Abstract

Patients with high levels of residual immune activation and suboptimal immune reconstitution may play a central role in disease progression, and patients with elevated suPAR (soluble urokinase-type plasminogen activator receptor) levels at baseline are at particular risk. In this study, we compared the effects of the immunosuppressive corticosteroid prednisolone with placebo in recently diagnosed asymptomatic HIV infection. We investigated the effects of corticosteroids such as prednisolone on disease progression in a randomized, placebo-controlled, double-blind study. Treatment with prednisolone resulted in significantly reduced numbers of AIDS-defining conditions (4 patients versus 11; p = 0.0196) (Fig. 1A) and the CD4/CD8 ratio increased significantly as compared with placebo (p = 0.039) (Fig. 1B). These findings were confirmed in a post-hoc analysis of the CD4/CD8 ratio (p = 0.039). Furthermore, prednisolone delayed the time to progression for CD4 counts (p = 0.039) (Fig. 1C). In addition, prednisolone improved CD4/CD8 ratio (p = 0.039) (Fig. 1D). These results suggest that corticosteroids such as prednisolone should be considered as an early treatment option for asymptomatic HIV infection in resource-limited countries. The conclusion that corticosteroids such as prednisolone are effective in reducing disease progression was supported by the results of a post-hoc analysis of suPAR levels, which showed a significant decrease in patients treated with prednisolone (p = 0.009) (Fig. 2). Furthermore, prednisolone treatment resulted in a significant increase in CD4 counts (p = 0.009) (Fig. 3). These findings suggest that prednisolone may be an effective adjunct to HAART in reducing disease progression.

Rationale of the Study

Corticosteroids such as prednisolone reduce HIV-immune activation.

If immune activation is a factor in HIV pathogenesis and not just a correlate, prednisolone may alleviate HIV disease progression.

Methods

Study design: 326 Patients Randomized: Double blind Randomization 1:1

Study drug: Prednisolone (5 mg/day)

Treatment duration: 2 years

Inclusion criteria: HIV positive CD4 > 350 no previous HAART no AIDS

Primary endpoint: Time to progression to AIDS (CD4 < 200 and/or AIDS-defining condition)

Results

Fig. 1: Consort Diagram

Fig. 2: Immune Activation and Viral Load

Fig. 3: CD4 Counts and CD4/CD8 Ratio

Fig. 4: Disease Progression

Prednisolone treatment (5 mg per day)...

• Reduces HIV-associated Immune Activation (Fig. 2B)
• Increases HIV viral load by factor 2 (Fig. 2C)
• Increases CD4 counts (Fig. 3C)
• Improves CD4/CD8 ratio (Fig. 3D)
• Attenuates Progression to AIDS-defining conditions (Fig. 4B)

Conclusions

• Reduction of HIV immune activation attenuates HIV disease progression, despite high-level virus replication
• This trial demonstrates that HIV immune activation is a causal factor in HIV pathogenesis
• Attenuation of HIV pathogenesis may result in viral suppression
• Improvement of CD4 counts and CD8/CD4 ratio may further be explored, e.g. in: (1) Immunological Nonprogressors (prednisolone plus HAART)
• HIV patients in resource-limited countries (prednisolone plus HAART)
• Patients with HAART failure in resource-limited countries (prednisolone as a salvage therapy)

References


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Abstract

The immune response to HIV infection is a crucial factor in disease progression. We investigated the effects of corticosteroids such as prednisolone on disease progression in a randomized, placebo-controlled, double-blind study. Treatment with prednisolone resulted in significantly reduced numbers of AIDS-defining conditions (4 patients versus 11; p = 0.0196) (Fig. 1A) and the CD4/CD8 ratio increased significantly as compared with placebo (p = 0.039) (Fig. 1B). These findings were confirmed in a post-hoc analysis of the CD4/CD8 ratio (p = 0.039). Furthermore, prednisolone delayed the time to progression for CD4 counts (p = 0.039) (Fig. 1C). In addition, prednisolone improved CD4/CD8 ratio (p = 0.039) (Fig. 1D). These results suggest that corticosteroids such as prednisolone should be considered as an early treatment option for asymptomatic HIV infection in resource-limited countries. The conclusion that corticosteroids such as prednisolone are effective in reducing disease progression was supported by the results of a post-hoc analysis of suPAR levels, which showed a significant decrease in patients treated with prednisolone (p = 0.009) (Fig. 2). Furthermore, prednisolone treatment resulted in a significant increase in CD4 counts (p = 0.009) (Fig. 3). These findings suggest that prednisolone may be an effective adjunct to HAART in reducing disease progression.

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Primary endpoint: Time to progression to AIDS (CD4 < 200 and/or AIDS-defining condition)

Second endpoint: CD4 counts, immune activation

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References