Time-Action Profile of Zinc Human Insulin (recombinant DNA) in Young Volunteers as Compared with Zinc Porcine Insulin (Monotard)

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Zinc human insulin (recombinant DNA) or zinc PPI (Monotard) 20 U was injected subcutaneously to study the time-action profile in six healthy volunteers. During the test period they received a 10-g biscuit containing 3% moisture, 7% protein, 10% fat, 80% carbohydrate, and 30 ml of water every hour. The onset of action with zinc human insulin occurred earlier than with zinc PPI. Also, the intensity of the blood sugar-lowering effect was more pronounced 3 and 4 h after administration of insulin. No other statistically significant differences were detected between the two blood glucose curves. The results show that it is possible to develop a zinc human insulin formulation with a duration of the blood sugar-lowering effect equal to a zinc PPI formulation. DIABETES CARE 5 (SUPPL. 2): 71–72, 1982.

An intermediate-acting human insulin (recombinant DNA) preparation was developed recently. It would be of interest to know whether this preparation combines the properties and possible advantages of human insulin (recombinant DNA) with a time-action profile that fits to the treatment of the majority of diabetic patients. To study the time-action profile of the human insulin-zinc formulation (zinc human insulin), Gerritzen tests were performed with both zinc human insulin and with a purified porcine insulin with prolonged action (PPI zinc; Monotard). The Gerritzen test provides useful information on the time-action profile of different types of insulin: onset, intensity, and duration of the blood sugar-lowering effect.[1] The occurrence of counterregulatory processes is minimized by carbohydrate consumption at regular intervals over the test period.

MATERIAL AND METHODS

Six healthy volunteers, aged 24–27 yr, within 10% of ideal body weight and with normal glucose tolerance, were studied. After an overnight fast they ate a 10-g biscuit containing 3% moisture, 7% protein, 10% fat, 80% carbohydrate, and 30 ml of water every hour from 7 a.m. until 10 p.m., the end of the test. An indwelling catheter was inserted in the brachial vein for blood sampling. At 8 p.m. 20 U of insulin was administered subcutaneously to the volunteers, who remained recumbent throughout the whole test period. Blood glucose was measured before the administration of insulin, every 30 min for 3 h after injection of insulin, and every hour thereafter for 50 h. Blood glucose was measured using the GOD/PAP method. The Gerritzen tests with zinc human insulin and zinc PPI were performed in a random crossover fashion 10 days apart. Differences between treatments were assessed with an analysis of variance at a 95% confidence level.

RESULTS

Figure 1 shows the mean and standard error of the mean of the blood glucose values observed in six volunteers after receiving zinc human insulin and zinc PPI. The blood glucose levels were significantly lower after zinc human insulin administration at 3, 4, and 5 h, but no other significant difference between zinc human insulin and zinc PPI was detected. Notwithstanding the substantial drop in blood glucose levels, none of the volunteers showed any clinical signs of heartbulb hypoglycemia.

DISCUSSION

The onset of hypoglycemia after subcutaneous administration of zinc insulin is faster after zinc human insulin than after zinc PPI. The intensity of the blood sugar-lowering effect after zinc human insulin appears also to be more pronounced than after zinc PPI. This difference, however, only occurs in the early part of the curve and, from 5 h on, no statistical difference could be detected. The duration of the blood sugar-lowering effect of both preparations appears to be equal. The

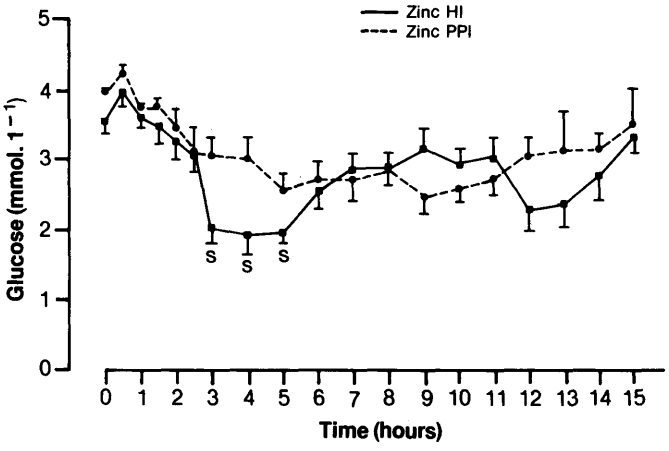

FIG. 1. Mean blood glucose levels of six healthy volunteers after subcutaneous administration of zinc human insulin and zinc PPI (20 U) under a constant oral carbohydrate load (Gerritzen test). s = statistically significant, $P < 0.05$.

rise in the blood glucose curve from 6 to 11 h after administration of zinc human insulin suggests that counterregulatory processes might have played a role. None of the subjects, however, showed any clinical evidence of hypoglycemia during the test period. The original Gerritzen procedure has to be adapted by either lowering the amount of insulin administered, or by increasing the carbohydrate load during the test period, to prevent too large a drop in blood glucose levels. The results show that it is possible to develop a zinc human insulin formulation with a duration of the blood sugar-lowering effect equal to a zinc PPI formulation.

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