NICE advice

COVID-19 rapid evidence summary: Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19

Evidence summary
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Key messages

The content of this evidence review was up-to-date on 20 April 2020. See summaries of product characteristics (SPCs), British national formulary (BNF) or the MHRA or NICE websites for up-to-date information.

In March 2020, the French Health Ministry issued advice to avoid using non-steroidal anti-inflammatory drugs (NSAIDs) to treat symptoms of COVID-19 because these medicines might aggravate the infection. In response to these concerns, NHS England issued a Central Alerting System (CAS) alert, in which the Medical Director, Professor Stephen Powis, gave interim advice that people who are currently on NSAIDs for medical reasons (such as arthritis) should not stop them and advised that the MHRA and NICE would review this topic.

NICE has produced an evidence review on acute NSAID use for COVID-19, which informed a subsequent NHS England and NHS Improvement policy statement. The policy states that, when patients, carers or healthcare professionals are starting treatment for fever and/or pain in adults or children with confirmed or suspected COVID-19, all treatment options should be considered and selected based on the greatest benefit compared to potential harms using each medicine's product information (see the NICE COVID-19 guideline on managing symptoms (including at end of life) in the community).

A proportion of people taking long-term NSAIDs for other conditions may be at higher risk of developing COVID-19 or more severe COVID-19 because of their chronic condition or concomitant medication; for example, people with rheumatoid arthritis taking immunosuppressants.

The purpose of this review is to assess the best available evidence to determine:

1. If long-term use of NSAIDs is associated with an increased risk of developing COVID-19.
2. If long-term use of NSAIDs is associated with an increased risk of developing more severe COVID-19.

For the purposes of this evidence review, long-term use of NSAIDs is defined as a regular, moderate dose of NSAIDs for at least 2 weeks, normally for chronic conditions.

A literature search identified 173 references, which were screened using their titles and abstracts. Thirteen references were obtained in full text and assessed for relevance; however, none were suitable for inclusion. This means that no evidence from published scientific studies was found to determine whether long-term use of NSAIDs is related to increased risk of developing COVID-19 or increased risk of more severe COVID-19.

There is no evidence to suggest that people taking NSAIDs for a long-term condition should be advised to stop treatment in the context of COVID-19. Gastrointestinal, respiratory, cardiovascular and renal adverse effects are listed among the possible adverse effects of NSAIDs in the BNF. COVID-19 may also lead to respiratory, cardiovascular and renal complications (BMJ Best Practice). In addition, certain comorbidities (such as diabetes, hypertension, cardiovascular disease and chronic respiratory disease) increase the risk of more severe COVID-19 (The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team 2020).

Factors for decision making

Effectiveness and safety

The searches performed for the evidence review found no evidence to determine if there is any increased risk of developing COVID-19 due to long-term use of NSAIDs, or if long-term use of NSAIDs can lead to an increased risk of developing more severe COVID-19.

Discussion and limitations of the evidence

Concerns over using NSAIDs for COVID-19 were raised by the French Health Ministry after 4 people with COVID-19 and no underlying health problems reportedly developed serious symptoms after using these medicines (Day 2020). On 14 March 2020, the French Health Minister issued advice to avoid using NSAIDs for COVID-19 based on a 2019 evaluation by the French National Agency for Medicines and Health Products Safety, which suggested that infection due to chickenpox (varicella) and some bacterial infections could be made worse by ibuprofen and ketoprofen.

On 18 March 2020, the EMA issued a press release stating there is currently no scientific evidence establishing a link between ibuprofen and worsening of COVID-19. The EMA is monitoring the situation closely and will review any new information that becomes available on this issue in the context of the pandemic. On 14 April 2020, the MHRA issued a similar statement, concluding there is currently insufficient evidence to establish a link between use of ibuprofen and susceptibility to contracting COVID-19 or the worsening of its symptoms..

Several scientists and senior doctors have expressed their views in the medical press about whether NSAIDs should be used or not in people with COVID-19, with all agreeing that the evidence is uncertain in this population (Day 2020, FitzGerald 2020 and Little 2020). Their opinions are generally based on studies in which NSAIDs were used to treat symptoms of pain and fever in people with other infections (not COVID-19), or on experimental studies.

In 2012, the MHRA advised that some non-selective NSAIDs, such as diclofenac, are associated with increased cardiovascular risk compared with naproxen and low-dose ibuprofen (up to 1,200 mg per day). This increased risk is particularly apparent with long-term use of high doses and in people who are already at high risk of cardiovascular disease. The MHRA also stated that NSAIDs (including COX-2 inhibitors) may rarely precipitate renal failure, and vulnerable (particularly elderly) people may be at increased risk.

COVID-19 may also lead to cardiovascular and renal complications (BMJ Best Practice). This suggests that NSAID use may not be appropriate in some people with COVID-19.

Conclusion

No evidence was found to suggest that people taking NSAIDs for a long-term condition should be advised to stop treatment in the context of COVID-19. Stopping or switching NSAID treatment could have a negative impact on some people.

Clinicians should follow advice in the BNF and the NICE Clinical Knowledge Summary on issues around prescribing NSAIDs. When considering an NSAID, individual risk factors for adverse effects should be taken into account, including any contraindications, drug interactions, medical history, and any monitoring requirements. The lowest effective dose of an NSAID should be used for the shortest period of time required to control symptoms and the need for long-term treatment should be reviewed periodically.

At this time, policy decisions on whether NSAIDs should be used long-term in people with confirmed or suspected COVID-19 will need to take into account the risk of adverse effects of NSAIDs, the risk of complications of COVID-19, and the presence of comorbidities that increase the risk of more severe COVID-19.

See the full evidence review for more information.

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