Pantoprazole treatment of Exogenous Obesity and Hyperinsulinism in Childhood

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Objective

Obesity in children and adolescents is an important health problem world over with increasing incidence. Studies carried out in the United States have shown that obesity cases have increased thrice in the last four decades. It has been reported that of chidren and adolescents 11.3% are obese, 16.3% are overweight, and 15.6% carry the risk of being overweight (1). In Turkey, the prevalence of obesity among 6462 children and adolescents aged 9-16 is 2.3% (2), and 15.3% in children aged 11-15 from families with low socioeconomic status, but 7.4% in other children (3). The enteroinsular axis which consists of gastrin, insulin, and islet cells has been known for many years. It has been shown that central obesity and IR develop in gastrin-gene knocked out mice (4). The following few studies have reported that proton pump inhibitors (PPIs) are associated with good glycemic controls particularly in type 2 DM patients (4,5). Pantoprazole is also a PPI and, as in adults, can be safely used for gastric acid suppression in children especially in those above age 6 (6). This study was conducted to assess the effect of pantoprazole on 46 children and adolescents aged 10-18 with exogenous obesity + insulin resistance +/- impaired glucose tolerance +/- type 2 diabetes mellitus (DM) who did not respond to therapy with diet and exercise.

Material and methods and Results

Material-methods

This study was conducted on 46children and adolescents with exogenous obesity + insulin resistance. The patients were randomly chosen and divided into therapeutic groups of metformin, pantoprazole, and metformin plus pantoprazole

Results

There was no difference between the groups in terms of age, gender and anthropometric measurements made before therapy. In the pre-therapy OGTT, the glucose levels at minutes 60 and 90 were highest in the metformin group and lowest in the pantoprazole group. In the post-therapy OGTT, the glucose level at minutes 60 and 90 were lowest in the metformin group which had the highest level prior to therapy. Likewise, the metformin group showed the lowest insulin levels at minutes 60,90 and 120. When the post-therapy values of HOMA-IR, Quick index, and fasting insulin/glucose ratio were compared, there was a significant improvement in all three groups, however, when the groups were compared with each other, there was no statistically significant difference between the groups in terms of improvement.

Table 1. Comparison of serum insülin and glucose level during oral glucose toleranse test before and after the treatment

