INTISARI

Latar belakang: Penelitian terapi *preemptive* anti-CMV pada penderita HIV menunjukkan hasil yang tidak konsisten. Efikasi dan keamanan terapi *preemptive* pada penderita HIV dengan viremia CMV belum diketahui.

Tujuan: Telaah sistematis ini dilakukan untuk mengevaluasi efikasi dan keamanan terapi *preemptive* dalam mencegah penyakit CMV pada populasi penderita HIV.

Metode: Pencarian literatur dilakukan melalui penelusuran *database* MEDLINE/PubMed dan CENTRAL (hingga Desember 2020). Uji random terkontrol, uji random terkontrol kuasi, dan uji observasional mengenai terapi *preemptive* anti-CMV dibandingkan plasebo atau tanpa terapi pada penderita HIV berusia ≥13 tahun diinklusi pada penelitian ini. Dua penulis secara independen menilai risiko bias dan mengekstraksi semua data luaran dari tiap studi. Analisis dilakukan dengan menggunakan model efek random dan hasil dinyatakan sebagai rasio risiko (RR) dengan interval kepercayaan (IK) 95%. Analisis sensitivitas diterapkan apabila terdapat heterogenitas studi yang diinklusi. Analisis subgrup dilakukan berdasarkan jenis studi.

Hasil utama: Sebanyak 10 studi diinklusi pada penelitian ini, terdiri atas 6 uji random terkontrol (2135 partisipan) dan 4 studi kohort obeservasional (395 partisipan). Lima dari enam uji random terkontrol dilakukan pada periode sebelum aplikasi klinis *highly active antiretroviral therapy* (HAART). Pemberian terapi *preemptive* tidak berhasil menurunkan kejadian penyakit CMV (RR 0,84, IK 95% 0,59-1,18), namun dapat menurunkan angka kematian semua kausa (RR 0,85, IK 95% 0,74-0,97) dengan kualitas bukti ilmiah rendah. Kejadian efek samping neutropenia meningkat secara bermakna (RR 2,47, IK 95% 1,12-5,45) dengan kualitas bukti ilmiah sedang. Analisis sensitivitas dilakukan berdasarkan 1) eksklusi studi pre-HAART dan studi dengan obat yang telah ditarik serta 2) eksklusi studi dengan risiko bias yang tinggi atau serius. Analisis subgrup dilakukan untuk tiap luaran berdasarkan jenis studi, baik uji random terkontrol maupun studi observasional.

Kesimpulan: Bukti ilmiah dari studi yang diinklusi pada telaah sistematis ini belum cukup untuk merekomendasikan pemberian terapi *preemptive* anti-CMV pada pasien terinfeksi HIV. Pemberian HAART dapat mempengaruhi luaran penderita HIV dengan viremia CMV, sehingga diperlukan uji random terkontrol pada periode HAART untuk mengetahui efikasi dan keamanan terapi *preemptive*.

Kata kunci: infeksi *human immunodeficiency virus,* infeksi sitomegalovirus, terapi *preemptive antisitomegalovirus, highly active antiretroviral therapy*

ABSTRACT

Background: Research on anti-CMV preemptive therapy in HIV patients has shown inconsistent results. The efficacy and safety of anti-CMV preemptive therapy in HIV-infected patients with CMV viremia are unknown.

Objective: This systematic review was conducted to evaluate the efficacy and safety of preemptive therapy for preventing CMV disease in a population with HIV infection.

Methods: Literature searching was carried out through the MEDLINE/PubMed and CENTRAL database searches (until December 2020). Randomized controlled trials, quasi-randomized controlled trials, and observational trials of anti-CMV preemptive therapy versus placebo or no therapy in HIV patients ≥13 years of age were included in this study. Two authors independently assessed the risk of bias and extracted all outcome data from each study. The analysis was performed using a random-effects model and the result was expressed as a risk ratio (RR) with a 95% confidence interval (CI). Sensitivity analysis was applied when there was heterogeneity of the included studies. Subgroup analysis was performed by study type.

Main results: A total of 10 studies were included in this review, consisting of 6 randomized controlled trials (2135 participants) and 4 studies of the observational cohort (395 participants). Five of the six randomized controlled trials were performed in the period before clinical application of highly active antiretroviral therapy (HAART). Preemptive therapy did not reduce the incidence of CMV disease (RR 0.84, 95% CI 0.59-1.18), but it could reduce the all-cause mortality rate (RR 0.85, CI 95% 0.74-0.97) with low quality of evidence. The incidence of neutropenia as an adverse effect increased significantly (RR 2.47, 95% CI 1.12-5.45) with moderate quality of evidence. Sensitivity analyzes were performed based on 1) exclusion of pre-HAART studies and studies with withdrawn drugs and 2) exclusion of studies with a high or serious risk of bias. Subgroup analysis was performed for each outcome based on the type of study, both randomized controlled trials and observational studies.

Conclusion: The scientific evidence from the studies included in this systematic review was insufficient to recommend the administration of anti-CMV preemptive therapy in HIV-infected patients. HAART administration can affect the outcome of HIV patients with CMV viremia, therefore, randomized controlled trials in the HAART period are needed to elucidate the efficacy and safety of preemptive therapy.

Keywords: human immunodeficiency virus infection, cytomegalovirus infection, anticytomegalovirus preemptive therapy, highly active antiretroviral therapy