Assessment of bronchodilator reversibility in asthmatic children

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Abstract

Aim: To assess the relationship between clinical control of asthma, forced expiratory volume in one second (FEV1) and bronchodilator reversibility in asthmatic children.
Methods: 69 asthmatic children were evaluated during their periodic controls at the University Hospital Centre "Mother Teresa" in Tirana, Albania. We selected the patients clinically stable during the last 4-6 weeks. Patients were classified into two groups: controller naive and controller therapy. All the children underwent assessment of FEV1 by means of spirometry and post bronchodilator spirometry 15 minutes after administrating 400mcgram Salbutamol. Bronchodilator reversibility (BDR) was considered positive in cases when FEV1 $\geq$ 9%.
Results: 61% of the patients belonged to the group controller naive, meanwhile 39% of the patients were on controller medication. All the patients on controller therapy and 97.1% in the controller naive group had normal FEV1. Only 2.9% of controller naive patients had FEV1 $\leq$ 80%. The controller naive group had positive BDR in 60.7% of cases, it had negative in 32.1%, and 3.5% had broncho-constriction from short acting beta agonist (SABA). The controller medication group had positive BDR in 33.3% of cases, negative in 55.5% and 5.5% had broncho-constriction from SABA.
Conclusion: BDR compares pulmonary function before and after administering short acting β2- agonists. BDR can help asthma follow-up and can guide changes in therapy. The children with uncontrolled asthma can be identified by BDR. If BDR is not performed regularly, a lot of useful information about asthma control is lost.

Key words: asthma, BDR, FEV1, SABA.

Introduction

Spirometry is currently considered essential for asthma diagnosis follow-up and monitoring asthma control in children ≥5 years (1). In spite of these recommendations, a US national survey of primary care providers reported that only 21% use spirometry routinely (2). One reason may be that the specific guideline which defined spirometric measures used to classify asthma severity and to control the forced expiratory volume in one second (FEV1), generally correlates poorly with asthma severity in children (3,4).

The bronchodilator response (BDR), as a physiological response, has traditionally been used to define the presence of asthma (1). It is very useful for the diagnosis of asthma (5). More recently, the BDR has been shown to reflect biomarkers of eosinophilic inflammation, such as NO (6-8), bronchial (9) and sputum (10) eosinophilia, as well as being associated with atopy (11) and bronchial hyper-reactivity (12). The BDR has also been reported to be a good predictor of responsiveness to inhaled corticosteroids (ICS) (13,14), or long-term prognosis (11,13). Hence, BDR is a valuable tool for the first diagnosis of asthma and also for its follow-up (15-17).

Our hypothesis was that the BDR, which may reflect both physiological and inflammatory biomarkers, is more sensitive than FEV1 in asthma monitoring. Since most asthmatic children have normal pre-bronchodilator spirometry regardless of severity classification (4), the purpose of our study was to identify a useful tool for monitoring asthma control in children with normal pre-bronchodilator spirometry.

Methods

We studied 69 children suffering from asthma. The children were evaluated in their routine follow-ups. The selection of the patients was based upon the following criteria:

Inclusion criteria:

1. They attended our tertiary-care asthma service (University Hospital Centre "Mother Teresa", Tirana, Albania) for the routine evaluation of asthma;
2. Were able to cooperate: all participants were required to demonstrate the ability to perform reproducible lung function tests (FEV1 and FVC within 5% reproducibly);
3. The patients were clinically stable during the last 4-6 weeks, without signs of viral infections;
4. During the check up the patients must be asymptomatic: clinically stable and normal breath sounds.

Exclusion criteria:

1. Patients were excluded if they had an asthma exacerbation in the past month;
2. The patients had taken short acting beta agonist (SABA) in the past six hours, and long acting beta agonist (LABA) in the past 12 hours.

Patients were classified into two groups: controller naive during 4-6 weeks and on controller therapy. All the children performed baseline spirometry according to the American Thoracic Society standards. Subsequently, we applied 400 mcg Salbutamol with MDI and aero chamber. Spirometry was repeated after 15 minutes in order to assess the reversibility (BDR). Reversibility was calculated according to the following formula: BDR= FEV1(l post-BD) – FEV1(l pre-BD)/ FEV1 (l pre-BD) X 100%; it was considered positive if FEV1 ≥ 9% (18,19).

The study was approved by the Albanian Committee of Biomedical Ethics.

Results

In this study, there were included 69 patients. About 61% were controller naive and 39% were on controller medication. All the patients of the group on controller medication had normal FEV1(≥ 80%). The group on controller naive: 97.1% had FEV1 ≥ 80% (normal), whereas only 2.7% had FEV1 ≤ 80% (Figure 1).

The results of bronchodilator reversibility (BDR):

- In the controller naive group: 60.7% of the patients had positive BDR, 32.1% had negative BDR and 3.5% reacted with broncho-constriction (Figure 2).
- In the controller medication group: 33.3% of the patients had positive BDR, 55.5% had negative BDR, and 5.5% reacted with broncho-constriction (Figure 2).

