Exploration of effect of metformin in Amyloid beta (1-42) and streptozotocin induced rodent models of Alzheimer's disease

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Background: Alzheimer's disease is a disease of aging brain. Metabolic disorder like diabetes mellitus can increase the risk of Alzheimer's disease and insulin resistance in brain. Metformin is commonly used in type-II diabetes, which helps in decreasing insulin resistance and can play neuroprotective effect. Hence we want to evaluate the effects of metformin in Amyloid beta (1-42) and streptozotocin induced rat models of Alzheimer's disease

Materials and Methods: Male wistar rats were used for the study. In first model, Alzheimer's disease was induced by injection of Amyloid beta 10 microgm/2microlitre (ICV) and in the second model by STZ 3mg/kg (ICV). The bilateral ICV injection was given stereotactically. Six groups were used for each model. Sham, disease control group (ICV amyloid beta and STZ respectively), Metformin (all received amyloid beta and STZ, followed by treatment 50mg/kg, 100mg/kg, 150 mg/kg) and positive control (memantine 1.8mg/kg). After 21 days of treatment, animals were subjected to a battery of behavioral tests (EPM, MWM), followed by sacrifice and estimation of amyloid beta level in brain by ELISA. $P \leq 0.05$ was considered significant.

Results: Regarding neurobehavioral tests, in both the models, compared to the Sham, disease control group showed significant ($P \leq 0.05$) increase in transfer latency in both the tests. When compared to disease control group, metformin treatment significantly decreased the transfer latency. In STZ model, compared to sham group, disease control showed significantly higher level of amyloid beta in brain. Treatment with metformin 100mg/kg ($p=0.02$) and 150 ($p<0.001$) mg/kg and memantine ($p<0.001$) significantly reduced the amyloid beta level in brain compared to the disease control group. In amyloid beta model, metformin 50mg/kg ($p=0.047$) and 100mg/kg ($p=0.002$) shows the significant decrease Amyloid beta (1-42) but and 150 mg/kg showed borderline significance ($p=0.063$). No significant difference was observed between the metformin and memantine groups in both the models.

Conclusion: In Present study metformin has shown positive effect on memory and reduced the level of neurotoxic amyloid beta burden in both Amyloid beta and STZ induced models of Alzheimer's disease in brain. So, further studies are needed to project metformin as therapeutic agent in dementia associated with AD