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EFFECT OF LONG-TERM INSULIN ADMINISTRATION ON SOME ANATOMICAL AND PHYSIOLOGICAL CHARACTERISTICS OF THE GASTROINTESTINAL TRACT IN SHEEP

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SUMMARY

Effect of long-term insulin injection on some anatomical and physiological characteristics of the gastrointestinal tract (GIT) were studied in 12 Saidi lambs. Animals were weaned at 12 weeks of age then divided into two treatment groups, a control group (A) with no insulin treatment and insulin treated-group (B). The treated animals were injected with 0.75 iu insulin per kg body weight daily for 28 weeks. At the end of the experiment four animals from each group were slaughtered and different anatomical and physiological characteristics of the GIT were measured. The results indicated that, insulin administration resulted in a significant (P<.02) increase in fresh tissue weight of the total digestive tract. Insulin treatment increased GIT weight by about 24% and this increase was mainly due to the increase in weight of both compound stomach and colon (23 and 42%, respectively). There were no significant differences in physiological volume of the different segments of the GIT between treatments. Capacity of the reticulo-rumen in insulin-treated animals was higher (P<.05) by 22 % compared to control, while that of omaso-abomasum had nearly similar value (1.56 vs. 1.51 l). Insulin treatment increased (P<.03) anatomical volume of colon and such increase was mainly due to larger (P<02) circumference rather than the length of colon in treated animals compared to control.

Keywords Sheep, insulin, gastrointestinal tract

INTRODUCTION

Insulin, is known to be released by butyric and propionic acids (Jordan and phillips, 1978) and is one of the most essential factors for mammalian cell proliferation in vitro (Bottenstein et al., 1979; Sakata et al., 1980b).

The higher volatile fatty acids production rate, particularly butyric acid stimulated the epithelial and underlying cell proliferation of both rumen (Sakata and Tamate, 1976, 1978, 1979) and colon (Sakata, 1984). There have been in vitro studies, however, that butyric acid inhibits mammalian cell proliferation (Ginsburg et al. 1973; Sakata et al., 1980b). This discrepancy, between in vivo and in vitro studies, may be due to a hormonal mediation, not present in the in vitro preparations. Indeed, Sakata et al. (1980a) reported that insulin has short-term anabolic effects on rumen epithelium. However, studies on the long-term effects of insulin on gastrointestinal tract (GIT) development are laking. Therefore, our objective was to examine the long-term effects of insulin on the GIT of sheep.

MATERIALS AND METHODS

The study was conducted during the winter and spring seasons in Animal Production Experimental Farm of the Faculty of Agriculture, Assiut University. Twelve Egyptian native lambs (Saidi) at the age of 12 wk were randomly assigned to two treatment groups, similar in average body weight, a control group (A) with no insulin administration and an insulin-treated group (B), injected with 0.75 iu insulin per kg body weight daily. Insulin dose was calculated weekly according to body weight. Insulin (Nova Industria, Denmark) was administred subcutaneously at about 10.00 h daily, 2 h after morning feeding. Animals were fed 60% of their requirements as concentrate while the rest was given as roughage (containing 1:1 white straw and berseem). The daily requirements of growing lambs were calculated according to Graham (1982). The trial conducted 28 weeks.

Four animals from each treatment were slaughtered, 2 h after morning feeding. The alimentary tract was ligated, from the esophagus up to the anus, care being taken to prevent the loss of ingesta. The separate parts of the digestive tract, reticulo-rumen, omaso-abomasum, small intestine, cecum and colon-rectum were isolated by tying off.

The physiological volume of stomach compartments and the intestinal segments were measured by the difference between the volume of each part when filled with its content and its volume after emptying the contents. Capacity of the two sections of the stomach, reticulo-rumen and omaso-abomasum, were measured by using the water-filling method (Kobeisy, 1990). Anatomical volume (AV) of intestinal segments, small intestine, cecum and colon, were estimated mathematically from the length and average diameter (5 loci) of each segment. $AV = K r^2 l$, where K = constant = 22/7, r = radius, l = length. Cleaned fresh tissue weight of each segment was recorded. Samples, each of 5x5 cm, were cut from the left wall of ventral sac of the rumen. The mucosal layer was separated manually from the muscular layer and weighed, the percentage of each of these layers from the total tissue weight of the rumen was calculated.

