



Budesonide Bests COVID-19

CLINICAL QUESTION

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

BOTTOM LINE

Early in the pandemic, inhaled budesonide shortened symptom duration and improved recovery rates among higher-risk unvaccinated outpatients with suspected or confirmed COVID-19 infection. However, with vaccines now available, the role of inhaled corticosteroids is less clear. Among younger healthy, vaccinated patients, inhaled steroids do not improve symptom duration or reduce hospitalization.

EVIDENCE

- Results statistically significant unless otherwise noted.

- Most recent and largest meta-analysis:¹ compared budesonide, ciclesonide or fluticasone furoate versus placebo or usual care. Among outpatients [6 randomized, controlled trials (RCTs), 4202 patients]:
 - Symptom relief at 7 days: no difference.
 - Symptom relief at 14 days: 57% versus 50% (PEER calculation), number needed to treat (NNT)=16.
 - Urgent care, emergency department visit, hospitalization: not different.
 - Adverse effects: not different.
 - Limitation: not stratified by lower/higher risk patients or vaccination status.
- Largest RCTs
 - Early pandemic (Nov 2020-March 2021): 1856 symptomatic COVID-19 positive patients aged ≥65, or ≥50 with co-morbidities comparing budesonide 800ug inhaled BID x14 days or usual care.²
 - Mean age 64, ~80% had comorbidities (most common: hypertension and diabetes), symptom onset 6 days prior, 12% had ≥2 vaccine doses.
 - First recovery day: ~12 days budesonide versus ~15 days usual care, difference ~3 days.
 - Hospital admission or death: 6.8% budesonide versus 8.8% (not statistically difference).
 - Other outcomes improved with budesonide:
 - Percent recovered by 14 days: 32% versus 22% (NNT=10), contact with health services: 54% versus 59% (NNT=18).
 - Later in the pandemic (Aug 2021-Feb 2022): 1407 symptomatic COVID-19 positive patients comparing fluticasone furoate 200mcg daily for 14 days or placebo.³
 - Median age 45 years, 65% had ≥2 vaccine doses; symptom onset 5 days prior.
 - Time to recovery: no different.
 - Mean days unwell: ~11days in both group (no difference).
 - Hospitalization, urgent-care visit, emergency room visit or death: 3.7% fluticasone versus 2.1% placebo.
- Primary differences between main RCTs:
 - First RCT:² early pandemic, 12% vaccinated, older patients, high-dose inhaled steroids and open-label.
 - Second RCT:³ later in pandemic, 65% vaccinated, younger, low-dose inhaled steroids and blinded.
- Limitations: Open label,² no placebo arm,² adverse effects poorly reported.²

CONTEXT

- Systemic steroids reduce mortality in hospitalized patients with COVID-19.
 - Greatest benefit in mechanically ventilated patients and no benefit in hospitalized not requiring oxygen.⁴
- Guidelines for management of COVID-19 outpatients variable: recommend against inhaled corticosteroids,⁵ include as potential option,^{6,7} or do not mention.⁸

- Cost per month: Budesonide 800ug BID: ~\$75, fluticasone furoate 200mcg daily: ~\$100.⁹

Updated November 1, 2023 by Samantha Moe, PharmD and G. Michael Allan, MD CCFP.

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