Figure 1. FEV1 and asthma control

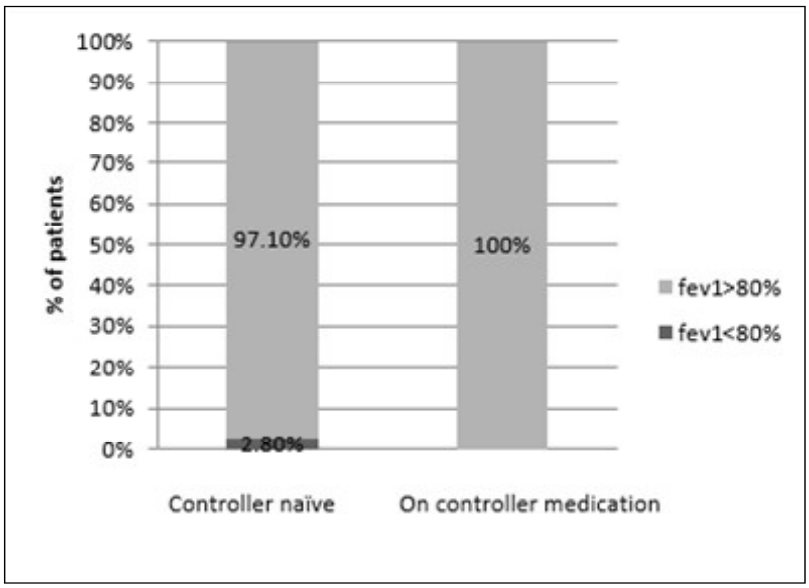
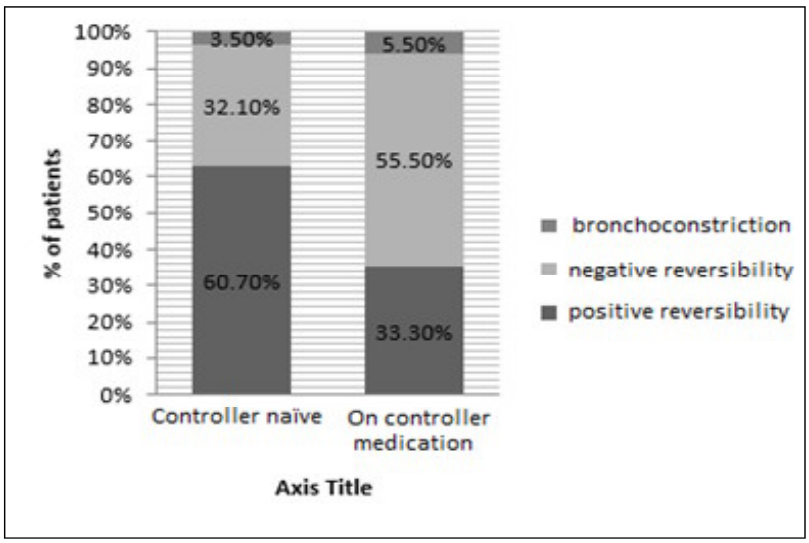


Figure 2. Bronchodilator reversibility



Discussion

Spirometry is the only objective in-office clinical tool the physician has, especially when the child is asymptomatic and the physical examination is normal. Unfortunately, pre-bronchodilator spriro-metry is usually in the normal range regardless of asthma severity (4). In our study, all the patients were on controller therapy and 97.1% of the patients in the controller naive group had normal FEV1. Only 2.9% of the patients in the controller naive group had FEV1 $\leq$ 80%.

In our study, differently from spirometry, BDR resulted at a dynamic parameter (6,20). In our study population with normal spirometry, up to 47% of the patients showed positive BDR, which provides evidence of poor control. BDR resulted positive in 60.7% of the controller naive and 33.3% of the group on controller medication. These patients merit to reevaluate their therapeutically scheme. In this situation, the clinician could miss potentially critical information regarding bronchial lability, which can

also associate poor asthma control if the BDR is not preformed (16).

BDR resulted negative in 32% of controller naïve patients, which means that their asthma was well-controlled. There were 55% of the patients in the group on controller medication who had negative BDR, which means reduction of the inflammation because of controller medication.

Broncho-constriction following bronchodilator is an adverse effect of SABA, and it may menace the life. There are several hypotheses trying to explain this paradoxical effect. Racemic albuterol has been shown to cause paradoxical broncho-constriction. Albuterol is a combination of 50:50 of (R) and (S) stereoisomer (21). (S) Stereoisomer has constrictive effects, meanwhile (R) stereoisomer has a greater affinity for the β-receptor and less sympathetic irritation than raceme form (22,23). Also, the other components (benzalconium, chlorofluorocarbonetc) may induce bronchospasms (24).

In the case of bronchospasms induced from the medication, the use of this medication should be stopped and alternative medications should be sought (25).

Even though the presence of broncho-constriction in our study was low (2.8%), the possibility of serious life consequences made it clinically relevant.

Conclusion

Our results support the hypothesis that BDR is more sensitive than FEV1 for monitoring asthma control. In a group of patients clinically stable and with normal spirometry, BDR can act as an earlier detector of lost asthma control and may guide important changes in therapy.

Conflicts of interest: None declared.

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