–2.88  | <.0001   |
| >119                       |                    | 20                          | 3.84 | 2.35–6.28  |          |
| Prolonged expirium         | Normal             | 77                          | 6.85 | 4.24–11.07 | <.0001   |
| Use of respiratory muscles | Non                | 10                          | 2.69 | 1.72–4.21  | <.0001   |
| Period B                   | Period A           | 46                          | 0.81 | 0.58–1.14  | .2       |

Notes: Concordance index = 0.75.

In this model, older age, higher pulse rate, prolonged expirium, and use of respiratory muscles were significantly associated with the occurrence of the combined negative outcome.

<sup>a</sup>Prevalence of pulse rate, prolonged expirium, and use of respiratory muscles are after imputation.

by the period variable, did not predict an increase in a combined negative outcome (odds ratio = 0.81, 95% CI 0.58–1.14).

## DISCUSSION

No changes in the combined negative outcome of young adult asthmatic patients were noted following an administrative change in policy to stop ipratropium bromide use in the ED at our medical facility. Using the estimate and 95% confidence limits for the odds ratio for the “period” effect, it seems that the change in policy did not worsen, and perhaps tended to improve the outcome (OR = 0.81), and that the study excludes any worsening greater than a 15% increase in the odds (95% CI: 0.58–1.14). We highlight the fact that this lack of deterioration in clinical outcomes occurred despite the fact that ipratropium bromide was administered to the patients with more severe symptoms during the period that it was available (Period A).

The marked increase in the use of steroids, particularly IV hydrocortisone, that occurred subsequent to the cessation of ipratropium bromide, may provide at least a partial explanation for the lack of change in the combined negative outcome between the two time periods. The fact that IV hydrocortisone is generally administered to patients with more severe asthma exacerbations supports this proposition. Other studies have shown increased steroid use to associate with improved clinical outcomes. The use of inhaled corticosteroids (ICSs) has been suggested to reduce the risk of hospitalization from exacerbation of asthma (9–11) and to decrease the risk of death from asthma (12–14). A study conducted in Israel during the same period as the current study is particularly pertinent. Sales of ICSs were found to increase almost ninefold from the 1980s to the 1990s, parallel to a decrease in asthma mortality rate (15). The most recent publication of the Global Initiative for Asthma (16) recognizes inhaled glucocorticosteroids as the most effective anti-inflammatory medication for the treatment of persistent asthma. Moreover, recently published guidelines of the National Asthma Education and Prevention Program Expert Panel recommend administration of systemic corticosteroids for all patients with moderate to severe exacerbations (6).

It is conceivable that the relatively low use of steroids in the ED, even during the second period of the study (only 61%), may be a cause of the high hospital admission rate following emergency room treatment we observed: 36%, compared to 20% reported by Weber et al. (17). It seems that in the environment of a busy ED, once the decision to hospitalize a patient is made, physicians may tend toward relying on the provision of a definitive treatment in the admitting ward. Alternatively, the high rate of hospital admission in the current study may also reflect better management of mild–moderate asthma attacks by the community health system in Israel, resulting in a higher proportion of severe cases reaching the emergency room. The rate of hospital admissions was similar between the two study periods, likely reflecting similarity in asthma severity in both. Further, this finding suggests that steroids may serve as an effective substitute for the treatment of acute and severe asthma attacks and can safely be used in the absence of ipratropium bromide.

We cannot refute the possibility that factors other than reduced use of ipratropium bromide may have accounted for the increased use in steroids, even between two consecutive years. Of note, during the same period of the current study, an opposing trend occurred in British Columbia. Significantly more patients with asthma discontinued the use of ICSs than those who initiated them, and the use of B agonists increased (18).

The change in policy at our medical facility, occurring prior to publication of the current guidelines (6), provided a quasi-experiment with a relatively controlled setting for investigation of the use of asthmatic medications. The characteristics and outcomes of the patients admitted to the ED due to asthma exacerbation prior and subsequent to the policy change were similar. Also similar were the characteristics and outcomes of the patients who did and did not receive ipratropium bromide during the year prior to the change, except that patients receiving ipratropium bromide as part of their treatment protocol were categorized in our study with a more severe asthmatic condition. This is in accordance with recommendations (2–4) that advocate administration of ipratropium bromide for severe episodes of asthma.

