Discontinuation of prophylaxis for *Pneumocystis carinii* pneumonia was safe after highly active antiretroviral therapy

Lopez Bernaldo de Quiros JC, Miro JM, Peña JM, et al., and the Grupo de Estudio del SIDA 04/98. **A randomized trial of the discontinuation of primary and secondary prophylaxis against *Pneumocystis carinii* pneumonia after highly active antiretroviral therapy in patients with HIV infection.** N Engl J Med. 2001 Jan 18;344:159-67.

QUESTION

In patients with HIV infection, can primary and secondary prophylaxis for *Pneumocystis carinii* pneumonia (PCP) be safely discontinued if antiretroviral therapy has improved immune function and CD4+ cell counts remain ≥ 200 cells/mm^3?

DESIGN

Randomized {allocation concealed*}†, unblinded*, controlled trial with mean follow-up of 20 months (primary prophylaxis group) and 12 months (secondary prophylaxis group).

SETTING

19 public hospitals in Spain.

PATIENTS

587 patients, of whom 474 (median age 36 y, 73% men) were in the primary prophylaxis group and 113 (median age 37 y, 76% men) were in the secondary group (previous PCP). Inclusion criteria were HIV infection and previous CD4+ cell counts < 200/mm^3 or PCP, current prophylaxis for PCP, sustained response to highly active antiretroviral therapy (HAART) (current CD4+ cell count ≥ 200/mm^3 and a plasma HIV-1 RNA level < 5000 copies/mL for > 3 months), and Karnofsky score > 80. Exclusion criteria were age < 18 years, pregnancy, or poor adherence to antiretroviral therapy. Follow-up was 97% (primary) and 100% (secondary).

INTERVENTION

In the primary prophylaxis group, 240 patients were allocated to discontinue prophylaxis and 234 were allocated to continue. In the secondary prophylaxis group, 60 patients were allocated to discontinue prophylaxis and 53 to continue. If the CD4+ count fell to < 200/mm^3, prophylaxis was started again.

MAIN OUTCOME MEASURE

Incidence of PCP.

MAIN RESULTS

No cases of PCP developed in any group in either the primary or secondary prophylaxis analyses. For both primary and secondary prophylaxis, the study groups did not differ for any outcomes, including infections, adverse effects, and CD4+ cell counts.

CONCLUSION

Discontinuation of primary and secondary prophylaxis for *Pneumocystis carinii* pneumonia, if antiretroviral therapy had improved immune function and CD4+ cell counts had remained ≥ 200 cells/mm^3, was associated with no new cases of PCP in patients with HIV infection.

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*See Glossary.

†Information supplied by author.

COMMENTARY

In the 1980s, PCP was an expected complication of HIV infection. PCP prophylaxis to prevent the first episode and lifelong suppression to prevent secondary recurrence were standard practices. Managing HIV infection is now directed toward disease modification by using HAART, which inhibits HIV replication and increases CD4+ cell counts, rather than prophylaxis for patients against opportunistic complications. What are the implications of this improved immune function on common events?

Lopez Bernaldo de Quiros and colleagues have addressed this question by clarifying when primary and secondary prophylaxis can be safely discontinued. Their results are supported by a recent study of primary prophylaxis (1) and secondary prophylaxis data from an observational database study (2).

Evidence supports discontinuing primary and secondary PCP prophylaxis when CD4+ counts are ≥ 200 cells/mm^3 for ≥ 3 months on highly active antiretroviral therapy. Situations in which we do not have sufficient evidence to discontinue PCP prophylaxis include patients with oral candidiasis or ongoing weight loss or those receiving cytotoxic chemotherapy or long-term corticosteroids.

This new information supports recent guidelines (3). PCP prophylaxis should, however, be restarted in patients who do not have sustained responses to antiretroviral therapy. Clinicians should monitor patients and their CD4+ cell counts and may reapply the same criteria for resuming prophylaxis as were initially used.

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