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Research Article

Outpatient Asthma Management without Rescue Bronchodilators?

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Abstract

Background: Overreliance on Short Acting Beta2 Agonists (SABA) is associated with increased risk of death from asthma in a dose-response fashion.

Objective: We wonder if there any subpopulation of asthmatic individuals that live without SABA. To face this possibility, we studied the rescue strategy of individuals that consecutively came for a first outpatient visit.

Methods: Individuals that did not have SABA for use as rescue medication in the last three months constituted the "NO SABA group"; and those who used SABA at least once in the last 3 months: "SABA group". They completed the Asthma Control Test (ACT) and performed spirometry.

Results: "SABA group" aged 38.82±15.13 yrs (n=65, 26 males) used inhaled salbutamol MDI as rescue therapy. The NO SABA group" (n=21, 8 males; mean (SD) aged 39.91±17.77 yrs) used for symptoms relief as follows: salmeterol/fluticasone (n=5), formoterol/budesonide (n=3); salbutamol/become thasone (n=2); budesonide (n=8); intramuscular dexamethasone (n=1); nebulized normal saline solution (n=1); and one individual did nothing. NO SABA group showed statistically significant better ACT (median= 18 vs SABA=11; p=0.0056, Mann Whitney test). NO SABA group had higher number of individuals under regular ICS (10/21 vs 21/65; p=0.0418; Fisher's exact test); and with higher doses (mean: 221.23 micrograms [95%CI: 59-384]; vs SABA group: 123.9 [95% CI: 63-184]; p=0.0318). Also, the number of individuals with poorly controlled asthma was lower in the NO SABA group.

Conclusion: We observed that asthmatic individuals could live at least 3 months without SABAs and with better outcomes. Increased preventer adherence could be a cause or a consequence.

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Introduction

Substantial progress was made against key outcomes such as asthma hospital admissions and mortality in the 1990s and early 2000s, but little improvement has been observed in the past 10 years, despite escalating treatment costs [1]. In 2015, 0.40 million people (95% UI 0.36 million to 0.44 million) died from asthma [2]. Overuse on short acting beta2 agonists (SABA) is associated with increased risk of death from asthma in a dose–response fashion [3]. SABA became a key agent for asthmatic individuals but fail to treat the underlying pathogenesis, namely the airway inflammation. This overreliance link between asthmatic individuals and SABA could be a modifiable cause of the observed plateau in mortality from asthma in the last decade and the poor adherence to the controller anti-inflammatory treatment [4]. Furthermore, SABA might not be considered as a treatment for asthma. We eradicated SABA in daily practice for the population under our service. We want to know if there any subpopulation of asthmatic individuals that live without SABA before entry into our asthma department. To face this possibility, we studied the rescue strategy of patients that consecutively came for a first outpatient visit.

Patients and Methods

During the period from March 10, 2017 to January 16, 2018 we described the rescue strategy in all new asthmatic individuals that came for a first visit to the outpatient pulmonary department. In this observational, non-intervention study, we divided the enrolled individuals according to SABA use. Individuals that did not have SABA for use as rescue medication in the last three months constituted the "NO SABA group"; and those who used SABA at least once in the last 3 months="SABA group". Individuals aged ≥16 years were entered in the study if they had a diagnosis of asthma, based on a history of episodic dyspnoea and wheezing, and/or documented bronchodilator reversibility in forced expiratory volume in 1 s (FEV_1) of 12% and 200 ml; to be non- or ex-smoker of less than 10 pack-yr, to be neither pregnant nor breast-feeding and to be capable of completing Asthma Control Test (ACT) and to perform spirometry [5-7]. After giving the informed consent, all the participants described what they did to relief asthma symptoms and whether they recognized the difference between relief and maintenance therapy. Then, individuals completed the ACT (scores <16: very poorly controlled; 16-19: not well-controlled; 20-25: well-controlled asthma). Finally, participants performed spirometry pre and 15 minutes post 200-400 micrograms of PMDI salbutamol with a daily calibrated MedGraphic spirometer [8].The sample size had a power of 90 and alpha two sided of 0.05 to detect a difference in ACT of 4. For non-normal distribution data, the Mann Whitney test was used and Fisher's exact test for comparison of categorical variables. Graphpad/Prism 7 was used as statistical software. This study was approved by the Hospital teaching and research committee. The protocol was registered at Clinical Trials Gov under the number=NCT03498742.

