Metformin for Preventing Diabetes Mellitus in HIV-Infected Patients with Prediabetes: A Randomized Controlled Trial

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Background: HIV infection and diabetes mellitus (DM) both increase the risk for cardiovascular diseases. Prediabetes (PreDM) is a condition preceded DM and commonly observed in HIV-infected patients receiving antiretroviral therapy (ART). Both metformin and lifestyle interventions have been shown to reduce risk of progression to diabetes in non-HIV infected population although the prescription of metformin in the real-world clinical approach to diabetes prevention remains limited.

Objective: This study aimed to evaluate the efficacy of metformin for preventing DM in HIV-infected patients.

Methods: We conducted a randomized controlled clinical trial in HIV-infected patients with preDM. We randomized patients into two groups: metformin group (received metformin) and control group (not received metformin). Patients in both groups were counseled regarding diet control and lifestyle modification. They were followed for 24 weeks. The primary endpoint was the development of DM. Fasting plasma glucose (FPG), 2-hr 75-gm oral glucose tolerance test (OGTT), HbA1c, computer-based homeostatic model assessment index of beta-cell function (HOMA%B), and insulin resistance (HOMA-IR) were analyzed.

Results: 74 patients were enrolled, with 37 in each group. Mean age was 49.6 years and 68.9% were males. Most patients (81.1%) received NNRTI-based ART. At baseline, mean CD4 cell count was 570 cells/mm3 and mean body mass index (BMI) was 24.6 kg/m2. Baseline characteristics including age, sex, BMI, waist-hip (W/H) ratio, CD4 cell count, duration of ART, and ART regimen were similar (p>0.05) between the two groups. Mean FPG, 2-hr OGTT, HbA1c, HOMA%B and HOMA-IR were also similar between both groups at baseline (p>0.05). After 24-week follow-up period, only one patient developed DM and in the control group. Mean HbA1c significantly decreased from baseline (p<0.001) only in the metformin group. HOMA-IR at 24 weeks was significantly lower in the metformin group (1.086 vs 1.478, p=0.042). However, BMI, W/H ratio, FPG, 2-hr OGTT, HbA1c, and beta cell function between the two groups were not significantly different at 24 weeks. No patient had adverse effects that led to discontinuation of metformin. No cardiovascular event observed in the study period.

Conclusion: Metformin appears to improve insulin resistance and prevents progression to DM in HIV-infected patients with preDM. However, further study with longer study period is needed to evaluate the long-term benefit of metformin.

Keywords: HIV, Prediabetes, Diabetes, Metformin, Insulin resistance, Randomized control trial