Data analysis was done according to Harvey (1987) computer program.

RESULTS AND DISCUSSION

Insulin injection improved fresh tissue weight of different parts of the gastrointestinal tract (GIT). Insulin treatment increased GIT weight by about 24 % (P<.02). Similar trend was found when the fresh tissue weight were calculated proportional to either body weight or metabolic body weight (13 % and 15 %, respectively). Such improvement was mainly due to the increase in weight of both compound stomach and colon (23 % and 42 %, respectively) (Table 1). Whether this was related merely to increased hypertrophy (increase in size) or to an increased hyperplasia (increase in number) of the cells could not be determined in this study. However, growth is a function of both hypertrophy and hyperplasia of the cells and both of actions were improved by insulin. Insulin improved hypertrophy through its stimulation of glucose metabolism (Waltan and Etherton, 1986), protein synthesis (Prior et al., 1984; Brockman and Laaveld, 1986; Weekes, 1986: Harvey and Kaye 1988) and lipid synthesis and inhibits libolysis (Krahl, 1961; Olefsky, 1977; Green, 1983; May and Mikalecky, 1983 Walton and Etherton, 1986). On the other hand, insulin promoted hyperplasia (Gardner and Kaye, 1991), may be through the stimulation of nucleic acid formation and protein synthesis (Heyner et al., 1989). Sakata et al. (1980a) found that infusions (6 h) of insulin resulted in higher mitotic index of biopsied rumen epithelium. It is important to note that the trophic effect of insulin was only pronounced in compound stomach, particularly rumen, and colon and not in small intestine (Table 1), becouse the rumen and colon are the major sites of fermentation and VFA production (Van Soest, 1983). The high level of the VFA production was considered as the promotor of the epithelial cell proliferation of both rumen (Kobeisy, 1990; Sakata and Tamate, 1976, 1978, 1979) and colon (Kobeisy, 1993 a,b and Sakata, 1984) in the presence of insulin (Sakata et al., 1980b).

Table 1. Fresh tissue weight of different parts of the gastrointestinal tract in sheep as influenced by long-term insulin administration

	Absolute weight (g)			Proportional to live body weight (g/kg BW)			Proportional to metabolic body weight (g/kg$^{.75}$ BW)		
	A	B	SE	A	B	SE	A	B	SE
Rumen	631.15c	785.78d	61.51	1.77	1.99	.12	4.32c	4.97d	.29
Reticulum	82.58	95.73	6.52	.23	.24	.02	.57	.61	.04
Omasum	70.75e	87.82f	4.85	.20	.23	.02	.49	.57	.05
Abomasum	153.65g	187.25h	8.62	.43	.48	.02	1.05q	1.20r	.05
subtotal	938.13i	1156.58j	71.84	2.63	2.94	.15	6.42k	7.34l	.32
Small intestine	639.80	676.68	54.88	1.76	1.76	.16	4.19	4.37	.34
Cecum	42.13	46.05	4.17	.12	.12	.01	.29	.30	.03
Colon	310.43k	440.93l	45.89	.87c	1.12d	.10	2.13c	2.80d	.24
subtal	992.36m	1163.65n	60.39	2.75	3.00	.22	6.60	7.47	.47
Total digestive tract	1881.40o	2330.22p	93.09	5.27c	5.93d	.26	12.86g	14.80h	.47

Values are least-squares means and SE = standard errors.
Treatments: A=control; B=0.75 iu insulin/kg BW daily.
c,d ($P<.10$); e,f ($P<.05$); g,h ($P<.03$); i,j ($P<.08$); k,l ($P<.09$) m,n ($P<.04$); o,p ($P<.02$); q,r ($P<.06$).