The only outcome measure that worsened after cessation of ipratropium bromide was the number of emergency room readmissions within 48 hours. It is possible that ipratropium bromide might have benefited those readmitted to the emergency room within 48 hours during Period B. Studies demonstrating the benefit of ipratropium bromide for severe cases may support such hypothesis (2–4, 6). However, in the current study, a subgroup analysis comparing severe patients during the first period who received ipratropium to severe patients in the second period who did not receive ipratropium (not shown) did not reveal a difference in combined negative outcome rates. For this analysis, asthma severity was determined by oxygen saturation of  $<90\%$  or, alternatively, by two of the following three criteria: (1) pulse rate greater than 119 beats per minute or breathing rate above 28 per minute, (2) wheezes or prolonged expirium, and (3) rhales.

The proportion of patients presenting with febrile disease was relatively high in both Periods A and B, over 20%, though statistically significant differences were not observed either between the periods or between those treated and not treated with ipratropium bromide. In a subanalysis that excluded all patients with febrile disease upon arrival to the ED (not shown), no change was observed in the prediction model for the combined negative outcome and the periods were still not associated with the outcome, thus refuting the possibility that febrile disease was a confounding variable.

The main limitation of this study is its retrospective design, including the dependency on recorded data, which were not always complete. However, imputation in the statistical analysis provided some compensation for this. Further, there is no apparent reason to expect that any resultant informational bias differed between the two study periods. Our analysis of the periods, not the treatments, prevented the biases that can arise from nonrandomized comparisons of treatments and provided an “intent-to-treat” type of analysis. Moreover, the two study periods were close enough in time to minimize biases due to secular trends in diagnosis or concomitant treatment. We note that while there was no statistically significant difference between the combined adverse outcome rates of the two periods (41% and 43%,  $p = .6$ ), the actual sample size, after applying exclusion criteria, was smaller than expected. Therefore, we cannot rule out type II error.

If, after discharge, a patient was admitted to the ED of another hospital, this would not be included in our data. While this is technically a limitation of the study, the likeliness of its occurrence is low, since patients in Israel are assigned to hospitals according to their residency. Moreover, hospital discharge letters state that patients should return to the ED if their health condition should deteriorate.

We do not have an explanation for the fewer number of acute asthma patients admitted to our emergency medical department during Period B than during Period A. However, the fact that patients in both the periods had the

same demographic and clinical characteristics minimizes the concern for a possible selection bias. Moreover, admission distribution according to months during the study periods did not reveal any outstanding difference between Periods A and B. Reports from the Allergenic Pollen Alert (Tel Aviv University) of the corresponding months and the 3 years preceding the study periods show seasonal variations in the distribution of airborne particles with a general identical pattern from 1 year to the next (19), corresponding to the month-to-month variation in the number of ED admissions of acute asthma attack in both the periods during our study.

A number of retrospective studies of the effectiveness of asthma medications have determined medication use from numbers of prescriptions (14) or from records of pharmacological sales (12, 13, 15). While the patient self-report in the current study, as recorded in the ED medical chart, may better reflect actual use of medication, the dichotomous category of use and nonuse does not account for the length and the consistency of the use. Describing medication use on a continuum is important for expressing patterns of use and adherence, particularly for asthma medications (20), whose effect may only become apparent some time after initiation or discontinuation. Relevant to this study, clinical deterioration of asthma may occur as long as weeks or months following discontinuation of ICSs (16). Nevertheless, the current study relates to immediate treatment and its short-term clinical implications.

The decision to stop purchasing ipratropium bromide for use in our ED was an administrative one, based on clinical experience, cost containment and the notion that no harm is expected. The consequences of this decision, including patient safety, were only evaluated subsequent to the action. This study was designed under that constraint, yet with full intention of using all available data and full collaboration with the ED staff. In that respect, this quasi-experiment represents “real-life” circumstances in which, in the pressured environment of an ED, administrative decisions with clinical implications are made without well-based scientific evidence, yet under the belief that safety is preserved. Emerging evidence regarding possible adverse outcomes of the use of ipratropium bromide for COPD patients and increased risk for cardiovascular events, as recently published, should also be considered (5).

In the United States alone, 16.4 million adults, comprising 7.3% of the population over age 18, currently suffer from asthma (21). Judicious use of therapeutic means is mandatory and obligates the primary caregiver in the ED both toward the patient and the sponsor, that is, the hospital management.

## CONCLUSIONS

By demonstrating no notable increase of adverse clinical consequences, this retrospective study provides clinical support for an administrative decision to stop the purchase of ipratropium bromide for the treatment of acute asthma

patients in an ED. Our study provides evidence that steroids can be a safe substitute for ipratropium bromide. In light of the lower costs of steroid treatment, this observation warrants further investigation.

#### DECLARATION OF INTERESTS

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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