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Low-Dose Cotrimoxazole Administered in Hematopoietic Stem Cell Transplant Recipients as Prophylaxis for *Pneumocystis jirovecii* Pneumonia Is Effective in Prevention of Infection due to *Nocardia*

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Although high-dose cotrimoxazole (trimethoprim-sulfamethoxazole [TMP/SMX]) is an effective treatment for systemic nocardiosis, the effect of low-dose TMP/SMX on disease prevention has not yet been clarified. Previous studies performed in solid organ transplantation recipients have shown that TMP/SMX when administered as *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis has no effect on prevention of nocardiosis [1]. On the contrary, Molina et al. [2] observed a significant increase in the incidence of nocardiosis among recipients of allogeneic hematopoietic stem cell transplant when TMP/SMX was replaced by atovaquone for PJP prophylaxis. The authors assumed that low-dose TMP/SMX has a significant impact in prevention of infection due to *Nocardia*. However, the assumptions raised by Molina et al. [2] have been criticized by other experts. Interestingly, in this report most cases occurred during a certain period of time, thus raising the possibility of an airborne *Nocardia* outbreak [3]. Although infection due to *Nocardia* occurs sporadically, several previous reports have raised the possibility of *Nocardia* outbreaks affecting bone marrow transplant units [4].

A retrospective review of patient medical files in our BMT Unit was performed with the aim to identify transplant recipients with infection due to *Nocardia*. Diagnosis of infection due to *Nocardia* was based on culture of blood, sputum, and/or biopsy material. Nocardiosis occurred in 3 of 164 consecutive patients treated with allogeneic stem cell transplant between January 2011 and December 2018. Administration of low-dose TMP/SMX (1 double-strength tablet 160/800 mg 3 times weekly on alternate days) was the standard policy for PJP prophylaxis. Twenty-six patients did not receive TMP/SMX because of suspected adverse reactions, mainly skin eruptions. TMP/SMX was substituted with intravenous pentamidine or atovaquone. Nocardiosis occurred in 3 of these 26 non–TMP/SMX-treated patients while they were on treatment for active graft-versus-host disease with systemic corticosteroids. On the contrary, no infection due to *Nocardia* was observed in the group of 138 patients who received low-dose TMP/SMX for PJP prophylaxis (P = .003). There was a trend for increased incidence of nocardiosis among the group of patients treated with systemic steroids for active graft-versus-host disease (P = .08). In multivariate analysis the only parameter statistically associated with decreased incidence of infection due to *Nocardia* was administration of low-dose TMP/SMX. Moreover, our data do not suggest the possibility of an outbreak because there was no clustering of infectious episodes in time. The 3 cases of nocardiosis among our patients occurred in 2012, 2013, and 2015, respectively.

In conclusion our data support the hypothesis, raised by others, that low-dose TMP/SMX administered for PJP prophylaxis has a significant impact on prevention of *Nocardia* infection. TMP/SMX should be preferred over atovaquone or pentamidine for PJP prophylaxis because there is a significant likelihood of a prophylactic effect on other microorganisms besides *Pneumocystis*. For patients not treated with low-dose TMP/SMX, suspicion of systemic nocardiosis should be raised during periods of steroid administration and in the presence of certain findings, including subcutaneous or lung nodules and/or brain abscess.

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