Insulin treatment increased physiological volume of the different segments of the GIT, absolute value or calculated proportional to either body weight or metabolic body weight, however such improvement was not significant (Table 2).

Table 2. Physiological volume in different parts of the gastrointestinal tract of sheep as influenced by long-term insulin administration

	Absolute volume (ml)			Poportional to live body weight (ml/kg BW)			proportional to metabolic body weight (ml/kg$^{.75}$ BW)		
	A	B	SE	A	B	SE	A	B	SE
Reticulo-rumen	3901.25	5145.00	609.21	108.69	128.56	9.91	265.63	323.00	27.00
Omaso-abomasum	362.50	420.00	74.95	10.32	10.75	2.14	25.07	26.86	5.14
subtotal	4263.75	5565.00	586.69	119.02	139.32	9.12	290.72	349.86	25.51
Small intestine	395.00	582.50	82.65	11.18	14.72	2.00	27.23	36.88	5.00
Cecum	250.00	291.25	42.91	7.08	7.32	1.24	17.24	18.35	3.06
Colon	458.75	568.75	88.93	12.37	14.93	1.80	30.48	36.13	4.73
subtotal	1103.75	1442.50	185.34	32.89	36.48	4.63	74.98	91.36	10.21
Total digestive tract	5367.50	7007.50	719.15	149.66	175.79	11.32	365.67	441.22	31.43

Values are least-squares mean and SE = standard errors.
Treatments: A=control; B=0.75 iu insulin/ kg BW daily.

Capacity of the reticulo-rumen in insulin-treated animals was higher (P<.05) by 22 % compared to control, while that of omaso-abomasum had nearly similar value (1.56 vs. 1.51 l) (Table 3). Such increase was mainly attributed to the increase in the fresh tissue weight of the rumen. Insulin treatment increased the weight of the rumen tissue by about 25 %, and this increase was mainly due to heavier mucosa rather than muscularis (Fig. 1), which, in turn, permit the rumen tissue to dilate more in treated animals compared to control. Similar effect of insulin on rumen epithelium has been reported by Sakata et al. (1980a).

Length and circumferences of the different intestinal segments showed always higher values in treated animals than control, but not significant with exception of the circumference of colon which was significantly (P<.02) larger in treated group than control. The anatomical volumes, which is a function of both length and circumference, of different segments (small intestine, cecum and colon) were higher in treated animals than in controls, however such increase was only significant (P<.03) in colon (Table 4).

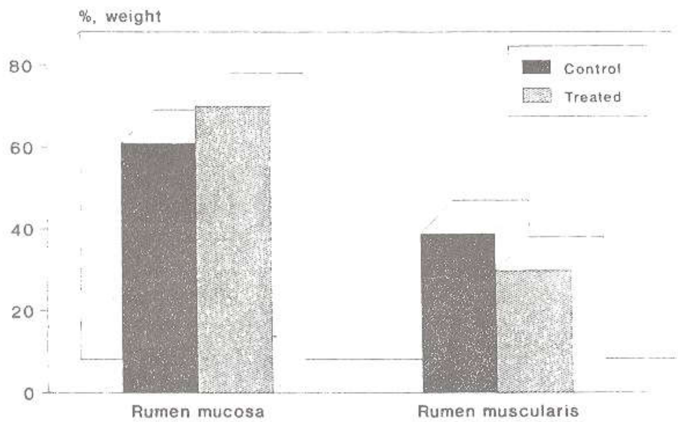

Fig. 1. Percentage weight of mucosa and muscularis of the rumen in sheep as influenced by insulin.

