

OPINION PIECE

Are Antipyretic Medications Compatible with SARS-CoV-2 Vaccines?

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Vaccine hesitancy is an issue that should be addressed to maximize protection from serious COVID-19. SARS-CoV-2 vaccination hesitancy in the United States ranges from 21 to 42%. [1] Fear of adverse effects and concerns about safety are some of the main reasons for refusing to be immunized. [2, 3] Vaccinations can induce adverse reactions, such as injection site tenderness, headache, myalgia, and arthralgia. Fever is occasionally a systemic side effect. [4] People often self-treat these problems with antipyretic and/or analgesic drugs; physicians sometimes recommend these as well.

The Centers for Disease Control and Prevention recommend avoiding antipyretic or analgesic medications prophylactically before immunization. [5] However, if inflammatory manifestations develop after vaccination, such as fever, pain, or swelling, these medications can be utilized, if approved by a physician. [5] Nevertheless, self-administration of over-the-counter pharmaceuticals is widely prevalent and leads to the question of whether the antipyretic drugs hamper vaccine immunogenicity.

The mRNA vaccines enhance specific T-cell activity, stimulate cytokine production, and generate antibodies that can bind and neutralize the virus. This immune reaction can be impeded by antipyretic agents, such as non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, or aspirin. [6] In a randomized trial,

serotype-specific IgG geometric mean concentrations (GMC) were measured after pneumococcal vaccination, with acetaminophen administered concomitantly in one group and delayed in another. [7] The IgG levels decreased in both, when compared to control population, but reached statistical significance ($P < 0.0125$) only in the concomitant group. The researchers catalogued decreased immune titers in five out of 13 serotypes of the vaccine. Hence, when antipyretic drugs are given a few hours after vaccination, there appears to be less impact on antibody titers. It is unknown whether the antibody response reduction is clinically significant since protective levels of antibodies remained present in either case. It remains to be established whether antipyretic pharmacotherapies affect long-term T-cell-mediated immunity.

The effect of duration and timing of antipyretic therapy on COVID-19 vaccine immunogenicity is yet to be defined. Vaccine acceptance might be enhanced by increased awareness of the availability of antipyretic therapies to diminish potential post-vaccination side-effects. Additionally, NSAID prophylaxis may offer protection against vaccine-related pericarditis and/or myocarditis. [8] Research may reveal that it is unnecessary to avoid these drugs if immune responses are satisfactory despite their use. However, currently, it is prudent to discourage prophylactic antipyretic medication before vaccination.

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