



CLINICAL CARE GUIDELINES

USE OF CORTICOSTEROIDS IN PALLIATIVE MEDICINE

DEFINITIONS AND PRINCIPLES

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Corticosteroids are produced by the cortex of the adrenal glands⁽¹⁾. There are two main forms- glucocorticoids and mineralocorticoids⁽¹⁾. The actions of glucocorticoids include gluconeogenesis, fat deposition, sodium retention, decreased protein synthesis and decreased immune response⁽¹⁾. Examples of glucocorticoids include Cortisol (Hydrocortisone), Prednisolone and Dexamethasone⁽¹⁾. Mineralocorticoids, such as Fludrocortisone, mainly act on the extracellular balance of sodium and potassium in the distal tubule of the kidney⁽¹⁾.

Glucocorticoids are commonly used within palliative care in a variety of doses to tackle both specific and non-specific symptoms of advanced cancer⁽²⁾. They are commonly referred to as steroids although as explained above they are one form of several corticosteroids⁽¹⁾. The corticosteroid used most commonly in palliative care is Dexamethasone, see below⁽³⁾. The use of corticosteroids within the general medical population is extremely closely monitored and there have been some concerns within the literature that this is not appropriately translated into palliative care patients^(4,5).

These guidelines are designed for all clinicians dealing with Palliative Care patients.

AIMS

- Corticosteroids should be considered for various symptoms as outlined below with the aim of treatment being clear.
- Treatment should be regularly monitored and if symptoms do not respond, stop responding or recur, steroids should be reduced and withdrawn.
- Corticosteroids have considerable side-effects and hence the LOWEST effective dose should be used for the SHORTEST time. Reduce the dose of steroids to the minimum required to achieve symptomatic effect.
- The prognosis of the patient should be considered when prescribing steroids. Side-effects from steroids may be a problem for patients with a prognosis of months or more.

PHARMACOLOGY OF CORTICOSTEROIDS

The corticosteroid of choice within palliative care is Dexamethasone but Prednisolone is used at times⁽³⁾. Below is a table of approximate anti-inflammatory equivalencies of several corticosteroids⁽⁶⁾.

NAME	DOSE (mg)	DURATION OF ACTION (hrs)
Hydrocortisone	20mg	8-12
Prednisolone	5mg	12-36
Dexamethasone	0.75mg	36-54

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Dexamethasone has several advantages for patients with malignancy⁽⁶⁾

- Lower sodium retention potency and hence reduced likelihood of fluid retention
- Ability to administer larger dose with small number of tablets.
- Tablets dispersed in small volumes of water.
- Available as subcutaneous injection.

SIDE EFFECTS

- Doses >4mg od are likely to lead to significant side effects after several weeks⁽³⁾.
- Doses <4mg od are often tolerated in patients with a prognosis of months⁽³⁾.

Early effects – days⁽⁶⁾

Diabetes mellitus (steroid induced or worsening of established type1 or type 2 diabetes)

Oral thrush

Fluid retention

Hunger

Mental disturbance – insomnia, agitation, euphoria, paranoia

Additive risk of GI bleed when used with NSAIDS

Later effects-weeks⁽⁶⁾

Cushingoid appearance – moon facies, central obesity, buffalo hump.