	Metformin		Pantoprazole		Metformin+ Pantoprazole		P1	P2
	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)		
Glucose0	100,63±18,11** (86-157)	91,38±6,37 (83-104)	90,64±7,83** (76-105)	86,75±6,82 (71-92)	100,06±20,95** (79-165)	112,60±26,15 (96-158)	>0,05	0,01
Glucose 30	151,63±36,28¥(47-202)	135±28,35 (112-189)	138,21±28,89** (95-188)	127,75±28,60 (88-173)	156,25±29,72** (109-214)	163,80±46,58 (140-247)	>0,05	>0,05
Glucose60	149,13±33,16£ (97-219)	109,25±24,05 (80-156)	121,14±19,41¥ (87-152)	117,75±16,99 (87-136)	146,19±40,32¥ (112-266)	180,20±86,61 (129-330)	<0,05	0,03
Glucose 90	132,75±24,96£ (104-178)	106,13±20,93 (83-147)	108,64±12,85* (85-125)	105,63±19,79 (82-132)	138,69±47,20£ (68-244)	153,80±79,43 (100-291)	<0,05	>0,05
Glucose 120	125,67±21,91* (97-188)	95,88±21,26 (72-137)	104,71±13,71** (79-123)	97,50±19,12 (58-123)	128,75±41,51** (93-231)	138±43,75 (94-204)	>0,05	0,02
İnsulin 0	21,94±10,04* (11-47)	13,96±6,61 (7-28)	16,45±5,63** (8-25)	23,02±14,04 (9-60)	21,40±13** (8,4-48)	30,96±46,75 (5,4-199)	>0,05	>0,05
İnsulin 30	166±91,27£ (42-300)	72,56±42,39 (28-137)	105,36±34,44* (28-178)	75,64±27,73 (48-133)	148,56±81,34£ (33-300)	74,25±25,45 (53-129)	>0,05	>0,05
İnsulin 60	134,56±66,12£ (46-300)	51,81±32,06 (20-154)	121,14±46,27£ (56-203)	79,79±39,2 (20-155)	135,63±54,19** (71-245)	113,44±33,39 (30-200)	>0,05	<0,001
İnsulin 90	126,75±65,28£ (63-300)	39,50±27,42 (16-133)	104,14±42,80** (49-177)	80,86±45,8 (26-155)	115,63±59,91* (61-224)	65,88±21,33 (28-120)	>0,05	0,004
İnsülin 120	118,06±73,48£ (59-300)	30,81±32,85 (10-146)	73,50±32,53* (26-157)	43,64±25,83 (9-92)	96,44±64,44** (40-294)	68,50±29,93 (14-115)	>0,05	0,003
İnsülin pik	185,69±76,78£ (79-300)	81,60±42,89 (35-154)	147,29±30,18£ (96-203)	99,36±34,98 (50-155)	169,38±62,55* (110-300)	116,31±43,70 (19-200)	>0,05	>0,05
Total insülin	567,3±257,8£ (296-1209)	208,6±115,25(110,4-576)	420,59±71,55£ (310,3-593)	302,95±121,30 (130-518)	517,65±191,59¥ (311-911)	353,03±93,72 (139-545)	>0,05	0,002
Mean insulin	113,4±51,5£ (59,2-241,8)	41,7±23,05 (22,08-115,2)	84,12±14,31£ (62,06-118,6)	60,59±24,26 (26-103,6)	103,5±38,32¥ (62,2-182,20)	70,61±18,74 (27,8-109)	>0,05	0,002
HgbA1c	5,44±0,35** (4,5-5,9)	5,4±0,41 (5,2-6,5)	5,28±0,34** (4,6-5,8)	5,2±0,19 (4,9-5,6)	5,93±1,61** (5-6,6)	5,8±0,57 (5,1-7,2)	>0,05	>0,05

p1: The comparison of pretreatment values between three group, p2: The cmparison of posttreatment values between three groups ; Superior letter shows comparison of laboratory values before and after the treatment in each group, *:p<0,05; ¥:p<0,01; £:p<0,001; **:p>0,05

Table 2. Comparison of HOMA-IR, quick index and fasting glucose-insulin ratio before and after the treatment

	Metformin		Pantoprazole		Metformin+ Pantoprazole		P1	P2
	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)	Before treatment mean±SD (Min-max)	After Treatment mean±SD (Min-max)		
HOMA-IR	5,29±2,13* (2,91-10,6)	3,40±1,29 (1,62-6,5)	4,17±0,93* (2,4-5,86)	3,31±0,88 (1,58-4,54)	5,74±3,30* (3-12,68)	3,61±1,59 (1,58-6,9)	>0,05	>0,05
Quick İndex	0,30±0,015¥ (0,27-0,32)	0,33±0,017 (0,29-0,35)	0,311±0,010¥ (0,29-0,335)	0,32±0,014 (0,306-0,35)	0,303±0,019¥ (0,269-0,32)	0,324±0,03 (0,234-0,36)	>0,05	>0,05
Glucose/insulin	5,52±2,52* (1,96-9,73)	7,33±2,79 (3,28-13,4)	5,06±1,09* (3,5-6,79)	6,28±1,55 (4,02-9)	5,08±1,99** (2,23-9,71)	7,08±6,09 (2,31-29,2)	>0,05	>0,05

Conclusion

In conclusion, as far as we know, our study is the first study in the literature that investigates the effects of metformin and metformin+pantoprazole combination on IR in children and adolescents. The results of our study are of importance because they imply that pantoprazole has a corrective effect on IR, and this effect is exerted through insulin-sensitizing mechanism without increasing insulin secretion but no additional affect superior to the metformin. Since pantoprazole can reduce the effect of metformin, patients receiving metformin+pantoprazole combination should be carefully monitorized.

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