EFFECT OF ORLISTAT ON TESTICULAR PALMITOYL PROTEIN THIOESTERASE 1 AND SEMENOGRAM IN OBESE RATS

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Introduction

Obesity is a growing public health issue causing health issues like diabetes, cardiovascular disease, hypertension, and hyperlipidemia and male infertility. It is suggested that obesity negatively impacts sperm function, even if this function does not render obese males infertile. Orlistat is an anti-obesity drug used in the management of obesity and its associated co-morbidities.

Aim of the work

To investigate the effect of orlistat (10 mg/kg b.w./day) on testicular palmitoyl protein thioesterase 1(PPT1) in high fat diet fed rats as a marker of infertility induced by obesity, in a rat model.

Patients and Methods

Experimental animals: 32 adult male wistar albino rats, weighted from 120 to 150 g were kept under standard laboratory conditions and randomly divided into group I (n=8): Normal group were fed on normal control diet, group II (n=8) were fed on high fat diet (HFD) only, group III (n=8) were fed on HFD with orlistat for12 weeks (preventive group) and group IV(n=8) were fed on high fat diet with orlistat for 6 weeks (from 7th week to 12week) (treated group).

Methods: After 12 weeks, laparotomy was conducted after anesthesia. Testes and epididymis were extracted and dissected. Sperm analysis and histological examination were performed to assess the changes in the seminiferous tubules. Immunohistochemical staining of all sections was done and PPT1 was assessed.

Results

Table 1 demonstrated statistically significant difference among the four groups in the sperms count, and sperm motility ($p<0.001$). Group I, III and group IV showed statistically significant higher mean values than the group II. Group I showed significantly lower dead sperm % levels than group II, III and group IV. immunohistochemical assessment of PPT1 is demonstrated in **Table 2.** There was significant higher difference in PPT1 levels in group II compared to group I, and group III ($p<0.001$), while no significant difference was found between groups III and IV.

Table (1): Comparison between the four studied groups according to semen parameters.

Semen analysis	Group I (n = 8)	Group II (n = 8)	Group III (n = 8)	Group IV (n = 8)	F	P
Active %						
Min. – Max.	76.02 – 86.56	14.59 – 33.02	25.76 – 80.04	57.07 – 66.12	46.688*	<0.001*
Mean ± SD.	80.32 ± 3.31	23.33 ± 7.11	71.31 ± 18.48	61.14 ± 3.10		
Median (IQR)	79.83 (78.01–82.14)	20.59 (18.22–30.70)	77.57 (75.71–79.08)	61.06 (58.69–63.22)		
p_0		<0.001*	0.307	0.004*		
Sig. bet. grps.	$p_1<0.001^*, p_2<0.001^*, p_3=0.211$					
Slow %						
Min. – Max.	3.55 – 12.31	15.71 – 44.89	1.10 – 5.15	6.31 – 17.98	31.277*	<0.001*
Mean ± SD.	8.50 ± 3.15	26.60 ± 8.73	2.60 ± 1.28	11.79 ± 4.36		
Median (IQR)	8.56 (6.20 – 11.31)	24.90 (22.11–29.07)	2.66 (1.57 – 3.06)	11.33 (8.16 – 15.54)		
p_0		<0.001*	0.126	0.586		
Sig. bet. grps.	$p_1<0.001^*, p_2<0.001^*, p_3=0.007^*$					
Dead %						
Min. – Max.	8.99 – 14.36	32.96 – 60.18	18.14 – 23.09	23.99 – 30.70	102.503*	<0.001*
Mean ± SD.	11.18 ± 1.92	50.08 ± 8.60	20.34 ± 1.84	27.07 ± 2.24		
Median (IQR)	10.57 (9.73 – 12.77)	50.32 (46.68–56.75)	19.99 (18.78–21.96)	27.02 (25.29–28.63)		
p_0		<0.001*	0.003*	<0.001*		
Sig. bet. grps.	$p_1<0.001^*, p_2<0.001^*, p_3=0.034^*$					
Count/ml						
Min. – Max.	41.50 – 54.23	19.10 – 24.60	43.81 – 52.78	47.0 – 57.10	126.739*	<0.001*
Mean ± SD.	46.97 ± 4.60	21.88 ± 1.89	48.15 ± 3.12	52.29 ± 3.70		
Median (IQR)	47.28 (42.69–50.06)	21.70 (20.45–23.50)	48.96 (45.24–50.10)	52.70 (49.0 –55.40)		
p_0		<0.001*	0.905	0.024*		
Sig. bet. grps.	$p_1<0.001^*, p_2<0.001^*, p_3=0.103$					

Table (2): Comparison between the four studied groups according to PPT1 score :

	Group I (n = 8)	Group II (n = 8)	Group III (n = 8)	Group IV (n = 8)	F	P
PPT score (0-3)						
Min. – Max.	0.0 – 2.0	2.0 – 3.0	0.0 – 3.0	0.0 – 3.0	7.464*	0.001*
Mean ± SD.	0.75 ± 0.71	2.63 ± 0.52	1.50 ± 0.93	1.25 ± 1.04		
Median (IQR)	1.0 (0.0 – 1.0)	3.0 (2.0 – 3.0)	1.50 (1.0 – 2.0)	1.0 (0.50 – 2.0)		
p0		<0.001*	0.282	0.621		
Sig. bet. grps.	p1=0.049*,p2=0.012*,p3=0.928					

Conclusion

Obesity was associated with testicular dysfunction, orlistat improved testicular dysfunction in HFD-fed rats indicating that it has potential preventive and therapeutic benefits in the obese testis.