The Effect of Botulinum Toxin A on Leptin, Ghrelin, Insulin, Glucagon, and Oxidative Stress in Diet-induced Obesity Rat Model

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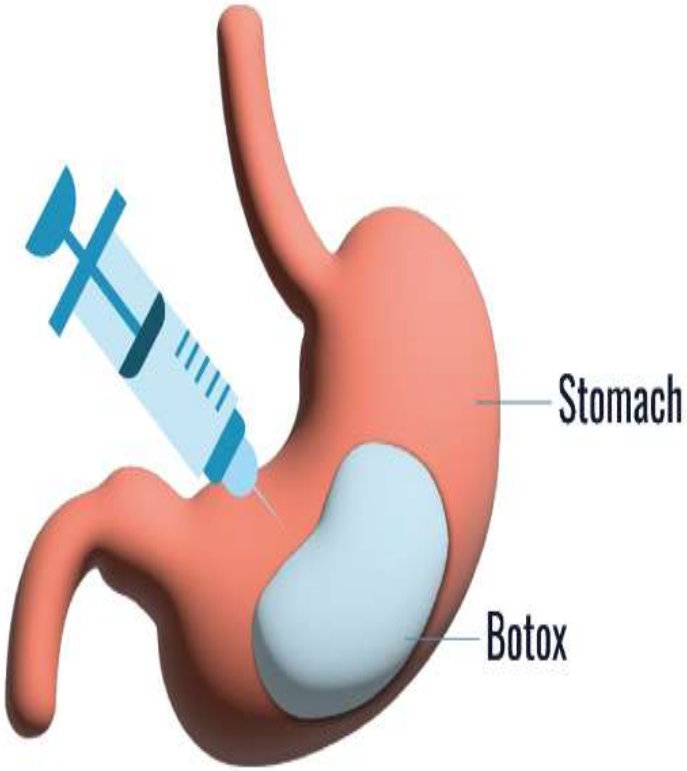
I have no potential conflict of interest to report

INTRODUCTION

- Obesity is a health problem that is increasing day by day all over the world.
- According to the World Health Organization data, in 2022, more than 1 billion people, including 650 million adults, 340 million adolescents and 39 million children, are obese worldwide.
- The World Obesity Federation's 2023 atlas predicts that 51% of the world, or more than 4 billion people, will be obese or overweight within the next 12 years.
- Bariatric surgery is becoming more popular every day.
- Non-surgical methods ? Botulinum Toxin ?



OBJECTIVE

Aim

The aim of this study is to show the effects of Btx-A, which is discussed for the treatment of obesity, on body weight and its effects on insulin, glucagon, ghrelin and leptin after its injection into the stomach.

Primary Outcome

- The effect of Btx-A on weight loss in obesity
- The effect of Btx-A on the metabolic hormones insulin and glucagon in obesity.
- The effect of Btx-A on ghrelin and leptin, which play a role in obesity

Secondary Outcome

- Effect of Btx-A on oxidant and antioxidant substances
- Effect of Btx-A on ischemia and angiogenesis in brown and white adipose tissue

MATERIAL and METHOD

- Thirty-five 12-week-old Wistar Albino rats with an average weight of 190-240 grams were examined in three groups as botox group (n = 15), control group (n = 15) and sham group (n = 5).

- Rats were allowed free access to water and cafeteria food (CAF) ad libitum (unlimited feed and water)for 70 days. CAF of four different products: cornflakes, chocolate, pastry, and chips. Every day, each component of the CAF was placed in cages as four distinct items. The amount of food consumed each day was documented.

- Botox group, after 70 days of feeding, a total of 20 IU of Btx - A period of 2.5 IU each in eight compartments in the stomach (large curvature, lesser curvature, antrum, anterior and posterior walls of the corpus regions).

- The control group was given 20 IU of saline in the same way.

- Only laparotomy was performed in the sham group.

MATHERIAL and METHOD

- After the procedure, all rats continued on the cafeteria diet and were weighed every 3 days.
- There was no loss of rats from any of the three groups after the surgical procedures.
- Rats were sacrificed on day 51.
- Insulin, glucagon, ghrelin, leptin, catalase (CAT), superoxide dismutase (SOD), malondialdehyde (MDA) and thiobarbituric acid reactive substance (TBARS) were studied with blood samples.
- VEGF was studied by taking samples of white and brown adipose tissue.

FINDINGS

Weight changes in all groups before surgery.