Result

Eighty six consecutive individuals visiting the outpatient pulmonary department were included in the description. Eleven individuals were excluded because they did not complete the ACT score and

twenty three because of lack of ATS/ERS statements accomplishment for spirometry [8]. General characteristics and main results were shown in table 1. We found 21 individuals that did not have SABA and hence they did not use it at all in the last 3 months before the visit (group=NO SABA) and 65 individuals that used SABA. Only 2 individuals of NO SABA group and 4 in the SABA group knew the difference between maintenance and relief therapy (p=0.63, Fisher exact test). For symptoms relief NO SABA group used extradoses of the maintenance treatment of combined salmeterol/fluticasone (n=5), formoterol/budesonide (n=3); Salbutamol/beclomethasone (n=2); budesonide (n=8); intramuscular dexamethasone (n=1); nebulized normal saline solution (n=1); and one individual did nothing. NO SABA group showed significantly better ACT, higher number of individuals under regular ICS; and with higher doses (Figure 1). Also, the number of individuals with poorly controlled asthma was lower in the NO SABA group (Table 1). These findings did not change after deleting question 4 in ACT.

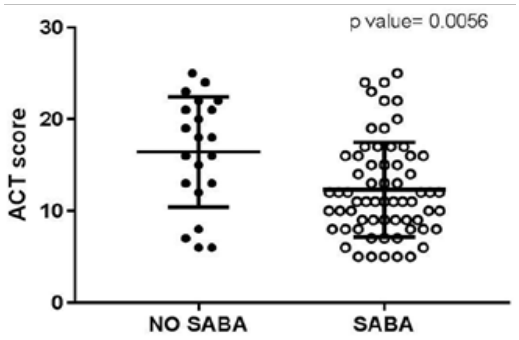

Figure 1: Graphical representation.

Variables	No SABA n=21	SABA n= 65	p
Age Yrs mean ± SD	39.91±17.77	38.82±15.13	0.78 NS*
Male/Female	8/16	26/39	0.574 NS#
History of asthma (yrs mean ± SD)	26.78±20.11	25.52±15.67	0.81 NS*
Reason for visit Not due to asthma (n)	8	20	0.6 NS#
ACT mean ± SD	15.70±6.80	12.32±5.27	0.0056*
FEV1% predicted	78.94±20.01	75.20±17.65	0.3676 NS*
Percent FEV1 Change post bronchodilator	9.69±10.63	15.83±14.46	0.088 NS*
Hospital/E Room visit 12 m (n)	4	22	0.5 NS#
Subjects with regular ICS (n)	10	21	0.0418#
ICS dose microgr Mean (95%CI)	221.23 (59-384)	123.9 (63-184)	0.0318*
Poorly controlled asthma (ACT<16)	8/16	48/17	0.0041#
Daily maximum of rescue medication mean (95%CI)	1.27 (0.45-2.1)	12.32 (6.37-18.27)	<0.0001*

Table 1: General characteristics and main differences between the group of subjects that did not use SABA as rescue medication and the control group of subjects that did use SABA. Daily maximum rescue medication for NO SABA group signified others agents than SABA; generally preventer therapy.

Discussion

We observed that asthmatic individuals that did not have SABA for use as rescue medication showed significant better Asthma Control Test, significant better preventer adherence, and significant higher ICS daily dose. It could speculate that SABA worked as a distraction factor for preventer adherence. Overreliance on SABA and poor adherence to preventer therapy could be both faces of the same coin. But what occurred first? Higher ICS dose and better adherence could clearly explain the difference in ACT that we found in NO SABA group. Possibly, SABA overreliance interfered with ICS adherence in this observational study. We notified to all the individuals when responding ACT question 4 (During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication?) to think not only on SABA but also to include what they had done for relieving asthma symptoms. We did not find any difference in demographic or asthma severity. Both groups had similar FEV_1% predicted, similar prior rate of asthma exacerbations, and no difference in reason for the consultation (Table 1).

Overreliance on SABA and relief behavior became an upward spiral of SABA consumption that was associated with increased risk of asthma death; and furthermore, it conspired to the pathogenic essence of asthma treatment; namely anti-inflammatory therapy and its adherence. Indeed, first step in asthma recommendations should not keep blank [9]. The strategy of Combined ICS/formoterol as needed for GINA step 3 to 5 is not widely accepted [5].

As observational design, this study had several limitations. Firstly, investigators implemented a "SABA free asthma management" [10]. The second bias is that as one of the questions of ACT was rescue therapy, the NO SABA group had lower use even when we explained to the individuals that their response should include all the agents used to relief symptoms. Anyway, the exclusion from the ACT of the item 4 did not change the results at all. The high rate of drop outs for a first outpatient visit and the low percentage of well controlled individuals constituted a faithful measure of how far away were GINA recommendations from daily practice.

Conclusion

In conclusion, we observed that asthmatic individuals could live 3 months without SABAs and they had better asthma control. Overreliance in SABA might interfere with preventer adherence.

Authors Contribution

The conception and interpretation of the manuscript was done by Luis Javier Nannini and important intellectual share by Nadia S Neumayer and Octavio M Fernández. The four authors participated actively with protocol procedures.

Conflict of Interest

Luis Javier Nannini received fees as speaker and advisory board for AstraZeneca, Argentina SA and Novartis Argentina SA. Nadia S Neumayer, Octavio M Fernández and Daniela M Flores had no conflict of interest to declare.

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