

LETTER

Isotretinoin in acne treatment during the coronavirus disease 2019 (COVID-19): A retrospective analysis of adherence to therapy and side effects

Dear Editor,

We read with great interest the letter by Abdelmaksoud et al¹ and we completely agree with authors that till further studies on the pathogenesis of COVID-19 infection, isotretinoin should be utilized at low dose with proper care of the nasal mucosa.

Isotretinoin is an oral retinoid approved for the management of severe cases of acne vulgaris, and recently utilized for mild to moderate acne.²

COVID-19, is a respiratory disease caused by the SARS-CoV-2 virus and it was stated a pandemic on 11 March 2020. Advanced age is recognized as a risk factor for a severe infection, however those of any age may suffer from severe disease from COVID-19.³

According to the British Association of Dermatologists isotretinoin could theoretically increase the risk of COVID-19 viral load because of its drying effect on the mucous membranes (<https://www.bad.org.uk/shared/get-file.ashx?itemtype=document&id=6661>).

Most isotretinoin side effects are skin related and associated with xerosis. Dry nasal membrane was also observed in two-thirds of patients. Isotretinoin treatment modifies nasal mucociliary clearance considerably, reduces normal and regenerated mucosal thickness, triggering severe inflammation.⁴

Angiotensin-converting enzyme 2 (ACE2) is the host receptor for SARS-CoV-2 entrance. As reported by Abdelmaksoud ACE2 receptor expression was found in the basal layer of the epithelium in nasal mucosa. Disruption of nasal mucosa, uncovering the basal layer, perhaps could increase nasal mucosa invasion by coronavirus.¹

However, data are still sparse and controversial. Sinha et al evaluated the ACE2 expression levels in control and drug-treated groups for the top significant drugs (vorinostat, panobinostat, and isotretinoin) among the 672 clinically approved drugs. According to their data the top ACE2 downregulator is isotretinoin.⁵

In the wake of these evidences, we retrospectively reviewed 34 patients in treatment with isotretinoin from March to August 2020 in our outpatient clinic in Naples (11 males and 23 females; median age 22.5 years, range 18 to 38; medium duration of isotretinoin treatment 5 months, range 2 to 8 months; medium dosage 22.7 mg/die). Female patients did not present any sign of hyper-androgenism.

16/34 patients (47%) reported nasal dryness. Overall, four of the 34 patients (11.7%) reported cough, rhinorrhea, of them only two patients (5.8%) reported a temperature not over 37.5 and up to 2 days. No patients reported to had been diagnosed with COVID-19.

6/34 patients (17.6%) declared to have suspended the therapy prematurely: 1/6 because of side effects related to the drug and 5/6 because of the fear of an increased risk of being infected by COVID-19. In particular, 1/5 started the therapy in the month of December, 2/5 in February and 2/5 in March and interrupted the therapy in March 1/5 (20%), April 3/5 (60%), and May 1/5 (20%).

We observed that 14.7% of patients prematurely interrupted the therapy in the months of Italian lockdown (March to May 2020) because of the fear of COVID-19. The lockdown period in fact has been characterized by a drastic reduction in the number of accesses in dermatological departments and different measures, such as the implementation of teledermatology, have been applied in order to limit coronavirus infection spread.⁶ Moreover, it is likely that there is an inclination of the patients to overestimate the incidence and severity of side effects of oral isotretinoin.⁷

According to our survey 47% of the patients reported nasal dryness. In the light of this data, we believe that a nasal moisturizer should be recommended during the treatment.

Our sample is mostly composed of non-hyperandrogenic females. This data could justify that patients do not report serious signs of disease. In fact, according to Cadejani et al the frequency of several common clinical symptoms of COVID-19 is significantly more pronounced in males and hyperandrogenic females than their non-hyperandrogenic counterparts.⁸

Finally, although the correlation between isotretinoin and the pathogenesis of COVID-19 infection is not clear, we believe is essential to start with low dose of isotretinoin associated to proper care of the nasal mucosa for isotretinoin patients to reduce side effects, and to improve adherence to therapy.

We believe that the absence of correct information about the treatment and the possible side effects may discourage patients, leading them to poor adherence. An adequate communication about the correct use of the medication and its possible correlation to COVID-19 infection could be a good strategy to improve the adherence to the treatment.⁹

The limit of our survey is that it is based on patients' statements. However, further studies on larger samples are needed to assess the possible effect of isotretinoin on SARSCoV-2 infection.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS


Marianna Donnarumma conceived the work and wrote the manuscript. Mariateresa Nocerino wrote the manuscript and analyzed data. Wanda Lauro wrote the manuscript and revised it critically. Maria Carmela Annunziata and Claudio Marasca drafted the work and ensured the accuracy of any part of it. Gabriella Fabbrocini approved the version to be published.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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