RETROSPECTIVE ANALYSIS OF IMPACT OF SMOKING ON THE TREATMENT RESPONSE TO INHALED CORTICOSTEROIDS AMONG PATIENTS WITH ASTHMA

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Abstract:

Objective: Asthma is commonly found in both, the developed and the developing world. Among the patients presenting to the emergency medical care settings, patients with acute exacerbation of asthma occupy a significant percentage. This study hopes to assess the impact of smoking on treatment response to inhaled corticosteroids among patients with asthma.

Methodology: This retrospective analysis was conducted upon a sample of 200 patients presenting at the department of general medicine and chest medicine at Liaquat University Hospital, Jamshoro with acute exacerbation of asthma (despite being on regular medication) from September 2017 to January 2018 after taking verbal informed consent. Inquiries were made regarding the habit of smoking, the treatment regimen and history of approaching an emergency healthcare setup due to acute exacerbation of asthma and mean hospital stay. In addition to the above, sputum samples were taken for investigating the sputum eosinophil level.

Results: Among the study subjects, 70% of the sample comprised of males, while the remaining 30% were females. The mean age of the study population was 31 years, with 62% of the total subjects i.e. 124 patients admitting to be regular smokers (at least a cigarette per day). The mean frequency of emergency hospital visits were higher among smokers than non-smokers. The mean sputum eosinophil proportion among smokers was 0.6% while the mean sputum eosinophil proportion among non-smokers was 3.4%.

Conclusion: After careful consideration, the obtained results show that the treatment response among non-smokers was markedly better than the treatment response observed in smokers. Thus asthma patients should be counselled against the use of cigarettes.

Keywords: Smoking, Cigarette, Asthma, Eosinophilia, Sputum, Treatment Response.

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INTRODUCTION:
Inhaled corticosteroids are the most effective treatment currently available for chronic asthma. [1] Patients with mild to severe asthma respond to inhaled corticosteroids as assessed by improved asthma symptoms and lung function as well as reduced bronchial hyper-reactivity and eosinophilic inflammation. [2–4]

Both national and international asthma guidelines emphasize the importance of the early introduction of inhaled corticosteroids as first line treatment for those with mild disease. [5, 6] A very small percentage of patients with asthma have been identified who do not benefit from corticosteroid treatment. [7] The mechanisms of steroid resistance in these individuals are poorly understood but are thought to include abnormalities in glucocorticoid receptor function, corticosteroid pharmacokinetics, or transcription factor protein activity. [7]

Clinical studies in asthma have concentrated on non-smokers, but cigarette smoking is common with about 20% of asthmatics being regular smokers. [8, 9] There is evidence for increased morbidity and mortality from asthma in individuals who are cigarette smokers. [9–12] Asthmatic patients who smoke have been reported to have more severe asthma symptoms than non-smoking asthmatics, [9, 11] an accelerated decline in lung function over time, [10] increased hospital based care, [13] and increased mortality following admission to hospital with an episode of near fatal asthma. [12]

There is comparatively little direct information about the effect of active smoking on drug treatment in asthma. In an uncontrolled study it was reported that improvements in airway function and plasma inflammatory markers in response to inhaled corticosteroid treatment might be attenuated in asthmatic smokers compared with asthmatic non-smokers. [14]

We have examined the effects of active cigarette smoking on the efficacy of inhaled corticosteroid treatment in subjects with asthma. To our knowledge, this is the first retrospective study, assessing the treatment response in this sort, for this issue.

METHODOLOGY:
This retrospective analysis was conducted upon a sample of 200 patients presenting at the department of general medicine and chest medicine at Liaquat University Hospital, Jamshoro with acute exacerbation of asthma (despite being on regular medication) from September 2017 to January 2018 after taking verbal informed consent. Inquiries were made regarding the habit of smoking, the treatment regimen and history of approaching an emergency healthcare setup due to acute exacerbation of asthma and mean hospital stay. In addition to the above, sputum samples were taken for investigating the sputum eosinophil level. Sputum induction is not always successful and thus only the subjects whose sputum was successfully induced (in quantities ample for investigation to be carried out), were included in the sample.

RESULTS:
Among the study subjects, 70% of the sample comprised of males, while the remaining 30% were females.

The mean age of the study population was 31 years, with 62% of the total subjects i.e. 124 patients admitting to be regular smokers (at least a cigarette per day).
The mean frequencies of emergency hospital visits were higher among smokers than non-smokers.

The mean hospital stay among smokers was higher than the mean hospital stay for non-smokers, owing to asthma exacerbation. The mean sputum eosinophil proportion among smokers was 0.6% while the mean sputum eosinophil proportion among non-smokers was 3.4%.
DISCUSSION:
We have demonstrated that smoking status has a significant effect on the response to inhaled corticosteroid treatment in patients with mild asthma. Non-smoking asthmatics experienced less adverse effects and paid less frequent visits to an emergency setting, while spending a lesser mean time at the hospital than smokers. The sputum eosinophil proportions for non-smokers yielded more promising results than the eosinophil proportions for smokers.

Although cigarette smoking is the major identifiable factor in the development of COPD, we do not believe that the smoking asthmatic group in this study represents a group of subjects with COPD. It is important to note that sputum eosinophilia is a valuable means of monitoring the control of asthma [15, 16]; however, it is not the perfect diagnostic test for asthma and sputum eosinophilia is not a universal finding even in exacerbations. [17] Thus arrays of other criteria were involved in our study, as mentioned earlier.

Pedersen et al [14] studied the responses to inhaled budesonide in asthma in a longer term study and found improvements in FEV1 and blood markers of inflammation which were not observed in a subgroup of smokers. The study was not placebo controlled, airway inflammation was not assessed directly, and the subgroup of asthmatic smokers studied had more severe airflow limitation than in the current study both before and after treatment.

Our results are consistent with the findings of Pedersen’s study, with additional direct information on history of emergency visits and mean hospital stay. The asthmatic patients in our study had mild asthma and had relatively low cigarette exposure, suggesting that the lack of effect of inhaled corticosteroids in smokers does not depend primarily on the severity of asthma or the extent of cigarette exposure.

The mechanism behind the lack of response to inhaled corticosteroids in smoking asthmatics is not known. Cigarette smoke has the potential to cause harm to the airways in a number of ways, including direct toxicity and pro-inflammatory activity. Cigarette dose dependent inflammatory responses are observed in the airways of healthy adults [18] and smokers exhibit altered airway cytokine regulation. [19] Other mechanisms by which cigarette smoking might prevent the anti-inflammatory actions of steroids include differences in drug access or clearance from the lungs due to increased mucus secretion or airway permeability. Alternatively, cigarette smoking might alter the molecular mode of action of steroids.

CONCLUSION:
After careful consideration, the obtained results show that the treatment response among non-smokers was markedly better than the treatment response observed in smokers. Thus asthma patients should be counselled against the use of cigarettes because cigarette smoking impairs responsiveness to inhaled corticosteroids in patients with asthma, and that studies assessing treatment in asthma should take smoking status into account in their conclusions about efficacy. The findings may have important clinical implications for asthmatic patients who smoke and further reinforce the need for smoking cessation in asthma, even in patients with mild disease.
REFERENCES: