The use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with COVID-19

Scientific brief

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Background

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs, and have a wide range of uses. NSAIDs include nonselective cyclooxygenase (COX) inhibitors (such as ibuprofen, aspirin (acetylsalicylate), diclofenac, and naproxen), as well as selective COX2 inhibitors (such as celecoxib, rofecoxib, etoricoxib, lumiracoxib, and valecoxib).

Concerns have been raised that NSAIDs may be associated with an increased risk of adverse effects when used in patients with acute viral respiratory infections, including COVID-19.[1,2] This review aimed to assess the effects of prior and current use of NSAIDs in patients with acute viral respiratory infections on acute severe adverse events (including mortality, the acute respiratory distress syndrome (ARDS), acute organ failure, and opportunistic infections), on acute health care utilization (including hospitalization, intensive care unit (ICU) admission, supplemental oxygen therapy, and mechanical ventilation) as well as on quality of life and long-term survival.

Methods

A rapid systematic review was carried out on 20 March 2020 on NSAIDs and viral respiratory infections using MEDLINE, EMBASE, and WHO Global Database. The review included studies conducted in humans of any age with viral respiratory infections exposed to systemic NSAIDs of any kind. All studies on COVID-19, the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) were included irrespective of their sample size.

Review of the evidence

A total of 73 studies were included (28 studies in adults, 46 studies in children, and one study in adults and children). All studies were concerned with acute viral respiratory infections or conditions commonly caused by respiratory viruses, but none specifically addressed COVID-19, SARS, or MERS. The review showed very low certainty evidence on mortality among adults and children.[3] Effects of NSAIDs on the risk for ischemic and haemorrhagic stroke and myocardial infarction in adults with acute respiratory infections are unclear.[4,5] Moderate to high certainty evidence showed little or no difference between ibuprofen and acetaminophen (paracetamol) among children with fever with regard to effects on death from all causes, hospitalization for any cause, acute renal failure, and acute gastrointestinal bleeding.[6-9] Most studies report that no severe adverse events occurred, or that only mild or moderate adverse events were observed. [10-13] There was no evidence regarding the effects of NSAID use on acute health care utilization, explicit quality of life measures, or long-term survival.

Limitations

No direct evidence from patients with COVID-19, SARS, or MERS was available. Therefore, all evidence included should be considered indirect evidence with respect to the use of NSAIDs prior to or during the management of COVID-19. Only one randomized controlled trial included a sufficiently large number of participants to identify rare severe adverse events. The remaining evidence derives from smaller randomized controlled trials, which are likely to be underpowered for detecting rare severe adverse events, and from case-control and cohort studies with methodological limitations. Studies included not only patients with confirmed viral respiratory infections and known pathogens, but also those with conditions commonly caused by respiratory viruses, such as upper respiratory tract infections and fever in children. It is likely that not all participants had viral respiratory infections. NSAIDs are a diverse set of drugs with different risk profiles for different populations and conditions. Not all studies distinguished between different types of NSAIDs. Some of the older studies are likely to have included patients taking specific NSAIDs that are no longer available owing to adverse effects.

Conclusion

At present there is no evidence of severe adverse events, acute health care utilization, long-term survival, or quality of life in patients with COVID-19, as a result of the use of NSAIDs.

References

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WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this scientific brief will expire 2 years after the date of publication.

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