

Use of NSAIDs in patients with COVID-19: what is the evidence?

Key Points:

- There is insufficient evidence that NSAIDs negatively impact morbidity or mortality of COVID-19.
- Health Canada continues to recommend both ibuprofen and acetaminophen for treatment of fever due to COVID-19.¹
- Evidence to date suggests that older people (>60 years of age) and those with underlying medical conditions are at higher risk of severe COVID-19 disease. As NSAIDs should also be used with caution in these populations, it is reasonable to avoid NSAIDs in the elderly and in those with comorbid conditions (e.g., cardiovascular disease, renal disease, chronic respiratory disease). If the use of an NSAID is unavoidable in these patients, it should be at the lowest effective dose and for the shortest duration.
- The [CPhA monograph Nonsteroidal Anti-inflammatory Drugs](#) (NSAIDs) contains detailed information on the contraindications, warning and precautions to consider when recommending or prescribing NSAIDs.²
- The potential impact of corticosteroids on COVID-19 is not within the scope of this statement.
- The COVID-19 situation is evolving and data collection is ongoing. The NSAID evidence will be reviewed as it becomes available and this statement will be updated accordingly.

Background:

March 15, 2020, news agencies reported that France's health minister, Dr. Olivier Véran, tweeted that anti-inflammatory medications "could be a factor in aggravating the [COVID-19] infection" with ibuprofen, a nonsteroidal anti-inflammatory drug (NSAID), and cortisone, a corticosteroid, listed as examples. Dr. Véran indicated that paracetamol (acetaminophen) should be preferentially used to treat fever and that patients should consult their physicians if they are already taking anti-inflammatory medications.³

Proposed risk of NSAIDs:

The mechanism of action of NSAIDs involves inhibiting the cyclooxygenase (COX) enzymes, COX-1 and COX-2, and thereby inhibiting the synthesis of prostaglandins and thromboxane A2 (TXA2). COX-2 is believed to be upregulated in activated human B lymphocytes and required for optimal antibody synthesis. An in vitro study designed to determine whether nonselective NSAIDs affect antibody synthesis found that ibuprofen, ASA, naproxen and acetaminophen inhibited antibody production at pharmacological doses; with ibuprofen having the greatest effect.⁴ A case-control study of 168 children with acute viral infections concluded that NSAID use was associated with an increased risk of empyema (bacterial infection of the pleural space).⁵

Possible benefit of NSAIDs:

The NSAIDs indomethacin and naproxen have both been found to have antiviral properties. Indomethacin was studied in vitro and in animal models and found to have potent direct antiviral activity against SARS-CoV (severe acute respiratory syndrome coronavirus) and CCoV (canine coronavirus) through interference with viral RNA synthesis.⁶ Animal models have shown that naproxen also has antiviral activity against influenza A and B viruses by interfering with the RNA replication process.^{7,8} As COVID-19 virus is single-stranded RNA virus, it has been proposed that naproxen could be "a probable agent for control of widespread novel coronavirus infection".⁹

Discussion:

Further research, including randomized controlled trials, is required to determine the impact of NSAIDs on coronavirus infection and subsequent disease. Confounding variables may appear to show an association between NSAID use and COVID-19 morbidity and mortality and must be taken into consideration, e.g., patients may have been taking NSAIDs to treat comorbid conditions which put them at increased risk of more severe COVID-19 disease; many patients may be self-treating COVID-19 symptoms with NSAIDs but only the most ill present at hospital.

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References

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