

P02-176 - EFFECTS OF CLOZAPINE AND ITS METABOLITES ON EXPRESSION OF GLUCOSE TRANSPORTER 2 LOCATED IN CELL MEMBRANE OF ISOLATED RAT'S ISLETS

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Objective: The aim of this study was to clarify effects of Clozapine and its metabolites on insulin resection and expression of glucose transporter 2 (GLUT₂) located in cell membrane of isolated rat's islets.

Methods: The cells of isolated rat's islets were prepared by a modified collagenase digestion methods. At 5.5 mmol/L glucose, the cells of islets was treated with 1mmol/L clozapine, desmethyl-clozapine(DCLO), clozapine N-oxide(CNO),respectively, blank control group was also set.

1. After incubation 48h, the insulin in supernatant was assayed by radioimmunoassay.
2. The cells of isolated rat's islets in each group were detected GLUT₂ mRNA level with RT-PCR and its protein expression with Western-blot.

Results:

1. Compared to control group, clozapine significantly inhibited insulin secretion ($P = 0.007 < 0.01$); DCLO has a tendency to inhibit insulin secretion after 48h of incubation, but no significant difference was found ($P = 0.154 > 0.05$). There was no difference of insulin secretion between CNO group and the control group after 48h of incubation ($P > 0.05$).
2. The mRNA and protein expression of GLUT₂ located in cell membrane of islets: clozapine group was significantly lower than control group ($P = 0.017 < 0.05$, $P = 0.035 < 0.05$), DCLO group was also lower than control group, but no significant difference was found ($P > 0.05$), and no significant difference between CNO group and control group ($P > 0.05$).

Conclusion: Clozapine can inhibit GLUT₂ expression of cells of islets, and then hamper glucose transport through cell membrane, which was one of mechanisms to explain the effect of clozapine on insulin secretion.

Keywords: Clozapine, islet, insulin, glucose transporter