Uncovering the Mechanism of Action of the Anti-Diabetic Effects of Bromocriptine: The Role of Prolactin

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Abstract:
The quick release bromocriptine mesylate (Cycloset®) was recently approved as a drug to treat type 2 diabetes mellitus. Although several studies have shown beneficial effects of bromocriptine to reduce hyperglycemia in diabetic rodents and humans, the exact mechanism of action of the anti-diabetic effects of bromocriptine remains unknown. In the present study, we hypothesized that the anti-diabetic effects of bromocriptine is due to reductions in basal prolactin levels. Thus, we studied 4 groups of genetically obese and diabetic (*ob/ob*) mice for 16 days: 1) control (one daily ip injection of vehicle), 2) prolactin (mini-osmotic pumps infusing ovine prolactin; 18 µg/day), 3) bromocriptine (one daily ip injection of bromocriptine mesylate; 12 µg/g), and 4) bromocriptine+prolactin. Bromocriptine group exhibited a reduction in serum prolactin levels compared to other groups. No changes in food intake were observed among the groups; however, bromocriptine and bromocriptine+prolactin groups showed a reduced weight gain along the experiment. To determine whether glucose homeostasis was affected by the treatments we performed glucose and insulin tolerance tests. Bromocriptine group exhibited an improved glucose tolerance and insulin sensitivity compared to other groups, including bromocriptine+prolactin group. Serum insulin levels were also decreased only in bromocriptine group. In conclusion, prolactin replacement did not change the energy balance of bromocriptine-treated *ob/ob* mice, but it blunted most of the improvements observed on their glucose control. Our findings suggest a possible mechanism of action of the anti-diabetic effects of bromocriptine.
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