Thinning of skin

Increased susceptibility to infection

Proximal muscle wasting and weakness

Longer term effects - months to years⁽⁶⁾

Avascular bone necrosis

Osteoporosis

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PRESCRIBING CORTICOSTEROIDS

General Points

- Always clearly document reasons for prescribing steroids^(4,6,7).
- Review treatment regularly and discontinue if no benefit after one week, ensure patients are aware of principle of aiming for short courses of steroids-not long-term medication^(6,7).
- Patients should be made aware of side-effects and the need to report to GP or ward staff if less well on steroids^(6,7,8). They should be given a steroid card if taking steroids for >3wks⁽⁶⁾.
- Give steroids before 1400hrs to minimize risk of sleep disturbance^(3,8).
- Give prophylactic gastric protection if also taking NSAIDs or consider if previous GI bleed⁽⁷⁾.
- Consider prophylactic topical oral anti-fungals - Nystatin 1ml QDS, if any present or prior oral symptoms⁽⁵⁾.
- Doses may need to be doubled if patients are also taking enzyme-inducers eg. Phenytoin, Carbamazepine^(3,7). In addition, Carbamazepine and Phenytoin levels can be reduced by corticosteroids and may need to be adjusted⁽⁷⁾.
- Consider switching to Prednisolone if proximal myopathy develops but benefit is still being achieved on Dexamethasone⁽³⁾.
- Consider prophylaxis against osteoporosis (eg; Risendronate 35mg once weekly) if patient is on steroids for >6months⁽³⁾.
- Weekly urinalysis or monitoring of blood sugars if on doses Dexamethasone \geq 4mg for first month of treatment (or after a dose increase) then if symptomatic thereafter^(7,9).

Reduction/Discontinuation^(3,6,10,11)

- If taken <4mg Dexamethasone for <3 weeks, it is generally safe to stop steroids abruptly unless:
 - Patients have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.
 - A short course has been prescribed within one year of cessation of long-term therapy (months or years).
 - Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy.
- If taken Dexamethasone for more than 3 weeks, reduction should not be abrupt but should largely be guided by whether the disease is likely to relapse as steroids are reduced.
 - If the latter is likely to occur, reduce steroids more slowly.
 - If not suggested guidance below:
Dexamethasone >2mg daily – reduce the dose by half every 3-5 days.
then/or
Dexamethasone <2mg daily (near physiological dose) – reduce dose by 0.5mg every 5-7 days or on alternate days to stopping.

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Recommended Doses

Below are suggested average starting doses of Dexamethasone according to indication^(3,6,7)

2-4mg/day	6mg/day	8mg/day	16mg/day
Anorexia Weakness Improvement in well being/mood Non-specific pain relief Anti-emetic	Co-analgesic in -nerve compression pain -liver capsule pain	Obstruction of hollow viscus - bronchus - bowel - ureter	Raised intracranial pressure Spinal cord compression SVC obstruction

Anorexia^(1,3,6,7)

- Is a universal symptom in the dying - often this concerns carers more than the patient.
- Careful discussion and reassurance that deterioration in condition is due to disease process can relieve anxieties about limited food intake.
- If the patient is concerned about poor intake, it may be appropriate to have a trial of steroid therapy.
- If the patient has no appetite undue pressure to eat will cause distress and or nausea.

Appetite / wellbeing^(1,3,6,7)

- Steroids can increase appetite, food intake and sense of wellbeing, although this is usually a short term benefit.
- If appetite not improved steroids should be rapidly tailed off. Progestogens e.g Megestrol Acetate up to 160mg od, may be prescribed for appetite stimulation or Mirtazapine 15-45mg.

Anti-emetic^(1,3,6,7)

- Thought to enhance anti-emetic tone in medulla.

Pain^(1,3,6,7)

- Mechanism of action not entirely clear but thought to be combination of:
 - an anti-inflammatory effect
 - a reduction in oedema and pressure e.g. nerve compression or raised ICP
 - Action on pain transmission through C-fibres.

Dyspnoea^(1,3,6,7)

- Mechanism unclear but some evidence of benefit in lymphangitis carcinomatosa, radiotherapy pneumonitis and airways obstruction.

SVCO/Cord Compression^(1,3,6,7)

- Both are medical emergencies and should be treated with high dose steroids on the basis of clinical suspicion

NB: See also care guidelines for above symptoms.

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Steroids at the End of Life

There is a lack of evidence over discontinuation of steroids at the end of life and each case should be considered in terms of the reason for taking the steroids, dose and duration along with burden of administering the steroids either orally or subcutaneously. Ideally the decision should be discussed with the patient and/or relatives.

OUTCOMES

1. Prescription of steroids should be carefully considered and documented.
2. Always aim for the lowest therapeutic dose for the shortest time.
3. Plans for review and reduction of steroids should be documented in the notes and acted upon accordingly.
4. Monitor urinalysis/random BM weekly whilst on Dexamethasone $\geq 4\text{mg}$.
5. Issue steroid card to patients when on steroids for $>3\text{weeks}$.
6. Consider prophylaxis against GI side-effects and thrush.
7. Audit prescription of steroids every 2 years.

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