Budesonide bests COVID-19

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Clinical question

What is the effect of inhaled corticosteroids on length of illness, emergency department visits, and hospital admissions in outpatients with COVID-19?

Bottom line

Based on 2 open-label trials, higher-risk outpatients (≥1 comorbidity) with suspected or confirmed COVID-19 may benefit from 800 µg of inhaled budesonide twice a day for 14 days. Compared with usual care, budesonide shortened the time to recovery (12 vs 15 days), increased the proportion of patients recovering by day 14 (32% vs 22%), and reduced the need for health services (53% vs 59%).

Evidence

Results are statistically significant unless otherwise noted.

- An RCT[1] randomized 1856 symptomatic patients with COVID-19 aged 65 or older, or 50 or older with comorbidities, to 800 µg of inhaled budesonide twice a day for 14 days or usual care.
  - -Mean age was 64, about 80% had comorbidities (most common were hypertension and diabetes), and symptom onset was 6 days prior.
    - —First recovery day was at about 12 days with budesonide versus about 15 days with usual care.
    - —Rates of hospital admission or death were 6.8% with budesonide versus 8.8% with usual care. Results were not statistically different, but analysis suggests a 96% probability that the benefit was real.
  - -Other outcomes improved with budesonide:
    - —The proportion who recovered by 14 days was 32% versus 22% with usual care (number needed to treat [NNT]=10); contact with health services was 53% versus 59% with usual care (NNT=18).
- Another RCT[2] of 800 µg of inhaled budesonide twice a day (for duration of symptoms; median 7 days) or usual care followed 146 (generally younger or lower-risk) adults with COVID-19 symptoms (94% confirmed):
  - -The mean age was 45, there was a median 1 comorbidity per patient, and symptom onset was 3 days prior:
    - —Urgent care or higher-acuity visits were needed by 3% versus 15% with usual care (NNT=9).
    - —The proportion of patients with symptoms present at 14 days was 10% versus 30% with usual care (NNT=5).
- Study limitations included open-label design,[1,2] no placebo arm,[1,2] 1% of study population fully vaccinated,[1] and poor reporting of adverse effects.[1] Studies were conducted before the Omicron variant was identified.

Context

- Systemic corticosteroids reduce mortality in hospitalized patients with COVID-19. Mechanically ventilated patients benefit the most; hospitalized patients not requiring oxygen experience no benefit or harm.[3]
- Management guidelines for COVID-19 outpatients vary regarding inhaled budesonide, from not mentioning it,[4] to not providing recommendations for or against it,[5] to including it as a potential option.[6]
- Cost is about $110 per inhaler.[7]

Implementation

Outpatients with COVID-19 have a growing number of treatments available to them. Antiviral agents (nirmatrelvir-ritonavir) and monoclonal antibodies (eg, sotrovimab) appear to reduce the risk of death or hospitalization,[8,9] but patient eligibility and access vary by jurisdiction. Family physicians can provide inhaled budesonide at the point of care to those not eligible for antiviral agents or monoclonal antibodies.[10] Fluvoxamine is also available, but its benefits are less certain than those of other treatments.[11]

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Competing interests
None declared

References

1. Yu LM, Bafadhel M, Dorward J, Hayward G, Saville BR, Gbinigie O, et al. Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. *Lancet* 2021;398(10303):843-55. Epub 2021 Aug 10. Erratum in: *Lancet* 2021;398(10303):e12. Epub 2021 Aug 19.
2. Ramakrishnan S, Nicolau DV Jr, Langford B, Mahdi M, Jeffers H, Mwasuku C, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. *Lancet Respir Med* 2021;9(7):763-72. Epub 2021 Apr 9. Erratum in: *Lancet Respir Med* 2021;9(6):e55. Epub 2021 Apr 14.
3. RECOVERY Collaborative Group; Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med* 2021;384(8):693-704. Epub 2020 Jul 17.
4. Bhimraj A, Morgan RL, Shumacker AH, Lavergne V, Baden L, Cheng VCC, et al. *IDSA guidelines on the treatment and management of patients with COVID-19.* Arlington, VA: Infectious Diseases Society of America; 2022.
5. COVID-19 Treatment Guidelines Panel. *Coronavirus disease 2019 (COVID-19) treatment guidelines.* Bethesda, MD: National Institutes of Health; 2022.
6. *Guidance for primary care management of adults in the community with suspected or confirmed COVID-19.* Vancouver, BC: BC Centre for Disease Control; 2021.
7. *Prescribe Smart* [website]. Prescribe Smart; 2019. Available from: **https://www.prescribesmart.com**. Accessed 2021 Oct 14.
8. Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. *N Engl J Med* 2022 Feb 16. Online ahead of print.
9. Gupta A, Gonzalez-Rojas Y, Juarez E, Crespo Casal M, Moya J, Falci DR, et al. Early treatment for COVID-19 with SARS-CoV-2 neutralizing antibody sotrovimab. *N Engl J Med* 2021;385:1941-50. Epub 2021 Oct 27.
10. Ontario COVID-19 Drugs and Biologics Clinical Practice Guidelines Working Group. *Clinical practice guideline summary: recommended drugs and biologics in adult patients with COVID-19. Version 10.0.* Toronto, ON: Ontario COVID-19 Science Advisory Table; 2022.
11. Ontario COVID-19 Drugs and Biologics Clinical Practice Guidelines Working Group. *Fluvoxamine: what prescribers and pharmacists need to know.* Ontario COVID-19 Science Advisory Table, University of Waterloo School of Pharmacy; 2022.

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