Australian Government
Department of Veterans' Affairs

Veterans' MATES

Therapeutic Brief 42

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Topic 42: Oral corticosteroids: minimising adverse effects

Corticosteroids are important medicines for their potent anti-inflammatory and immunosuppressant properties.[1] When used for longer than 3 months, particularly at doses higher than the equivalent of prednisolone 5 mg per day, corticosteroids are associated with a high incidence of adverse effects.[2-4] Although the risk of adverse effects is lessened with lower doses, patients may still be at risk; cumulative dose, current or past use of corticosteroids, concomitant medicines, age and gender may influence the extent and severity of adverse effects experienced.[4, 5]

Their use is indicated in a wide variety of inflammatory and other conditions. The proportion of people for whom long term oral corticosteroids are prescribed increases with age.[6-8] Analysis of Department of Veterans' Affairs (DVA) administrative claims data indicates most veterans dispensed oral corticosteroids are elderly (median age of 85 years), with 15% living in residential aged care facilities.[7]

When corticosteroid therapy is necessary, it is good practice to prescribe the lowest therapeutic dose for the shortest possible time to achieve the desired clinical outcome and reduce the risk of adverse effects.[3] When managing adverse effects, consider the dose of all steroids prescribed for your patient, including inhaled and topical steroids, as they are often overlooked. When making clinical management decisions, consider the individual needs of your patient to balance risks, burdens, benefits and quality of life, especially in your older patients with multimorbidity.[9]

This therapeutic brief identifies adverse effects associated with oral corticosteroid use and provides strategies to minimise those effects.

Inside

Key points

Corticosteroid-related adverse effects increase with dose and duration of use

Consider

- Reviewing your patient's dose with an ongoing view to tapering or ceasing as soon as is clinically appropriate
- Bisphosphonates in the prevention and treatment of corticosteroid-induced osteoporosis
- Glucose monitoring in all patients receiving corticosteroids
- Encouraging the application of an appropriate, twice daily skin emollient as well as instigating preventive strategies to reduce skin tears, particularly in your older patients

Monitor for fracture risk

Fracture risk is increased by bone loss and muscle weakness and atrophy. If corticosteroids are prescribed for longer than one month, instigate early preventive measures to help reduce the overall fracture risk.[10]

Bone loss

Analysis of DVA administrative claims data indicates only 26% of veterans dispensed oral corticosteroids receive a medicine for osteoporosis prevention (bisphosphonates, strontium, teriparatide, denosumab, calcitriol or raloxitene) and 23% receive a bone mineral density (BMD) test within the recommended testing period.[7]

When does the risk of fracture start to increase?

- The risk of fracture increases rapidly during the initial 3 to 6 months of therapy, continues to increase at a lesser rate for as long as steroids are used and decreases substantially after ceasing therapy.[2, 11]
- Bone loss is usually asymptomatic, becoming apparent only when a fracture occurs (most often in a vertebra, hip or forearm).[2]

Who are most likely to be affected?

- Patients receiving more than the equivalent of 5mg of oral prednisolone per day for longer than 3 months.[2, 3, 10]
- Patients receiving frequent short courses of corticosteroids.[3]

See Module 28: osteoporosis available at: www.veteransmates.net.au/TB_osteoporosis

How do I monitor and minimise bone loss and fractures?

- Assess fracture risk by measuring the lumbar spine and proximal femur BMD using the DXA (dual-energy X-ray absorptiometry) scan before starting therapy and repeat every 2 years or if it is likely to change management.[3, 10]
- Encourage patients to eat a balanced healthy diet, rich in calcium and vitamin D, participate in weight bearing exercise at least 3 times a week, minimise alcohol intake and stop smoking.[3, 12]
- Initiate a calcium supplement if dietary intake is inadequate.[3, 12] Glucocorticoids cause reduced intestinal calcium absorption.[3]
- Initiate a vitamin D supplement, especially in residents of aged care facilities.[12, 13] Recent evidence suggests there is a significant association between corticosteroid use and vitamin D deficiency.[14]
- Alendronate, risedronate and zoledronic acid are available on the PBS for prevention and treatment of corticosteroid-induced osteoporosis in patients receiving continuous therapy of equal to or greater than 7.5 mg oral prednisolone or the equivalent per day for longer than 3 months and have a BMD T score less than -1.0 for alendronate and risedronate and -1.5 for zoledronic acid.[13, 15]
- Consider:
  - the Health Assessment for people aged 75 years and older.[16]
  - an ongoing review of corticosteroid dose with reduction or cessation if clinically appropriate.
  - the use of inhaled or topical corticosteroids instead of oral where possible, although these still carry a risk of osteoporosis.[1, 3]
  - the use of glucocorticoid-sparing agents where possible.[3, 17]
  - other alternative treatment approaches where appropriate - refer to a specialist if unsure.

