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Oral corticosteroids

Oral corticosteroids (OCS) are potent anti-inflammatory and immunosuppressant medications used in the treatment and prevention of many conditions including asthma, chronic obstructive pulmonary disease (COPD), rheumatology, skin conditions and some cancers. They are highly effective for both acute and chronic disease; however, over-use and indiscriminate use poses a risk for serious side effects and irreversible harm.

Prednisone and prednisolone are the most commonly prescribed oral corticosteroids, with equivalent potency. Prednisone must be converted into prednisolone in liver, therefore prednisolone should be chosen to avoid low treatment efficacy if patients have abnormal liver function. Prednisone and prednisolone are best administered as a single dose in the morning.

Dexamethasone tablets are also classed as a corticosteroid, with a longer duration of action (half-life) than prednisone/prednisolone.

Benefits

Corticosteroids are used in a wide range of conditions for their anti-inflammatory and immunosuppressant effects. Some indications include:

- Autoimmune or inflammatory diseases (e.g. inflammatory bowel disease)
- Acute asthma
- COPD exacerbations
- Acute gout
- Croup
- Multiple myeloma, lymphoma, some leukaemias

Oral corticosteroids are effective and fast-acting for treatment of rheumatoid arthritis. They provide rapid relief of symptoms and short-term low dose OCS are effective in reducing pain associated with rheumatoid arthritis. The introduction of disease-modifying and biologic therapies for rheumatoid arthritis has dramatically shifted the place for low-dose maintenance treatment with prednisolone. For some other inflammatory conditions such as polymyalgia rheumatica, the use of long-term corticosteroids remains an important treatment.

Long-term oral corticosteroids are not recommended for management of COPD. Oral corticosteroids may be required for treatment of acute exacerbations. A 5-day course of prednisolone or prednisone in dose of 30 to 50mg daily is adequate to treat exacerbations. Longer courses add no further benefit and have a higher risk of adverse effects, including mortality and pneumonia.

Prednisolone or prednisone is recommended in the Australian Asthma Handbook for the management of severe acute flare-ups or asthma attacks. The recommended daily dose is oral prednisolone 37.5–50 mg for 5 to 10 days. Oral dexamethasone can be used as an alternative to prednisolone, in a dose of 16mg for 2 days only for adults. Based on these recommended doses, a potentially toxic level can be achieved in as little as four short courses of prednisolone.

Daily maintenance therapy may also be prescribed for people with severe or difficult-to-treat asthma. These people often require recurrent bursts of oral corticosteroids or long-term OCS treatment. Studies have shown an increased incidence of type 2 diabetes, osteoporosis, gastric/duodenal ulcers and dyspepsia, depression/anxiety pneumonia, and cataracts with long-term maintenance use for severe asthma.

Adverse effects

Side effects are rarely serious with short-term use (less than one month). These may include:

- Sleep disturbance
- Increased appetite
- Weight gain
- Increase in postprandial blood sugar
- Psychological effects, including increased or decreased energy

The risk of a serious side effects increases with increasing dose and duration of use. Potentially serious side effects can occur, even with short-term use, including:

- Severe infection
- Heart failure
- Peptic ulceration
- Diabetes mellitus
- Skin changes
- Mania, psychosis, delirium, depression

Concerns associated with long-term maintenance use of oral corticosteroids (more than 3 months) are infection, hypertension, dyslipidaemia, diabetes, osteoporosis, myopathy, redistribution of body fat and weight gain, osteonecrosis (particularly in the hip), fatty liver, cataracts and glaucoma and neuropsychiatric effects such as insomnia, depression and behavioural disturbances.

Signs and symptoms of infection may be masked. Latent tuberculosis (TB) may be reactivated, and wound healing may be delayed with corticosteroids.

Oral corticosteroids may cause hyperglycaemia, type 2 diabetes and worsen diabetes control. More frequent blood glucose monitoring is required during treatment with corticosteroids. The risk of onset of type 2 diabetes is almost nine times greater for patients prescribed more than 7.5mg prednisolone per day compared to 0.5mg or less per day.

Hypertension and heart failure may be worsened due to sodium and water retention.

Long-term corticosteroid use increases the risk of osteoporotic fractures and accelerates bone loss. This risk is dose-dependent. Patients on long-term oral corticosteroid therapy (> 7.5 mg prednisolone daily for more than 6 months) have a 2-fold risk of developing osteoporosis. Prevention and treatment of corticosteroid-induced osteoporosis should be considered if ongoing use is considered necessary.

Oral corticosteroid use is associated with an increased risk of depression and anxiety. It has been shown that depression and anxiety are three times more likely in people with asthma taking maintenance OCS than in those with severe asthma who do not take oral corticosteroids.

Monitoring for adverse effects should include glycaemic control, bone mineral density, blood pressure, cataracts and glaucoma, weight change and fracture risk score.

Cumulative use

The risk of many long-term adverse effects on oral corticosteroids increases once lifetime cumulative exposure exceeds 1000mg prednisolone equivalent. Repeated short-term use of OCS increases the risk of complications. As little as 2 to 4 short courses can cause serious adverse events.

A recent Australian study showed one-quarter of patients with asthma who use inhaled corticosteroids (ICS) were dispensed 1000mg prednisolone over a 5-year period. Good inhaler technique and better adherence to ICSs, together with use of biologics (omalizumab, benralizumab, dupilumab, mepolizumab) when appropriate can reduce harmful use and toxicity of prednisolone. The steroid-sparing effects of biologics has been well demonstrated. Modifiable risk factors such as smoking should be addressed.

Tapering

It is usually not necessary to taper prednisolone or prednisone for courses of less than 14 days.

After several weeks or months of oral corticosteroids careful weaning may be required. Cessation or a decrease in dose may trigger adrenal insufficiency. Signs and symptoms include weakness, fatigue, malaise, gastrointestinal upset, anorexia and weight loss, headache, fever, myalgia and psychiatric symptoms. Maintenance OCS can be weaned slowly whilst monitoring disease control. Typically, a 25% to 50% dose reduction every 1 to 4 weeks is recommended.

Summary

Oral corticosteroids are effective for reducing inflammation and for immunosuppression in a number of chronic conditions. However, there is now an increased awareness that serious adverse consequences of OCS arise at lifetime cumulative doses as low as 1000mg prednisolone. Oral corticosteroids should be used at the lowest dose for the shortest duration, as appropriate. For some conditions such as asthma and rheumatoid arthritis, biologics are steroid-sparing and provide better and safer control of these conditions.

References

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