Average Weight (gr)	BTX Group Mean ±SD	Control Group Mean ± SD	ShamGroup Mean ±SD	*p**
İnitialDay	214.2±22.6	217.1±26.4	211.7±12.6	0.06
70th. Day	274.1±28.7	261.6±30.1	262.8±33.9	0.59
*p**	<0.001*	<0.001*	<0.001*	

SD: Standart Deviation

*p** *<0.05* was considered sufficient for statistical significance.

FINDINGS

Weight changing in all groups after surgery.

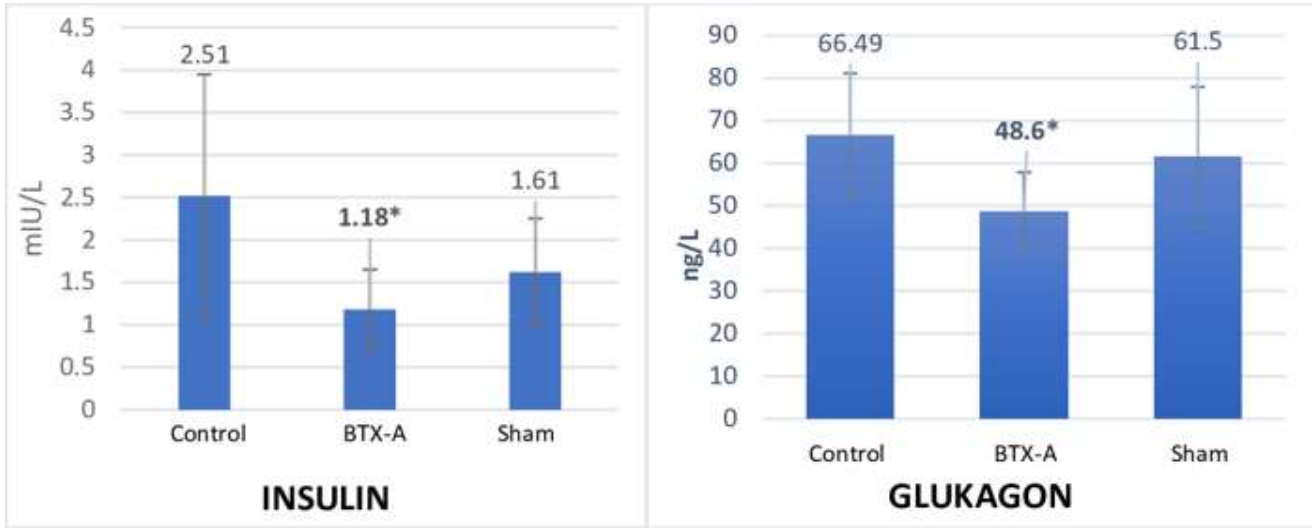
Average Weight (gr)	BTX Group Mean ±SD	Control Group Mean ± SD	ShamGroup Mean ±SD	p*
SurgeryDay	274.1±28.6	261.6±30.1	262.8±33.9	0.59
3rd Day	258.2±25.2	255.1±32.4	254.9±19.0	0.48
6th Day	251.8±27.8	252.3±29.9	253.4±20.5	0.30
9th Day	248.5±29.8	249.0±31.3	253.6±28.9	0.34
12th Day	246.0±31.6	258.4±30.5	255.2±20.5	0.21
15th Day	237.6±34.1	260.1±28.6	258.2±18.6	0.52
18th Day	236.8±37.2	258.3±28.8	261.3±21.0	0.62
21th Day	235.8±35.7	260.9±28.8	260.4±19.4	0.54
24th Day	238.0±39.1	263.4±31.9	264.0±21.6	0.55
27th Day	237.6±37.2	263.4±34.4	268.0±22.7	0.50
30th Day	244.7±41.9	265.7±35.0	270.5±24.8	0.54
33th Day	242.8±40.0	267.2±33.6	269.8±23.9	0.53
36th Day	244.5±41.9	265.6±32.4	268.2±24.4	0.51
39th Day	246.7±40.9	266.9±34.3	271.5±23.7	0.62
42th Day	244.8±43.7	264.1±33.8	271.6±26.1	0.59
45th Day	248.5±44.1	267.8±33.9	272.6±24.4	0.51
48th Day	264.5±34.9	273.2±30.6	278.7±26.0	0.65
51th Day	262.1±35.9	273.2±30.0	280.1±27.4	0.62