Muscle weakness and atrophy

When is it most likely to occur?

- There is no clear length of time, but chronic (or classic) corticosteroid-induced myopathy usually develops slowly over several weeks to months after prolonged use of steroids.[18]
- Acute corticosteroid-induced myopathy, which is less common, tends to occur abruptly 5 to 7 days after initiation of high-dose corticosteroids and is often more severe.[19]

Who are most likely to be affected?

- Patients receiving high-dose corticosteroids or after prolonged use.[20]
- People with a sedentary lifestyle may be at an increased risk of being affected.[19]
- Women may be more likely to be affected.[19]

How is the patient likely to be affected?

- The patient typically presents with a gradual onset of proximal muscle weakness, first in the legs and then in the arms.[3, 20]
- The weakness may be sufficiently severe to hinder mobility and increase the risk of falls, thereby increasing the risk of fracture, especially in your elderly patient.[21]
- If symptoms are severe enough to prevent your patient from walking, a tapered withdrawal of corticosteroid therapy is recommended.[20]

How do I monitor and minimise effects?

- Ascertain if your patient is having any progressive difficulty rising from a chair, climbing stairs or performing overhead reaching activities.[19]
- Encourage your patient to report any of these symptoms to you.
- Emphasise the benefits of weight-bearing exercise to maintain muscle strength and balance.
- Symptoms generally improve with dose reduction and resolve on cessation of treatment, however recovery may take weeks to months.[18, 19]

Monitor for hyperglycaemia

Corticosteroid use may increase blood glucose levels in both diabetic and non-diabetic patients.[3] The risk of developing new onset diabetes more than doubles in the elderly after initiation of oral corticosteroids.[22]

When is hyperglycaemia likely to occur?

- The effect of corticosteroids on blood glucose levels may be observed within hours or days after starting therapy and is dose dependent.[3]
- Blood glucose levels typically rise during the day and fall slowly overnight if the corticosteroid dose is given in the morning.[3]

Who are most likely to be affected?

- Patients prescribed high doses of oral corticosteroids or with prolonged use.[3]
- Patients prone to diabetes or those who already have diabetes.[3]
- Patients taking corticosteroids for the first time in conditions such as, polymyalgia rheumatica, giant cell arteritis or disseminated malignancy.[3]

How do I monitor and minimise effects?

- Monitor blood glucose levels starting from initiation of therapy.[3]
- Monitor glycaemic levels using a HbA1c test in high risk patients using long term corticosteroids (a new MBS item 66841, available from 1st November 2014, allows diagnosis of diabetes in asymptomatic high risk patients from a raised HbA1c alone).[23]
- Be aware blurred vison may indicate acute hyperglycaemia.[24]
- Hyperglycaemia often improves with corticosteroid dose reduction and reverses with cessation of therapy.[3, 18]
- In some cases, diabetes may persist even after corticosteroid therapy is ceased.[18]

Monitor for weight gain and Cushingoid features

Perhaps the most commonly reported and distressing adverse effect for many patients taking oral corticosteroids is weight gain and Cushingoid features (moon face, truncal obesity, buffalo hump, double chin and thinning of the arms).[5, 25]

Recent evidence suggests patients who are treated with corticosteroids and develop Cushingoid features are at a high risk of cardiovascular disease and features of metabolic syndrome, including increased blood pressure, triglycerides and blood glucose and cholesterol levels.[26]

Weight gain and Cushingoid features may lead to non-adherence of therapy.[27] Reassure your patient that these features are a common and transient adverse effect of corticosteroid use and will resolve with dose reduction and cessation of therapy.

When are symptoms likely to appear?

- Weight gain and Cushingoid features may begin to develop within the initial 2 to 3 months of therapy and affect approximately two thirds of patients.[18, 25]

Who are most likely to be affected?

- Patients taking high dose, long term corticosteroids are most likely to be affected.
- Weight gain and Cushingoid features occur more often in:
  - women
  - people less than 50 years of age
  - people with a high BMI at steroid initiation and
  - people who have a high calorie intake.[25]

How do I monitor and minimise effects?

