Dexamethasone

What is it?

- A corticosteroid with anti-inflammatory and immune-modulatory activity.
- Viral activity with COVID-19 infection may elicit a strong host immune response leading to local and/or systemic inflammatory damage. Corticosteroids mitigate inflammatory response and may prevent damage to the lungs and other organs.

Nova Scotia Health recommends **dexamethasone 6 mg PO/NG/IV daily x 10 days or until hospital discharge (whichever comes sooner)** in **adult** patients hospitalized with COVID-19 with SpO_2 ≤ 94% on room air or supplemental oxygen, or mechanical ventilation including extracorporeal membrane oxygenation (ECMO).

Evidence: Supported primarily by RECOVERY, a multi-arm, open-label RCT taking place across many UK centres:[1]

- The arm investigating corticosteroids included over 6000 patients hospitalized with COVID-19. Patients were included if, in the opinion of the attending physician, they had no contraindication to dexamethasone treatment.
- Randomized to receive dexamethasone 6 mg oral/IV daily for up to 10 days (median 7 days) or usual care alone. Eligible pregnant or lactating individuals could receive prednisolone or hydrocortisone as an alternative to dexamethasone, and pediatric patients could receive hydrocortisone or methylprednisolone as alternatives.

RECOVERY: Key findings of corticosteroid arm

- **Lower mortality:** Overall 22.9% (482/2104) dexamethasone vs 25.7% (1110/4321) usual care patients died by 28 days (RR 0.83; 95% CI 0.75-0.93; p<0.001). Pre-specified patient stratification indicates that **the degree of respiratory support is associated with the magnitude of mortality reduction. There is a trend towards possible harm in those that do not require oxygen support.**
  Death at 28 days (dexamethasone vs usual care; RR and 95% CI):
  - **Invasive mechanical ventilation:** 29.3% (95/324) vs 41.4% (283/683) [0.64 (0.51-0.81)]
  - **Supplemental oxygen without invasive ventilation:** 23.3% (298/1279) vs 26.2% (682/2604) [0.82 (0.72-0.94)]
  - **No oxygen:** 17.8% (89/501) vs 14.0% (145/1034) [1.19 (0.91-1.55)] – no mortality reduction, and numbers trend towards potential harm.

  Number needed to treat (NNT): For every:
  - 9 COVID-19 patients requiring invasive mechanical ventilation and
  - 35 COVID-19 patients requiring supplemental oxygen who receive dexamethasone, one death is prevented at 28 days versus usual care alone.
- **Shorter hospitalization:** Median 12 days in dexamethasone arm vs 13 days usual care, and greater probability of discharge alive within 28 days [overall RR 1.10 (95% CI 1.03-1.17); no difference amongst subgroup on no oxygen at baseline].
- **Few serious adverse events (SAEs):** 4 SAEs deemed by investigators to be related to dexamethasone: two hyperglycemic events, one gastrointestinal hemorrhage, one psychosis event.

Findings are similar when results are combined with other study data in meta-analyses.[2-4]

Infectious Diseases Society of America (IDSA): recommends dexamethasone in hospitalized COVID-19 patients with severe illness (SpO2 ≤ 94% on room air or supplemental oxygen), or in critically ill mechanically-ventilated patients. Use is not recommended in non-severe illness.[5]

National Institutes of Health (NIH): strongly recommends dexamethasone for hospitalized patients requiring supplemental oxygen, oxygen through a high-flow device or non-invasive ventilation, or mechanical ventilation or ECMO.[6]

Practical Considerations

- In the setting of COVID-19 in critical illness and septic shock, hydrocortisone may be a reasonable alternative to dexamethasone.
- In pregnancy, depending on gestational age, a methylprednisolone-based regimen may be appropriate. Refer to the Nova Scotia Health *Corticosteroid Treatment for a Pregnant COVID-19 Patient* order set for guidance.

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References:

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