Critical Care

LETTER

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Study find that COVID ARDS was associated with a low risk for possible or proven PCP: still true after dexamethasone use

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Razazi et al. conclude that in their study of patients with COVID acute respiratory distress syndrome (ARDS), they found a low risk for possible or proven *Pneumocystis jirovecii* pneumonia (PCP) [1]. Their findings are in accordance with two smaller studies in France [1] retrieving a low risk of pneumocystis colonization in COVID-19 patients [1]. In their limitation section nothing was said about the fact that none of these COVID patients did receive dexamethasone [1]. We would like to comment as indeed the adjunction of dexamethasone has completely changed the occurrence of COVID-19-associated opportunistic infections including PCP [2]. Coinfection of PCP and COVID-19 has been reported in some patients with COVID-19 till now [2], in which most of them received immunosuppressive therapies, such as corticosteroids [2]. The case reports and reviews are extremely numerous with the use of dexamethasone regarding co-infection of COVID-19 and PCP [2]. Chong et al. reviewed 12 cases of COVID-19 and PCP coinfection [3]. Accordingly, all PCP infections were reported in critically ill patients with COVID-19, which most of them were upon long-term exposure to immunosuppressants (91.7%, 11/12), such as high-dose corticosteroids [3]. Numerous cases were also diagnosed after post-mortem examination [3]. Since PCP is usually reported in patients with T-cell immunodepression, less attention has been paid to PCP in non-immunocompromised intensive care unit (ICU) patients although it accounts for 7% of the co-infections reported in those admitted with Influenza [4]. After the use of dexamethasone in COVID-19 ARDS, these researchers did find an unexpectedly high proportion of ICU COVID-19 patients detected with PCP (10/108 patients; 9.3%) [4]. According to their unexpectedly high proportion of pneumocystis-positive pulmonary samples observed in ICU COVID-19 patients and based on their findings, they advocate systematically searching for pneumocystis in deep respiratory specimens in these patients [4]. They believe that this strategy may be useful in limiting enhanced inflammation due to the presence of pneumocystis in the lung and avoiding inter-patient pneumocystis transmission [4]. It stands to reason that the statement by Razazi et al. that in their study of patients with COVID ARDS, they found a low risk for possible or proven PCP is no longer valid as the systematic use of dexamethasone has increased to an unexpectedly high proportion of ICU COVID-19 patients detected with *P. jirovecii* [4]. It remains somewhat strange that Razazi et al. were not expecting high levels of co-infection of COVID ARDS and PCP after the systematic use of dexamethasone.

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Authors' response

Romain Arrestier, Armand Mekontso-Dessap, Francoise Botterel and Keyvan Razazi

To the Editor,

We thank Honore and colleagues for their comments on our research letter about low risk of *Pneumocystis* pneumonia in COVID-19 patients with acute respiratory distress syndrome (ARDS).

We point out in the discussion that patients of our cohort were included before the systematic use of dexamethasone, but we may not have sufficiently discussed it.

Enrolment of patients during the first wave is indeed a limitation of our study because of the lower use of corticosteroid therapy compared to the other waves. To explore further this potential bias, we analysed 239 consecutive COVID-19 patients, hospitalized in our intensive care unit during the following waves from 26th May 2020 to 11th April 2021 (*Anticovid study Clinical trials NCT04433105*). All were treated with corticosteroids, 39 (16.3%) with tocilizumab and 29 (12.1%) were immunocompromised.

Of these, 73 had a *Pneumocystis* examination, including 131 PCR and 107 direct examinations (43 May Grunwald Giemsa stainings and 64 Grocott colorations) which were all negative. Only three patients (4%) had a positive PCR with a cycle threshold range of 35.5–37. All were classified as *Pneumocystis* colonization. Two of them did not have any pre-existing risk factors besides 10 days of corticosteroid for COVID-19 and had a negative β-D-glucan. One patient with liver transplantation and long-term corticosteroid therapy and calcineurin inhibitor treatment had a positive PCR with only one low titer positive β-D-glucan (178 pg/mL); he was classified as P*neumocystis* colonization, because his state improved without Trimethoprim-sulfamethoxazole treatment.

These findings are consistent with the finding of Alanio et al. [4] who found 9.3% of *Pneumocystis* positive RT-PCR. We would like to highlight that when discussing *Pneumocystis jirovecii* it is important to differentiate *Pneumocystis* pneumonia and *Pneumocystis* colonization. In the study of Alanio et al., none of the ten patients had *Pneumocystis* pneumonia (PCP) criteria (i.e. positive direct examination for proven PCP or positive RT-PCR with 2 positive β-D-glucan for possible PCP [5]) and were identified as "carriers". Only 4 of them were treated with prophylactic dose of co-trimoxazole without evident effect on mortality.

All these data are consistent and the statement that *Pneumocystis* pneumonia (PCP) risk is low in COVID-19 ARDS patients is still true in the "era of dexamethasone", whereas colonization seems to be higher than in the first wave but not associated with mortality. However, further studies are needed to explore if colonized patients have a higher risk of mortality.

Abbreviations

ARDS: Acute respiratory distress syndrome; PCP: *Pneumocystis jirovecii* Pneumonia; ICU: Intensive care unit.

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Authors' contributions

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