



# A Single Dose of Dexamethasone To Prevent Postbronchoscopy Fever in Children\*

## A Randomized Placebo-Controlled Trial

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**Study objective:** To assess the effectiveness of one dose of dexamethasone (0.5 mg/kg; maximum, 10 mg) to prevent fever after bronchoscopy with BAL.

**Design:** Randomized, placebo-controlled study.

**Patients:** Immunocompetent nonfebrile children undergoing fiberoptic bronchoscopy with BAL.

**Measurements and results:** Sixty-nine children were included in the study. Thirty-eight children received saline solution, and 31 children received dexamethasone. The two groups were similar regarding the number of children < 2 years old, the percentage of abnormal bronchoscopic findings, the number of positive BAL culture findings, and the index of lipid-laden macrophages. Twenty-six children (68%) in the saline solution group (SG) had fever, compared to 3 children (9.6%) in the dexamethasone group (DG) [ $p < 0.001$ ]. Fever after the procedure appeared later ( $12.3 \pm 5.5$  h) in the DG compared to  $5.4 \pm 2.7$  h in the SG.

**Conclusions:** One dose of dexamethasone administered prior to performing bronchoscopy with BAL may prevent fever subsequent to the procedure. Further studies are necessary in order to determine the optimal dosing regimen for dexamethasone when used for this purpose.

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**Key words:** fever; fiberbronchoscopy in children; lavage; steroids

**Abbreviations:** BALF = BAL fluid; DG = dexamethasone group; FB = fiberoptic bronchoscopy; IL = interleukin; LLM = lipid-laden macrophages; SG = saline-solution group; TNF = tumor necrosis factor

Fiberoptic bronchoscopy (FB) is a useful procedure to diagnose pulmonary diseases in childhood.<sup>1</sup> The procedure is regarded as safe; however,

rare serious complications such as arrhythmia, bleeding, transient hypoxemia, and bronchospasm have been reported.<sup>2,3</sup> By contrast, transient fever in the hours following bronchoscopy is frequently noted, mainly when the procedure is performed with BAL. The fever, abrupt in onset, is usually accompanied by rigors and malaise, and responds to antipyretics.<sup>4</sup> The incidence of postbronchoscopy fever varies according to different reports.<sup>5</sup> We have reported in a prospective study<sup>6</sup> an incidence of 48% in children undergoing FB with BAL. It has been shown that the transient fever is not due to bacteremia,<sup>7</sup> although bacteremia and sepsis after FB with BAL may occur among immunodeficient patients.<sup>8–10</sup> Consequently, prophylactic antibiotics are not routinely recommended for the procedure. Several studies<sup>11</sup> have demonstrated that the fever following bronchoscopy

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and BAL is related to the release of cytokines into the bloodstream by the alveolar cells. Prevention of this uncomfortable side effect, which usually warrants medical evaluation and laboratory investigations, and which may also alarm parents and caretakers, would be beneficial.

Steroids are known to decrease the release of cytokines from T-lymphocytes.<sup>12</sup> The aim of our study was to examine prospectively the effect of one dose of corticosteroid administered prior to performing bronchoscopy and BAL on the incidence of fever following the procedure.

