

Primary Prophylaxis with Triazoles for Fungal Infections in HIV Patients with Low Absolute CD4 Count: a Meta-analysis of Randomized Controlled Trials

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Abstract

Background Fungal infections are a major cause of mortality and morbidity in HIV patients. These infections range from mucosal involvements to deep mycoses.

Methods We searched PubMed and EMBASE databases for randomized controlled trials (RCT) on triazoles for primary prophylaxis in HIV patients using the search term “HIV AND (fluconazole OR itraconazole OR posaconazole OR voriconazole OR isavuconazole) AND prophylaxis AND randomized controlled trial [Publication Type]” and found 27 results. Both authors filtered the results independently by titles, abstracts and full text. Seven papers met the inclusion criteria.

Data extraction and analysis was carried out using RevMan 5.3 software. Four outcomes were selected- mucosal candidiasis, deep fungal infections, adverse drug reactions and death. Outcome analysis was carried out in two subgroups- fluconazole and itraconazole, using random effect models.

Results The total number of subjects was 4535, among them 2271 received a triazole drug and 2264 received placebo. Included studies used different cut-off for absolute CD4 count, median being 200 cells/ μ L.

The odds-ratio of developing mucosal candidiasis was 0.42 (0.21-0.83) for triazole drugs, the overall effect being $Z=2.49$ ($P=0.01$). Sub-group analysis showed 0.31 (0.10-0.96) odds-ratio for fluconazole group, and 0.59 (0.33-1.05) odds-ratio for itraconazole group. Heterogeneity was high ($I^2=89\%$) probably due to different cut-offs for absolute CD4 count.

The odds-ratio of developing deep fungal infection was 0.27 (0.15-0.50). The overall effect was $Z=4.22$ ($P<0.0001$). The odds-ratio in the fluconazole group was 0.29 (0.10-0.86) and in the itraconazole group it was 0.22 (0.10-0.50). Heterogeneity was low ($I^2=19\%$).

Analysis of adverse reactions showed no significant difference between drugs and placebo, overall effect being $Z=0.31$ ($P=0.76$). The odds-ratio was 1.04 (0.79-1.37) and heterogeneity was $I^2=0\%$.

There was no significant mortality benefit for the drugs. Odds-ratio for death was 0.94 (0.68-1.28) and overall effect was $Z=0.41$ ($P=0.68$). Heterogeneity was $I^2=63$

Conclusion Primary prophylaxis with triazole drugs have the benefit of preventing mucosal candidiasis (fluconazole better) and deep fungal infections (itraconazole better). Both drugs are well tolerated, but none of them have any mortality benefit.