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Belatacept is diabetogenic at therapeutic dose.

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Background: Belatacept is a promising immunosuppressant for replacing calcineurin inhibitors in kidney transplantation but its side effect is not fully studied. We evaluated whether belatacept is diabetogenic at therapeutic dose.

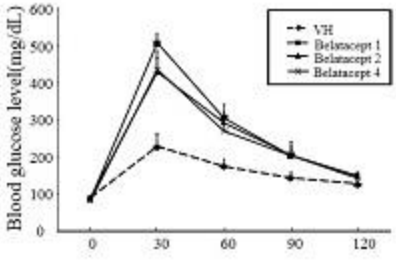
Methods: Three doses of belatacept (1, 2, 4 mg/kg) were chosen based on previous animal studies that 2 mg/kg of belatacept is effective in preventing acute rejection in rats. Belatacept were administered intravenously via tail vein at weekly basis for 4 weeks in rats and VH group rats received a saline via tail vein injection at weekly basis for 4 weeks. Body weight, urine volume, and water intake were measured daily before sacrifice. The diabetogenicity of belatacept was evaluated by intraperitoneal glucose tolerance test (IPGTT) and area under the curve for glucose (AUCg) calculated by trapezoidal estimation from the values obtained during the IPGTT.

Results: After four weeks, there is no significant difference of body weight, water intake and 24hr-urine volume between control and belatacept-treated groups. IPGTT revealed that fasting blood sugar level was normal among study groups (VH: 91±3 vs. other groups: 85±2, 89±4, 81±3; $P>0.05$), but belatacept treatment significantly increased blood glucose level at 30 min (VH: 229±35 vs. other groups: 507±25, 429±40; 436±50, $P<0.05$), and this increase was persisted until 2 hrs (Figure 1) compared with control group and AUGg was significantly increased in belatacept-treated rats (VH: 329±33 vs. other groups: 566±36, 523±44; 510±64, $^{\#}P<0.05$) (Figure 2). However, there was no dose dependent effect among three doses.

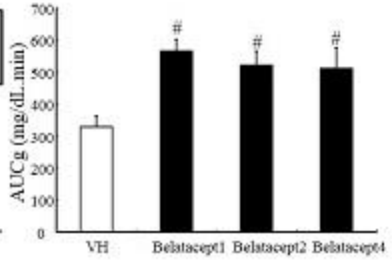
Conclusion: Our preliminary study clearly defines that belatacept is diabetogenic at therapeutic dose. Further evaluation is needed to confirm diabetogenicity of belatacept in clinical practice.

Figures:

IPGTT(**Figure 1**)



AUCg (**Figure 2**)



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