Corticosteroids and COVID-19 vaccine: a challenging issue

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To the editor;

In the pandemic era of COVID-19 vaccines, patients on immunosuppressive medications need special considerations. Immunosuppression can disturb the effectiveness of the vaccine responses. Thus establishing a proper recommendation for vaccination in these patients would be challenging. The immunosuppressive effects of corticosteroids (CS) vary and depend on its duration of use and doses. Doses more than 40 mg/ day prednisone for more than one week or [?] 20 mg of prednisone or equivalent for [?] two weeks, induce immunosuppression (1, 2). Till now the current recommendations for COVID-19 vaccines and CS administration are mostly based on the available evidence for killed vaccines (e.g., influenza).

Choosing the best time to increase the efficacy of vaccination is important in immunosuppressed patients. Also each country's vaccine policy is important to set out vaccination times in these specific groups. In some countries, especially developing countries, the COVID-19 vaccination schedule is not adjustable by the patients or physicians, and selecting a particular time window for the best efficacy of immunization is impossible. However, if the vaccination schedule is not adaptable, vaccination is recommended with any vaccine when available. If the schedules are adjustable, the following issues are considered:

Evidences showed that with the dose of up to 20 mg/day prednisone or equivalents, the response to inactivated vaccines could not be suppressed, and these patients can receive vaccine safely. Patients treated with prednisone at a dose of less than 20 mg/day are not immunocompromised and have sufficient immune response (1, 2).

The immunosuppressive doses of CS are [?] 20 mg/day for [?] 2 weeks, or $>$ 40 mg prednisone for $>$ 1 week. The ideal time for vaccination in this group is one month after discontinuation of the CS treatment to elicit an adequate immune response (1). If it was not possible to end the CS treatment, a vaccine should be given when receiving the lowest dose of CS. For example, the dose of CS can be reduced to less than 20 mg with or without the addition of steroids sparing drugs (e.g., azathioprine) , and then at least two weeks after vaccination, the dose of the drug returns to the previous state (3).

Suppose the patient is a candidate for CS therapy with doses of [?] 20 mg prednisone for [?] two weeks or $>$ 40 mg prednisone for $>$ 1 week. In this case, it is suggested that vaccine be administered at least 2 weeks before immunosuppression initiation because two weeks are required to develop an immune response (2). But if the CS administration cannot be withheld after vaccination because of disease flare or if the patient may not have access to the vaccine with the recommended interval, we recommend ordering the vaccine considering a suboptimal response to the vaccine.

Corticosteroid pulse therapy does not cause immunodeficiency, and the vaccine should not be delayed (4).

If a country's vaccination policy is such that the clinicians can choose the type of vaccine, it is better to choose a vaccine based on the underlying disease and the number of days that they can reduce the steroid

dose. If the patient's corticosteroid dose cannot be reduced for an extended time and there is a risk of disease flare, it is better to use vaccines with less interval time between two doses.

The immunogenicity of a single dose of some vaccines is likely to be acceptable in patients who have natural antibodies and are infected before. In the future, only one dose of the vaccine may be sufficient in these patients (5, 6). Therefore, it is better to adjust vaccination in this group of patients to gain the most effect from one of the two doses. It is better to focus on boosting the impact of at least one of the vaccine doses.

For patients under CS therapy who are immunocompromised, we suggest using a highly effective vaccine. The best vaccines with the best efficacy in this group of patients are not determined. These vaccines may be with mRNA or vector-based systems. Further clinical trial studies are required. These considerations can be used as long as more data are available.

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