- Monitor your patient's weight and observe for signs of Cushingoid appearance.
- Recommend a low-calorie diet, keeping in mind it is often difficult for the patient to maintain because of a steroid-induced increase in appetite.[1]
- Encourage physical exercise.
- Assess cardiac risk and monitor lipid profile, blood pressure and glucose levels.[28]
- Consider reviewing the dose and tapering or ceasing therapy, if clinically appropriate.[3, 28]

Monitor for cardiovascular disease

Corticosteroid daily doses greater than 7.5 mg prednisolone or the equivalent are associated with a significantly increased risk of cardiovascular events.[29] Hypertension and heart failure may also be worsened due to sodium and fluid retention.[1, 29]

When are symptoms likely to appear?

- Fluid retention can occur almost immediately after beginning corticosteroid therapy.
- Myocardial infarction, heart failure, transient ischaemic attacks and stroke associated with corticosteroid use have been identified within the first year after commencing therapy.[26]

Who are most likely to be affected?

- Patients taking doses greater than the equivalent of 7.5 mg of prednisolone per day are most likely to be affected.[3, 29]
- Patients taking corticosteroids continuously for prolonged periods may also be at risk.[18, 29]

How do I monitor and minimise effects?

- Assess cardiac risk and monitor for weight gain, peripheral oedema, cardiac insufficiency, and increased lipid, blood pressure and glucose levels depending on your patient's individual risk, corticosteroid dose and duration of therapy.[13, 26, 28]
- Consider reviewing the dose and tapering or ceasing therapy, if clinically appropriate.[29]

Monitor for neuropsychiatric effects

Mild neuropsychiatric effects appear to be common with serious adverse effects occurring in approximately 6% of people receiving oral corticosteroids.[27, 30]

Who are most likely to be affected?

- Patients prescribed high doses or those on long term therapy are most likely to be affected.[30, 31]
- Women may be affected more often than men.[32]

When are symptoms likely to emerge?

- Symptoms can emerge at any time, even after cessation of corticosteroid therapy, but they typically emerge during the first few weeks after initiation.[30-32]
- The progression from mild to severe symptoms may only be a short time.[31]

How are patients likely to be affected?

- The effect on patients can be varied and unpredictable and may include insomnia or vivid dreams, irritability with mood swings, depression/anxiety, mania or hypomania, catatonia and depersonalisation.[30]
- Delirium and psychosis are less common.[1]
- The euphoric effect and general feeling of wellbeing that is sometimes associated with corticosteroid use may lead your patient to resist dose reduction and cessation of therapy.

How do I monitor and minimise effects?

- Be alert to early symptoms including anxiety, irritability, insomnia or mood swings.[31]
- Consider dose reduction or cessation of therapy if clinically appropriate.[30, 31]
- If your patient displays signs of acute psychosis, refer for a psychiatric assessment immediately.[30, 31]
- If your patient shows signs of acute psychosis and has been taking corticosteroids for longer than 3 weeks, a tapered withdrawal of corticosteroid therapy is recommended. The tapering may need to be more rapid in acute situations.[30, 31]

Monitor for cataracts and glaucoma

The formation of posterior subcapsular cataracts (PSC) is a relatively common adverse effect of prolonged corticosteroid use.[1, 5] Corticosteroid induced glaucoma is much less common, but can lead to visual field loss and optic nerve atrophy which may become permanent.[18]

When are cataracts and glaucoma most likely to occur?

- The occurrence of glaucoma is rare and unpredictable.[1, 33]
- Cataracts develop slowly; they may not be apparent for at least one year after initiation of therapy.[18]

Who are most likely to be affected?

- Patients with increasing dosage and duration of treatment are most likely to be affected, however occurrence can be unpredictable.[18]
- Patients at an increased risk of glaucoma appear to be those with a personal or family history of open angle glaucoma, diabetes, high myopia or connective tissue disease, such as rheumatoid arthritis.[18]

How do I monitor and minimise effects?

- Consider reviewing the corticosteroid dose with reduction or cessation if clinically appropriate.
- Refer your patient annually to an optometrist or ophthalmologist for a comprehensive assessment or earlier if symptoms of cataracts are present.[10, 18]

Monitor for gastrointestinal effects

Gastrointestinal effects associated with corticosteroid use can include gastritis, dyspepsia, ulcers with perforation and bleeding, abdominal distention and oesophageal ulceration.[18]

Who are most likely to be affected?

