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This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Dexamethasone for the management of metastatic spinal cord compression & brain metastases in adults

Dexamethasone is used in the management of metastatic spinal cord compression (MSCC) and brain metastases in order to improve patients' symptoms and reduce neurological impairment.

Dexamethasone is the corticosteroid of choice for both MSCC and brain metastases because of its biological properties. It has low mineralocorticoid activity, therefore low rates of peripheral fluid retention. The half-life is 36-54 hours, allowing once or twice daily dosing. However, the long half-life may increase the risk of adrenal suppression, which can occur after as little as 2 weeks of dexamethasone[1].

MSCC

Background

Dexamethasone decreases spinal cord oedema which prevents further neurological deterioration and reduces pain[2].

There is limited evidence to guide clinicians on the optimal starting dose. Four randomised trials investigated the use of 96-100mg/day initially as an adjunct to radiotherapy, but over 10% patients experienced significant side-effects including hypomania, psychosis and gastric ulceration[2-5]. International consensus is that the toxicity of this dose of dexamethasone is too great[6]. UK national audits have identified 16mg/day in two divided doses as the most common starting regimen, and the NICE guidelines recommend this to be started as soon as the diagnosis of the MSCC is suspected[6].

Dexamethasone-related toxicity is a consequence of both the dose and the duration of treatment, and can be minimised by using the lowest effective dose for the shortest possible time.

Recommendations

Unless contraindicated, a loading dose of 16mg dexamethasone PO should be given as soon as possible after the suspicion of MSCC is raised.

If there is a significant suspicion of lymphoma, senior Oncology or Haematology advice (SpR on call, bleep 5054 9am-9pm, via switchboard overnight) is urgently required prior to dexamethasone administration (which can impair the histological diagnosis of lymphoma).

If MSCC is not confirmed on MRI scan, dexamethasone should be stopped immediately unless steroids have been administered for more than 3 days.

Reducing regimen:

Abrupt cessation of dexamethasone is **not** recommended if it has been given for more than 3 days, due to the potential for both worsening of symptoms and precipitation of acute adrenocortical insufficiency.

The following reducing regimen is based on consensus from the literature, and senior Oncologists within Oxford University Hospitals NHS Foundation Trust:

Day	Dexamethasone Daily Dose (PO)*	Administration
Until surgery or completion of radiotherapy	16mg	8mg BD**
Day 1-2 post treatment (2 days)	8mg	8mg OD***
Day 3-4 post treatment (2 days)	4mg	4mg OD
Day 5-6 post treatment (2 days)	2mg	2mg OD
Day 7 post treatment	Discontinue	

*__These are oral doses, and cannot be directly converted to IV doses, which should be prescribed as base. Please seek advice from a Pharmacist if IV dosing is required.__

BD: 8am and **2pm (any later increases the risk of sleep disturbance)

***OD: 8am

If at any point in the dose reduction neurological symptoms deteriorate, or pain increases, return to the previous dose level and seek senior Oncological advice (SpR on call, bleep 5054 9am-9pm, via switchboard overnight).

Patients who do not go on to receive definitive treatment (radiotherapy or surgery) should have dexamethasone gradually reduced and stopped as described above.

Following surgery, a quicker dose reduction schedule may be used. Steroids are not routinely required during adjuvant radiotherapy, but neurology should be closely monitored and steroid treatment reinitiated if there is any deterioration in findings (after discussion with the Spinal Surgical team). A slower reducing regimen may be required for patients who have received previous courses of steroids.

Brain Metastases

Background

Dexamethasone provides symptomatic relief for patients with raised intracranial pressure from cerebral oedema, most likely by decreasing blood brain barrier permeability, but this relief reduces over time and undesirable side effects increase.

There is randomised evidence showing 4mg daily dose gives the same degree of improvement in performance status as 16mg daily after 7 days, with decreased side effects[7] However, inadequate reporting in clinical trials has resulted in a lack of clear guidance for dosing. Published evidence regarding the optimal tapering schedule varies, but the most commonly reported involve a gradual decrease in dose over a period of 2-4 weeks, after radiotherapy-related oedema has resolved, with longer periods for patients who were symptomatic at baseline[1].

Recommendation

The starting dose of dexamethasone should be **4mg OD or BD (PO) depending on raised**

pressure symptoms. Patients with severe symptoms, or impending hydrocephalus, can be treated with higher doses (up to 16mg daily) pending definitive treatment.
Dexamethasone dose should be reduced 2 weeks after starting whole brain radiotherapy, and should be tailed down gradually over 4 weeks using 0.5mg tablets to enable a steady reduction. The exact schedule depends on the starting dose.
There can be periods of brain oedema up to 16 weeks following radiotherapy, which may require dexamethasone to be re-instituted.

For stereotactic radiosurgery (SRS), a shorter course of dexamethasone will be prescribed by the SRS team (usually 6mg OD for the duration of treatment and the following day, reducing to 4mg for 2 days, 2mg for 2 days, then stopped). In the case of larger metastases, the initial dose may be increased above this and the tailing down course last up to a month.
If no radiotherapy is to be given, the dose of dexamethasone should be tapered according to symptom response.

General guidance for prescribing steroids

Oral bioavailability of dexamethasone is high, so there is no benefit to using IV dosing unless the patient is strictly nil-by-mouth. IV dexamethasone is prescribed according to base, and therefore oral doses given here should not be used for IV dosing.

Prophylactic gastric protection should be continued for the duration of steroid treatment: Proton pump inhibitor (once daily omeprazole 20mg or lansoprazole 15-30mg orodispersible tablets for patients with dysphagia).

Concurrent *NSAIDs* increase the risk of gastric ulceration, and should therefore be avoided.

Blood glucose should be monitored in all inpatients (at least once daily, more often if known to have diabetes mellitus – see MIL for management of hyperglycaemia in adults).

Serum concentration of dexamethasone may be decreased in patients receiving *phenytoin or carbamazepine,* and the dose of dexamethasone may need to be higher in these patients. This should be discussed with the patient's Consultant or the Neurology team.

References

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