letter to the editor

Is It Safe to Use Long-Acting G-CSF for Febrile Neutropenia Prophylaxis in COVID-19 Pandemic?

TO THE EDITOR:

We have read the article of Lasagna et al[1] with great interest. First of all, we would like to thank them for drawing attention to this issue. After three patients with COVID-19 in whom Nawar et al[2] described a worsening of their clinical condition after administration of granulocyte colony-stimulating factor (G-CSF), one patient with a similar scenario was also reported by Taha et al.[3] A 47-year-old male patient using immunosuppressive agents for renal transplantation worsened 6 hours after filgrastim administration, and he was intubated because of respiratory failure. It cannot be said with certainty that the cause of clinical deterioration in all these four patients was the use of G-CSF, but it should be accepted that there are some concerns related to G-CSF.

Recently, concerns about the use of G-CSF during the COVID-19 pandemic have also been acknowledged by ASCO and the European Society for Medical Oncology; it was emphasized that G-CSF should be used with caution as its use may increase pulmonary infiltration.[4,5] Warnings about therapeutic use will likely reduce the use of G-CSF in patients with COVID-19.

The main issue we want to draw attention to is which formulation should we choose for prophylaxis? Considering that concerns about therapeutic uses of G-CSFs are generally accepted, what will happen if a patient using long-acting G-CSF becomes infected with severe acute respiratory syndrome coronavirus 2 during this period? As it is known, long-acting G-CSFs have a self-regulating mechanism of action, and as the neutrophil count increases, their elimination increases and blood levels decrease. Since they increase the neutrophil count in a more balanced way compared with short-acting G-CSFs, they may not have any effect on the clinical situation. However, there is evidence that G-CSFs do not only affect neutrophils but may also affect cells and cytokine pathways that play a role in the immune system.[6] That is, potential lung damage because of G-CSF may not be related to neutrophil count alone but may also be associated with activation or inactivation of various cytokines. In this context, since a patient using prophylactic long-acting G-CSF will be exposed to G-CSF in the blood circulation for a long time, if infected with severe acute respiratory syndrome coronavirus 2 during this period, the clinical condition may worsen like a patient using therapeutic G-CSF during COVID-19. There is no evidence for the effect of these hypotheses on COVID-19, but until these issues are clarified, it will probably be more appropriate to choose short-acting G-CSFs for febrile neutropenia prophylaxis.

Of course issues such as health policies of countries, cost-effectiveness, and insurance coverage of patients are also important for drug selection. For example, it is accepted that a single dose of pegfilgrastim in primary prophylaxis in the United States is more cost-effective than filgrastim administered daily (compared with more than 10 doses of filgrastim).[7] In addition, the fact that long-acting G-CSFs are single-use per cycle provides convenience for patients. Despite these advantages, considering the potential concerns during the pandemic period, G-CSF selection according to clinical considerations seems to be a more appropriate approach. As a matter of fact, the Update Committee formed by ASCO in 2015 stated that clinical considerations, not costs, should guide G-CSF prophylaxis.[7] If it is desired to reduce the patients' coming to the hospital for injections, the patients and their relatives can be educated about the injection administration. When any symptoms related to COVID-19 develop, it may be advised to stop the injection and reach the physician urgently.

Consequently, given the potential risks associated with therapeutic G-CSF use during the COVID-19 pandemic, the use of long-acting G-CSF preparations in prophylaxis should be carefully considered. Considering that the pandemic will continue for a while, it is clear that the prophylaxis indications and which agent to choose should be clarified in the near future with strong evidence.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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