- Patients taking concomitant bisphosphonates, NSAIDs, calcium channel blockers or nitrates may be at risk of developing symptoms of dyspepsia, reflux or ulcers.[1]
- Although the risk of ulcers and bleeding or perforation is low in ambulatory patients prescribed corticosteroids, concomitant use of NSAIDs and corticosteroids is associated with a significantly increased risk of gastric ulceration and bleeding.[34, 1, 35]
- Patients with high alcohol intake may be at an increased risk of gastrointestinal ulceration or bleeding.[20]
- The effect of warfarin is increased when taken with corticosteroids, resulting in an increased risk of bleeding.[1]

How do I monitor and minimise effects?

- Suggest corticosteroids are taken with food; it may help reduce stomach upsets.[1]
- Avoid NSAIDs in patients prescribed corticosteroids if possible; ask your patient whether they are taking over the counter NSAIDs.[36, 37]
- Consider a proton pump inhibitor (PPI) when corticosteroids and NSAIDs are both necessary with consideration given to the possibility of an increased fracture risk, particularly in your older patients.[13, 38] A recent meta-analysis identified an increased fracture risk, particularly of the spine and hip, associated with the use of PPIs.[38]
- Advise your patient with a high alcohol intake to limit consumption while taking corticosteroids.[20]
- Monitor the International Normalised Ratio closely if your patient is taking warfarin and corticosteroids together and decrease warfarin dose as required.[1]

Monitor for dermatological effects

Thinning of the skin, skin tears and bruising are common dermatological effects of corticosteroid use, especially in the elderly.[5, 39]

Who are most likely to be affected?

- Patients taking the equivalent of 7.5 mg of prednisolone or more per day for several months are most likely to be affected.[20]
- Older people are more likely to be affected as they are predisposed to skin fragility and skin tears which can become chronic wounds.[39]

What are the potential adverse effects?

- Effects may include skin atrophy, easy bruising, rosacea, acne and facial flushing, striae to the thighs, buttocks and shoulders, purpura and hirsutism.[1]
- A potentially serious adverse effect is impaired wound healing.[1, 18]

How do I monitor and minimise effects?

- Advise your patients to take extra care to avoid injuries and to promptly seek medical attention after an injury.[11]
- Encourage your patient to apply an emollient (moisturiser) twice a day to reduce the incidence of skin tears, especially in your elderly patients and residents of aged care facilities.[39]
- Examples of skin emollients listed on the RPBS include Alpha Keri® Lotion, Urederm®, Aquacare H.P.® or Calmurid® cream, Eucerin® ointment and Hamilton® Skin Therapy Oil.
- Avoid emollients that contain sodium lauryl sulfate, for example aqueous cream or emulsifying ointment, as they may cause skin irritation.[1]
- For further information about emollients and corticosteroids see Module 33: www.veteransmates.net.au/TB_emollients
- Consider preventive strategies to protect your patient's skin, especially those in aged care facilities. Refer to the Pan Pacific Clinical Practice Guideline for the Prevention and Management of Pressure Injury for details.[40]

Tapering the dose or withdrawing therapy

When tapering your patient's dose or withdrawing therapy, watch for signs of recurrent activity of the underlying disease and symptoms of adrenal suppression and slow the withdrawal regimen if symptoms arise.[18] The risk of adrenal suppression is variable and difficult to predict.[1, 20] However, doses less than the equivalent of prednisolone 7.5 mg per day or treatment for less than three weeks are unlikely to cause adrenal suppression.[1, 3] The adrenal response may return to normal quickly or may be suppressed for a year or more after long term therapy has been withdrawn. In this case the production of hydrocortisone in response to stress situations, such as infection or surgery may be insufficient and need to be supplemented.[1, 20] Seek specialist advice if you are unsure about how and when to taper the dose or withdraw therapy.[1]

Be alert to the patient's perception of recurrence of symptoms associated with their underlying disease due to the loss of euphoric effects and general feelings of wellbeing often associated with oral long term corticosteroid use; this may lead the patient to resist reduction and cessation of therapy. Explain to your patient there may be some discomfort when tapering therapy, but emphasise the importance and value in trying to persist.

There is a lack of clinical evidence to support any particular regimen of tapering or weaning of patients from long-term high dose corticosteroid use.[18] The rate of tapering will depend on your patient's underlying disease, previous dose, duration of therapy and individual response.[3]

Consider recommending a Medicines Review (HMR or RMMR) by an accredited pharmacist to review your patients' medicines and talk with them about:

- the corticosteroid medicines they are taking
- how they can help to minimise corticosteroid-related adverse effects
- how to optimise the benefits of therapy
- other medicines that may increase adverse effects

Full reference list available on the website: www.veteransmates.net.au

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