SD: Standart Deviation

p <0.05was considered sufficient for statistical significance.*

FINDINGS

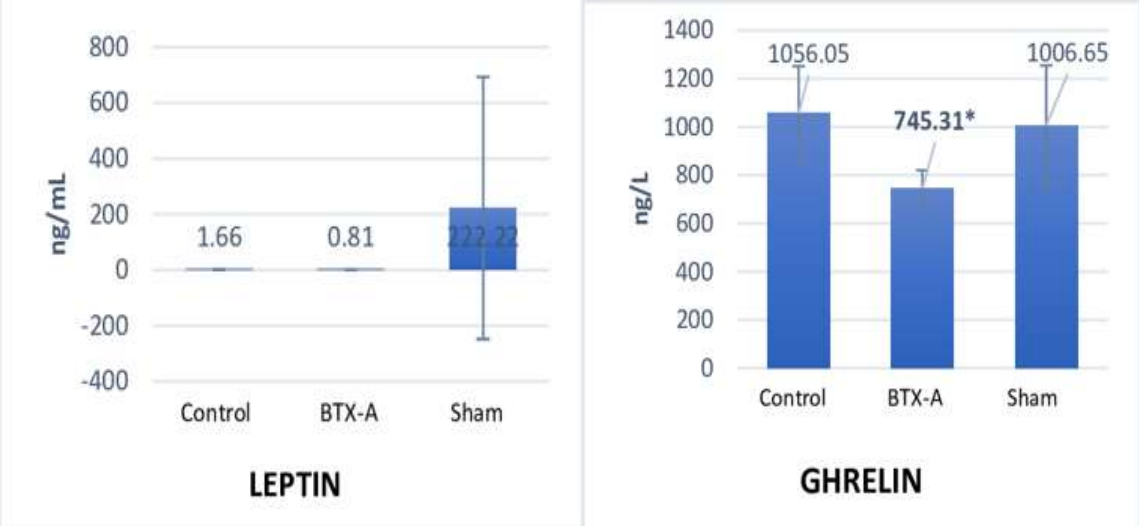
Results of hormone concentration measurements - 1



Insulin and glucagon levels were observed to be statistically significantly lower in the BTX group compared to the C group (both *$p < 0.05$).

FINDINGS

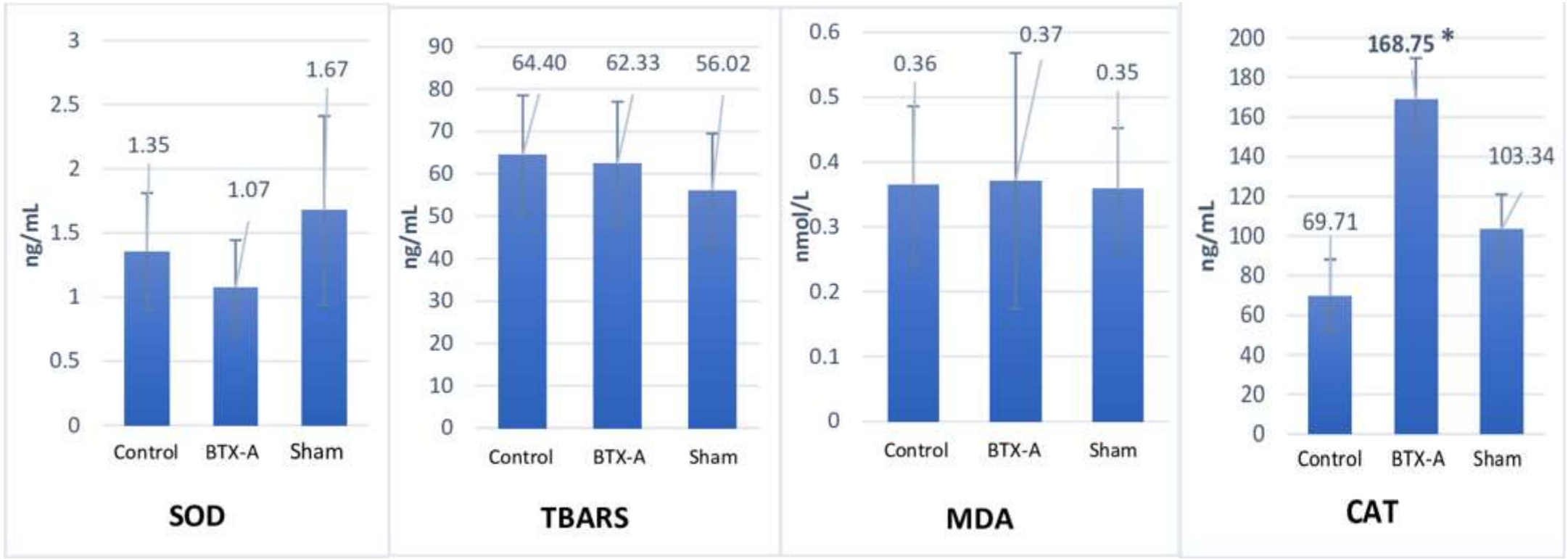
Results of hormone concentration measurements - 2



The ghrelin levels in the BTX group were found to be statistically significantly lower than in the C and S groups (*$p < 0.05$). The difference in leptin levels between the groups was not statistically significant ($p > 0.05$).

