

Drugs Used in Respiratory Conditions.

Abstract

In this article in the series of 'bite sized' pharmacology, we will look at the pharmacological actions of drugs used in respiratory conditions. This article will illustrate the common therapeutic interventions in asthma and chronic obstructive pulmonary disease (COPD) and then go on to examine the main types of drug used in these interventions and their pharmacodynamic actions.

Exercises will be provided to help you apply this knowledge to your prescribing practice.

Respiratory Conditions

Respiratory conditions are a common area of prescribing due to their prevalence and the fact that they are often long term chronic conditions that once diagnosed need prescribed for the rest of the patient's life. Respiratory conditions can be classified as seen in table 1. This article will focus on the restrictive respiratory conditions of asthma and the obstructive condition COPD.

The primary goal of drug therapy in respiratory conditions is to improve lung function and reduce the clinical symptoms associated with the underlying condition. Improving lung function along with long term condition management can dramatically improve the clinical symptoms.

The primary function of the lung is gas exchange. It takes oxygen from the air and allows its passage into the blood stream where it can be taken up by the haemoglobin of the red blood cells whilst at the same time allowing the carbon dioxide to pass back into the exhaled air.

Lung function is dependent on three things

- Air entry into the lungs
- The area available for gas exchange

- The blood flow through the lungs

Restrictive or obstructive airways diseases such as asthma and COPD cause a narrowing of the bronchi and bronchioles. This narrowing produces a significant reduction in the rate at which air can flow through the airways and thus significantly reduces the air available for gas exchange.

Classifications of Respiratory Conditions
– Inflammatory
– Obstructive
– Restrictive
– Infective
– Malignant

Table 1

Asthma

The British Thoracic Society (2016) propose a stepwise management plan for the treatment of asthma. They start by stating that the aim of management is to establish control over the symptoms of asthma. They lay out seven criteria fulfilments of which defines complete control.

- No daytime symptoms
- No night time wakening due to asthma
- No need for rescue medication
- No exacerbations
- No limitation to activity including exercise
- Normal lung function (defined as a FEV1 and or a PEF of > 80% of predicted or best)

- Minimal side effects from the medication

The step wise approach advocates a step up or down approach using the following drugs;

- Intermittent Reliever Therapy
 - Inhaled short acting beta 2 agonists as required
- Regular Preventer Therapy
 - Add in inhaled steroids
- Initial Add on Therapy
 - Add in long acting beta2 agonists (LABA)
 - If control is still inadequate consider starting other therapies such as leukotriene receptor antagonists or theophylline.
- Additional Add on Therapies
 - Increase inhaled steroids
 - Consider a trial of leukotriene receptor antagonists or theophylline
- High Dose Therapies including Regular Oral Therapies
 - Use daily oral steroid tablets in the lowest dose possible to maintain control
 - Continue with the high dose inhaled steroids

Many of the drugs stated in the above guidelines are also used in COPD, so let us now look at the pharmacodynamics of these in turn.

Beta2 adrenoceptor Agonists

Short acting beta2 agonists such as salbutamol and terbutaline are used in the treatment of asthma and in the treatment of COPD. They act at the level of the smooth muscle coat of the bronchi and bronchioles and have their actions on the beta adrenoceptors located there

causing relaxation of the smooth muscle and thus dilatation of the airways. The drugs are, for this reason, referred to as bronchodilators. The beta adrenoceptors are G-protein coupled receptors which lead to changes in the levels of adenylyl cyclase an enzyme that regulates cyclic adenosine monophosphate (cAMP). This regulation begins a chain of events that controls airway diameter and is therefore a perfect target for drug action. These drugs can be given either as inhaled preparations as powders, aerosols or nebulised solutions. Salbutamol is also available as an oral preparation, though there is a marked inter individual variation in its absorption and metabolism that makes its effect and duration of action unpredictable and therefor limits its use.

Long acting beta2 agonists are also available such as the drugs formoterol and salmeterol. These work in the same way as their short acting brethren but have a longer duration of action. They can be used in asthma but are more the mainstay of COPD treatment.

[Can we have a picture of a blue salbutamol inhaler here?](#)

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out the doses, strengths and regimes used for asthma and/or COPD in a patient you are likely to manage of inhaled beta2 agonists.

Corticosteroids

Inhaled corticosteroids of the glucocorticoid type such as beclomethasone, budesonide and fluticasone are commonly used in the management and treatment of respiratory conditions.

The oral corticosteroid prednisolone also acts predominantly as a glucocorticoid and acts in a similar way to the inhaled glucocorticoids.

These drugs, regardless of route of administration cause their effects by binding to the glucocorticoid receptors within the cells of the lung tissue. This binding in turn, up-regulates and increases the expression of normally produced anti-inflammatory proteins in the cell. As well as the production of more anti-inflammatory proteins, corticosteroids also act in a way that suppresses the expression of endogenously produced proinflammatory proteins. This produces an overall down regulation of the inflammatory response meaning these drugs are anti-inflammatory in action. In large doses or when given for a period of time they are also immunosuppressant.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out the dose and regime for the type of steroid you are most likely to use in the patients you manage.

Can we have a photo of a BNF here please?

Leukotriene Receptor Antagonists

Montelukast and zafirlukast are the main leukotriene receptor antagonists used in respiratory conditions. These drugs block the cysteinyl leukotriene 1 (CysLT1) receptors on smooth muscle cells found in the lungs. Activation of this receptor results in contraction and proliferation of smooth muscle, oedema, eosinophil migration and damage to the mucus layer in the lung, so inhibiting them promotes bronchodilation and a reduction in inflammatory response.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out how and when you might prescribe leukotriene receptor antagonists for a patient in your care.

Theophyllines

Theophylline and aminophylline are the two main drugs in this category.

These drugs act as competitive nonselective phosphodiesterase inhibitors which raises intracellular cAMP and in turn activates Protein Kinase A. This mimics the effects of beta adrenoceptor stimulation in smooth muscle as described above. Theophyllines also inhibit Tumour Necrosis Factor-alpha and inhibit leukotriene synthesis, and thus act to reduce inflammation.

Theophyllines have a narrow therapeutic window and are toxic in overdose when they can cause cardiac arrhythmias and convulsions. It is recommended that plasma concentrations are measured 5 days after starting the medication and three days after each dose adjustment. The blood sample should be taken 4 to 6 hours after dosing.

Exercise

Using pharmacologically available resources such as textbooks, the BNF or online electronic medicines compendium, find out the specific monitoring requirements for theophylline in a patient you would prescribe this for.

References & Further Reading

Barber and Robertson (2015) Essentials of Pharmacology for Nurses 3rd Edition McGraw Hill London

BNF Online <https://www.bnf.org/products/bnf-online/>

British Thoracic Society and Scottish Intercollegiate Guidelines for the Management of Asthma (2016) retrieved from <https://www.brit-thoracic.org.uk/standards-of-care/guidelines/btssign-british-guideline-on-the-management-of-asthma/>

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