Is Dexamethasone underutilized at End-of-Life Care?

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Disclosure!

None

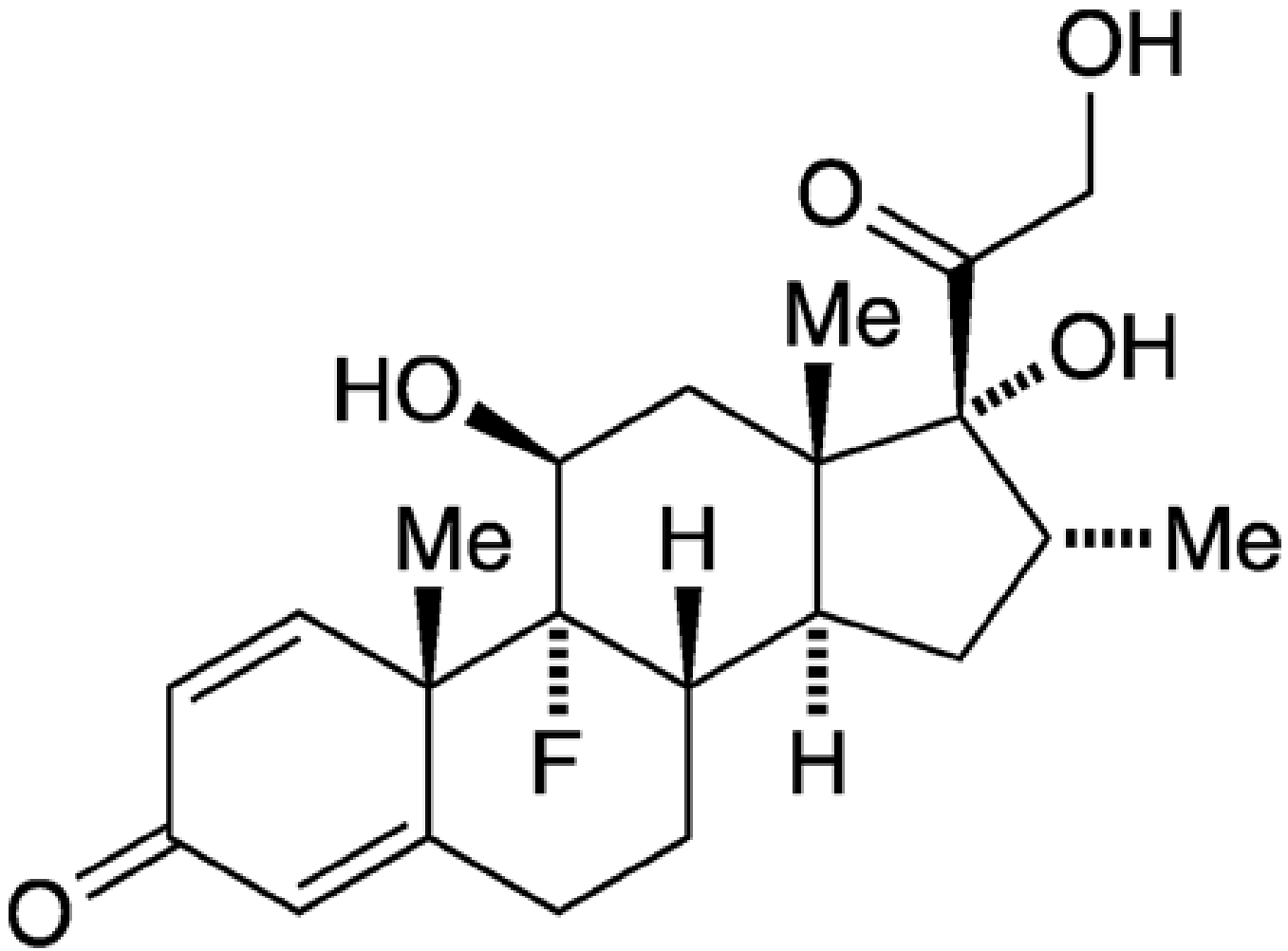
Objectives

- Review on Dexamethasone
- Dosage/Practice review
- Questions/Discussion

Case

- Terry is 81 yr Male
- After multiple hospital admissions for advanced CHF/COPD decided to forego active treatment and focus on comfort.
- Just finished cocktail of therapy mainly prednisone and felt the best when on steroids
- Few days after arrival , became more symptomatic
- Hydromorphone added to maximized inhalation therapy + Mucomyst with some response
- Still dyspneic but not ready for sedation

Dexamethasone



Dexamethasone

- First **synthesized** by **Philip Showalter Hench** in 1957
- Nobel Prize 1/3 1950
- FDA approval on 30 October 1958
- Merck marketed a brand name Decadron in 1959

