ABSTRACT

Background: In hypertensive diabetic patients, renal nerve denervation (RDNX) has been shown to improve glucose handling. However, our studies found that RDNX in hypertensive obese female Schlager mice (BPH/2J) adversely affects glucose handling. With the anatomical proximity of the renal and ovarian nerves in mice, we hypothesize that, removing ovarian nerves in female BPH/2J mice will adversely affect glucose handling. In this study, we investigated the effects of ovariectomy (OVX) on fasting glucose levels, glucose tolerance and the insulin tolerance in obese female BPH and BPN mice. Methods: After 10 weeks of high fat diet, fasting blood glucose in the BPH/2J and control (BPN/3J) mice, was measured on week 11. The mice then underwent bilateral surgical removal of ovaries (ovariectomy or OVX) in some mice and sham surgery in the red. Two weeks after OVX/Sham surgery, fasting blood glucose and glucose tolerance test (GTT) was measured. One week later insulin sensitivity test (ITT) was performed. Results: At 18 weeks of age and with high fat diet, the weight of BPH/2J mice (23 ± 1 g, n=6) was lower than the control BPN/3J mice (51 ± 4 g, n=3). The OVX/sham surgery did not significantly affect the body weight in mice. The fasting blood glucose levels in BPN mice after two weeks of sham surgery was (78.75 ± 7.432 mg/dl, n=4) and ovariectomy was (84.67 ± 19.64 mg/dl, n=3). In contrast, the OVX procedure increased fasting glucose levels in BPH/2J mice (97.25 ± 11.16, n=4) compared to sham BPH/2J mice (69.33 ± 5.948 mg/dl, n=6). The OVX procedure also caused a slight increase in the area under the curve for the GTT and slight decreased in the ITT curve in BPH/2J mice but it was not statistically significant.

Conclusion: Ovariectomy increased fasting blood glucose in BPH/2J mice similar to renal denervation suggesting a role of ovarian nerves in glucose regulation.

INTRODUCTION

- Previous study demonstrated improved glucose metabolism but in contrast female BPH mice had poor glucose handling.
- OVX study observed high blood glucose levels after surgery, and remained elevated by 20% in OVX group for the entire experiment (OVX will result in lower estrogen levels). OVX relevant to renal denervation because renal nerves are close in proximity to the ovarian nerves. If ovarian nerves are ablated it will result in decreased sympathetic nerve stimulation to the ovaries which will in turn result in decreased amounts of norepinephrine. This decreased amount of norepinephrine can then suppress the amount estrogen produced by the ovaries.
- Adverse effects of renal denervation would be most prominent in post-menopausal women due to the lower estrogen levels which are replicated with the OVX procedure.

HYPOTHESIS

Ovariectomy will result in an increased area under the curve for the glucose tolerance test (poor glucose handling), and a decreased insulin tolerance in female HFD both sham and OVX mice.

MATERIALS AND METHODS

- Materials: Materials included experimental mice, surgical instruments, and glucose solution.
- Methods: Methods included surgical removal of ovaries, fasting blood glucose measurement, and glucose tolerance test.

RESULTS

- Glucose Tolerance: Ovariectomy increased fasting blood glucose levels in BPH/2J mice similar to renal denervation suggesting a role of ovarian nerves in glucose regulation.
- Insulin Tolerance: Ovariectomy increased fasting blood glucose levels in BPH/2J mice.

CONCLUSION

Conclusion: Ovariectomy increased fasting blood glucose in BPH/2J mice similar to renal denervation suggesting a role of ovarian nerves in glucose regulation. These results can also have clinical application. Since there is evidence suggesting that renal denervation can potentially sever the ovarian nerves, it can help identify patients seeking renal denervation treatments who are at risk for the adverse glucose handling effects. Such patients would be at risk would be older middle aged women (post-menopausal) who also have hypertension.

REFERENCES


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