## MATERIALS AND METHODS

The study population included all children who underwent FB and BAL in the Shaare Zedek Medical Center from 2001 to 2003. Exclusion criteria were immunocompromised state, and concurrent treatment with steroids and fever  $> 38^{\circ}\text{C}$  at the time of bronchoscopy. The study received the approval of the internal review board, and informed consent was obtained from the parents of each patient enrolled in the study. Children were randomized to receive either IV dexamethasone (0.5 mg/kg; maximum, 10 mg) or normal saline solution immediately prior to the procedure in a double-blind fashion. The solutions were prepared and administered to the patients on an alternating basis by the bronchoscopy nurse. The attending physicians were blinded to the group assignment. This dose of dexamethasone was chosen because it is similar to that used for prevention of postextubation airway obstruction.<sup>13</sup> All procedures were performed with a bronchoscope (model BF-3C20, or BF-P200 for the older patients; Olympus; Tokyo, Japan). Sedation was achieved with midazolam (0.1 to 0.2 mg/kg) and propofol (1 to 3 mg/kg) administered IV. After local lubrication of the nostrils with lignocaine HCl 2% ointment, the bronchoscope was inserted through the nasal passages and advanced through the vocal cords into the tracheobronchial tree. Lidocaine 1% was atomized as needed for topical anesthesia through the channel of the bronchoscope at a maximum dose of 7 mg/kg. BAL was usually performed in the right lower lobe except in cases with localized pathology elsewhere. Three aliquots of 1 mL/kg of 0.9% sterile saline solution were instilled through the working channel after wedging the bronchus. Fluid was recovered by manual suction through a sterile specimen trap. All BAL fluid (BALF) specimens were tested in our microbiology laboratory for quantitative bacterial culture. In accordance with previous studies,<sup>14</sup> we considered the BALF culture finding positive if there was growth of one bacterium at a concentration  $> 10^4$  cfu/mL. BALF was also analyzed for lipid-laden macrophages (LLM) scoring to rule out pulmonary aspiration. For the scoring of LLM, the specimens were stained with oil red O, and an index as described by Colombo and Hallberg<sup>15</sup> was assigned. An index  $> 90$  was considered positive. After the procedure, the patients were monitored in the bronchoscopy unit by a nurse for a minimum of 4 h before discharge. An oral or rectal temperature during this time period  $> 38^{\circ}\text{C}$  was considered fever.

Blood culture specimens were obtained in all children with a temperature  $> 38^{\circ}\text{C}$ . All parents were instructed to monitor the body temperature during the 24 h following discharge by assessing for tactile fever which, if suspected, was to be confirmed by oral or rectal temperature measurement. Parents were advised to bring the child to the emergency department if fever occurred. After 24 h, one of the researchers contacted the family in order

to ascertain that all episodes of fever were indeed reported, and to inquire if any other side effects were noted.

## Statistical Analysis

We expected fever to develop in approximately 52.5% of patients undergoing BAL who received saline solution,<sup>6</sup> and in approximately 15% of those who received dexamethasone. In order to achieve statistical significance at  $p < 0.05$  and power  $\geq 90\%$ , the calculated study size was 36 patients in each group. We applied the *t* test (nonpaired, two tailed) and  $\chi^2$  test (Fisher Exact Test when applicable) for continuous and categorical variables as appropriate. Comparison of time (hours) until onset of fever was performed by the Wilcoxon signed-rank test. Significant *p* value was set at 0.05.

## RESULTS

During the study period, 178 children underwent FB in our unit and 69 of them were enrolled in our study. Reasons for exclusion were FB without BAL, fever at the time of FB, or refusal to participate in the study. All pertinent patient data are summarized in Tables 1, 2. Thirty-eight children received saline solution, and 31 children received dexamethasone. The male/female ratios of the two groups were similar: 22 children (58%) in the saline solution group (SG) and 19 children (61%) in the dexamethasone group (DG) were male ( $p = 0.81$ ). The average age ( $\pm$  SD) in the SG was  $5.43 \pm 5.3$  years, slightly older than in the DG ( $3.1 \pm 2.9$  years) [ $p = 0.023$ ]. The median age was similar in both groups: 3.28 years in the SG vs 2.22 in the DG ( $p > 0.05$ ). The number of children  $< 2$  years old did not differ between the two groups (SG,  $n = 12$  vs DG,  $n = 13$ ;  $p = 0.37$ ). Thirteen patients in the SG group (34%) had a chronic disease, comparable to the 10 patients (47%) in the DG ( $p = 0.86$ ) [Table 2]. Indications for FB in the SG were stridor and noisy breathing ( $n = 13$ ), BAL for microbiology and pathology ( $n = 9$ ), persistent pulmonary infiltrate ( $n = 8$ ), persistent wheezing ( $n = 4$ ), recurrent pneumonia ( $n = 3$ ), and cyanotic spells ( $n = 1$ ). In-

**Table 1—Comparison Between Patients in the SG and DG\***

Variables	SG	DG	<i>p</i> Value
Patients, No.	38	31	
Male/female gender, No.	22/16	19/12	0.81
Age, yr	$5.43 \pm 5.3$	$3.1 \pm 2.9$	0.04
Patients $< 2$ yr old, No.	12	13	0.37
Abnormal bronchoscopy findings, %	74	61	0.31
Positive culture findings, %	68	45	0.15
Index of LLM	40	28	0.55
Fever, %	68	9.6	$< 0.001$

\*Data are presented as mean  $\pm$  SD unless otherwise indicated.

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