

FOCUS ON RESEARCH

ROLE OF ENVIRONMENTAL FACTORS (SMOKING AND ALLERGEN EXPOSURE) IN STEROID RESISTANCE IN ASTHMA

Researchers

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Aim

1. To examine the influence of active smoking and allergen exposure on steroid resistance in asthma
2. To study the mechanisms of steroid resistance in asthma

Project Outline/Methodology

Various different tests of steroid sensitivity, mechanistic studies, and assessments of asthma control and airway inflammation were undertaken in the following subject groups:

1. Steroid sensitivity in asthmatic and non-asthmatic smokers and non-smokers

Subjects with asthma (smokers and non-smokers) were recruited from our hospital outpatient clinic. Normal volunteers (smokers and non-smokers) acted as controls. The asthmatic patients received a 2-week course of prednisolone 40mg daily to assess airway steroid sensitivity.

2. Seasonal allergen exposure on steroid sensitivity

Steroid sensitivity was assessed at 3 separate time points in a group of grass pollen-sensitive subjects: prior to the grass pollen season, during the peak of grass pollen season, and 6 to 8 wk after the grass pollen season.

Key Results

Smokers with asthma show a reduced response to a course of oral steroid tablets compared with non-smokers. The skin of smokers with asthma show a reduced response to steroids placed on the skin suggesting that smoking may not only affect the airway response to steroids in asthmatics but may also make other tissues of the body resistant to the effect of steroids. Different mechanisms have been implicated in the development of this reduced response. Different forms of the steroid receptor exist (isoforms) and a change in the numbers or ratio of the different receptors have been suggested as a cause of steroid resistance. We have shown for the first time that smokers have a reduction in the ratio of active steroid receptor (alpha) to the inactive receptor (beta) in peripheral blood cells and this may result in the reduced response of smokers to steroids.

It has been difficult to show any effect of seasonal allergen exposure on the various tests of steroid sensitivity.

Conclusions

Smokers with asthma respond less well to steroids than non-smokers. This may be a systemic effect and not only related to the airways. Various different mechanisms may be involved, but an alteration in the ratio of steroid receptor isoforms may be implicated.

What does this study add to the field?

Our research group has previously shown that smokers with asthma are resistant to the effect of both inhaled and oral corticosteroids. We have highlighted that this may be a systemic effect and not only an effect on the airways. We have shown that smoking alters the ratio of steroid receptor isoforms and this may be a mechanism behind the development of steroid resistance.

Implications for Practice or Policy

Asthma is a common condition and still has a high morbidity and mortality. Asthmatic smokers are known to have poorer asthma control but still up to 30% of asthmatics smoke. Given that we have shown that the effects of smoking are not only related to the airways, this may have implications for other chronic inflammatory conditions where steroids are used. Smoking cessation is of the utmost importance. Alternative or additional therapies to inhaled corticosteroids are needed for individuals with asthma who are unable to quit smoking

Where to next?

Further work looking at the mechanisms behind the reduced response to steroids in smokers with asthma is required. It is not known what happens to the response to steroids when people stop smoking and this would obviously be an important follow on to this study.

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