Mechanism of Action

- Potent glucocorticoid with very little mineralocorticoid activity
- Anti-inflammatory activities
- Suppresses the migration of neutrophils and decreasing lymphocyte colony proliferation.
- Decreases capillary membrane permeability
- Increases Lysosomal membranes stability
- Inhibits vitamin A compounds in the serum, prostaglandin, and some cytokines (interleukin-1, interleukin-12, interleukin-18, tumor necrosis factor, interferon-gamma, and granulocyte-macrophage colony-stimulating factor)

Anti-inflammatory activity

• Natural cortisol (or hydrocortisone)	1
• Prednisone / prednisolone.	4
• Methylprednisolone.	5-7
• Triamcinolone	5
• Betamethasone	25-30
• Dexamethasone.	25-80

Pharmacokinetics

- Absorption: Peak concentrations (Tmax) 1 hour (range: 0.5 to 4 hrs)
- Half-life = 4 hours (18%).
- Clearance is 15.7 L/hr following a single dose .
- Metabolism: Dexamethasone is metabolized by CYP3A4.
- Excretion: Renal ,<10% of dexamethasone is excreted in the urine.

Common Palliative uses (Non Specific)

- Pain
- Stimulate appetite
- Suppress nausea
- Alleviate fatigue

Specific Palliative indications

- Spinal cord compression
- Raised intracranial pressure
- Bowel obstruction

Contraindications

- Systemic fungal infections
- Hypersensitivity to dexamethasone
- Cerebral malaria
- Live or live-attenuated vaccines

- Caution :cirrhosis, diverticulitis, myasthenia gravis, renal insufficiency, or ulcerative diseases such as peptic ulcer disease or ulcerative colitis

Common side effects

- Increased appetite or weight gain
- Proximal muscle weakness
- Insomnia
- Gastrointestinal side effects
- Psychiatric side effects, such as delirium, depression, anxiety, and psychosis
- Osteoporosis with long-term use Less frequent side effects include the following:
- Infections
- Hyperglycemia
- Cushing syndrome

Life-threatening side effects

- Gastrointestinal bleeds
- Thromboembolism

Dosage
Up-to date

- Low-dose regimen *:* **Oral, IV: Initial:** 0.75 to 1.5 mg once or twice daily; usual effective dose range: 1 to 2 mg IV or orally twice daily .
- *Higher-dose regimen :* **Oral, IV:** Initial: 8 to 10 mg once; if responsive, then may consider 4 mg twice daily or 8 mg once daily; use the lowest dose that maintains pain relief while other analgesic treatments are added, if indicated .

Literature

- 1992 Feb;
- **High incidence of serious side effects of high-dose dexamethasone treatment in patients with epidural spinal cord compression**
- K Heimdal [1], H Hirschberg, H Slettebø, K Watne, O Nome

- High-dose dexamethasone (96 mg i.v. loading dose, decreasing doses to zero in 14 days)
- Total rate of serious side effects of 14.3 % , FOUR events
- one fatal ulcer with haemorrhage,
- one rectal bleeding
- one gastrointestinal perforation from undetermined origins,
- one perforation of the sigmoid colon
- Regimen was abandoned in favor of a standard dexamethasone dose of 16 mg daily reduced to zero in 14 days

Literature

- 2002 Sep;24,
- **A retrospective observation of corticosteroid use at the end of life in a hospice**
- Craig Gannon [1], Penny McNamara
- 51 % of 178 patients received corticosteroids, which were continued until death in 53%

Literature

- Published: 18 November 2014
- **Corticosteroids in palliative care - perspectives of clinicians involved in prescribing: a qualitative study**
- Anne Denton & John Shaw
- Differences in the understanding of the place of corticosteroids ,particularly in the treatment of non-specific symptoms and in the use of guidelines.
- Dose range of 1 mg to 40 mg
- median dose of 8 mg.
- The median duration 29 days

Literature

- Epub 2018 May 8.
- **Prescribing Trends of Palliative Care Team's Use of Dexamethasone for Cancer-Related Pain**
- Katayoun Barghi, Kyle P Edmonds, Toluwalase A Ajayi, Rabia S Atayee

- Average dose of 13 mg (SD = 10)
- decrease of 23% and 19% in MEDD and NPS (numeric pain score)

Literature

- Epub 2022 Apr 1.
- **Do Patients Benefit from a Trial of Corticosteroids at the End of Life?**
- Sriram Yennurajalingam [1], Eduardo Bruera [2]
- Limited evidence in regard to the effectiveness of corticosteroids in the improvement of the symptoms, side-effect profile, most optimal duration of use, dose, type of steroid.

Back to Terry

COVID 19 positive

Symptomatic .. Is it CHF/COPD/COVID?

Dexamethasone Trial started with out antiviral

More symptom control achieved

Conclusion

- Inflammation is the main physiology in symptoms
- More cancer/ Disease > More inflammation > More symptoms?

Thank You