FINDINGS

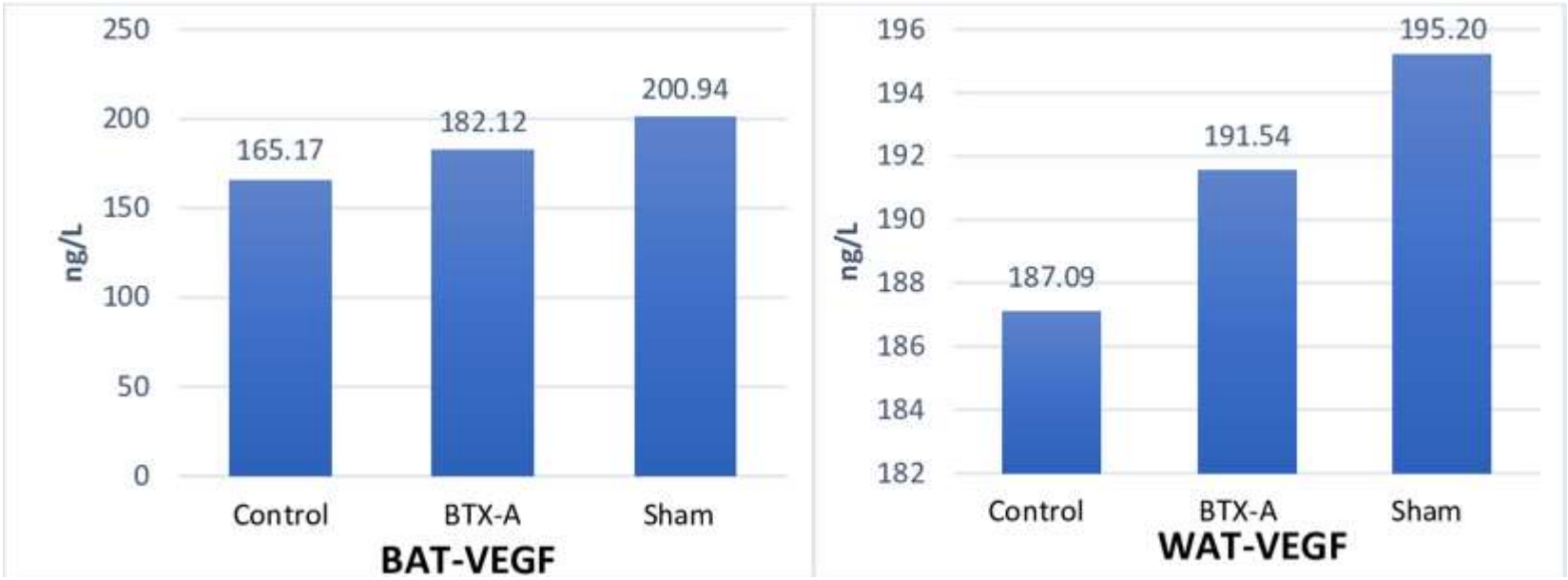
Results of oxidative stress product



SOD, TBARS, and MDA levels did not differ statistically significantly across the groups ($p > 0.05$). The BTX group had a substantially greater concentration of CAT than the C and S groups ($*p < 0.05$).

FINDINGS

Results of brown and white adipose tissue analysis



There was no statistically significant difference in VEGF concentrations between BAT and WAT ($p > 0.05$).

RESULTS - CONCLUSION

- As a result of the study, it was shown that botulinum toxin injection into the stomach in experimental animals in the diet-induced obesity model did not have a significant effect on weight loss.

- While botulinum toxin injection in the stomach has been shown to have a reducing effect on insulin, ghrelin and on glucagon and not on leptin.

- The fact that it has an increasing effect on antioxidant CAT shows that it has a positive effect on the antioxidant system. This positive effect was not observed in another antioxidant, SOD, in our study.

- The lack of reduction in adipose tissue appears as hypoxia and non-reduction of inflammation. This situation causes no significant decrease in VEGF level.

- All these results show that the use of Btx-A for weight loss in obese patients will not be effective enough and the possible positive effects are short-lived.

THANK YOU

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