Table 3. Capacity of stomach compartments in sheep as influenced by long-term insulin administration

	Absolute volume (ml)			Poportional to live body weight (ml/kg BW)			proportional to metabolic body weight ($ml/kg^{.75}$ BW)		
	A	B	SE	A	B	SE	A	B	SE
Reticulo-rumen	10137.5c	12375.0d	678.21	280.73g	315.74h	8.57	687.09i	789.11j	19.38
Omaso-abomasum	1512.5	1562.5	188.05	42.50	39.81	5.40	103.75	99.54	12.79
Total	11650.0e	13937.5f	722.89	323.29e	355.55f	9.97	790.84i	888.65j	20.74

Values are least-squares mean and SE = standard errors, Treatments: A=control; B=0.75 iu insulin/ kg BW daily and c,d (P<.05); e,f (P<.06); g,h (P<.02); i,j (P<.01).

Table 4. Length, circumference and anatomical volume of the intestinal segments of sheep as influenced by long-term insulin administration

	Length (cm)			Circumference (cm)			Anatomical volume (ml)		
	A	B	SE	A	B	SE	A	B	SE
Small intestine	2049.0	2082.3	118.85	3.32	3.40	.08	1811.25	1927.00	161.82
Cecum	31.0	35.3	2.76	9.73	9.85	.49	232.25	275.25	30.95
Colon	505.5	529.3	20.06	4.75c	5.30d	.12	910.50e	1187.25f	70.82

Values are least-squares mean and SE = standard errors, Treatments: A=control; B=0.75 iu insulin/kg BW daily and c,d (P<.02); e,f (P<.03)

In conclusion, results from this study indicate that long-term insulin injection led to an increased the GIT weight, particularly compound stomach and colon. The physiological volume of the GIT, capacity of the reticulo-rumen and anatomical volume of the colon were improved in treated animals. This in turn, insulin may act as somatotropin (growth hormone), since at high concentration will bind to somatomedin receptors (Hadley, 1984). Somatotropin mediates its major growth promoting activity indirectly by its action on hepatic somatomedin production (Phillips et al., 1980). Furthermore, isulin can stimulate incorporation of amino acids into protein in the absence of growth hormone, but growth hormone has no such anabolic effect in absence of insulin (Krahl, 1961).

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تـأثير الحقن لفترة طويلـة بالانسيولين علـى بعض الصفـات التشـريحية والفسيولوجية للقناه الهضمية فى الاغنام

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تم دراسة الحقن لفترة طويلة بالانسولين على بعض الصفات التشريحية والفسيولوجية للقناه الهضمية لعدد ١٢ حمل صعيدى ٠ تم فطام الحيوانات عند ١٢ اسبوع من العمر وقسمت بعدها الى مجموعتين ٠ المجموعة الاولى ضابطة ولم يتم حقنها بالانسيولين والثانية تم حقنها بالانسيولين بمعدل ٠,٧٥ وحدة دولية / كيلو جرام من وزن الحيوان يوميا ولمدة ٢٨ اسبوع ٠ عند نهاية التجربة تم ذبح ٤ حيوانات من كل مجموعة وتم قياس الصفات التشريحية والفسيولوجية المختلفة للقناة الهضمية ٠ ولقد اوضحت النتائج ان هناك زيادة معنوية (P< 0.02) فى وزن القناة الهضمية فارغة٠ فكانت هذه الزيادة حوالى ٢٤٪ بالمقارنة بالمجموعة الضابطة التى ترجع اساسا الى الزيادة فى وزن كل من المعدة المركبة والقولون (٢٣٪ ، ٤٢ ٪ على التوالى) ٠ ليس هناك فروق معنوية فى الحجم الفسيولوجى لمختلف اجزاء القناة الهضمية بين المعاملتين ٠ سعة الكرش – شبكية فى الحيوانات المعاملة بالانسيولين زادت (P<0.05) بمقدار ٢٢٪ بالمقارنة بالمجموعة الضابطة فى حين سعة الورقية – انفحه كانت متقاربة فى المعاملتين (١,٥٦ مقابل ١,٥١ لتر)٠ المعاملة بالانسيولين ادت الى زيادة معنوية (P<0.03) فى الحجم التشريحى للقولون وكانت هذه الزيادة ترجع اساسا الى الزيادة فى المحيط (P<0.02) عنها فى الطول فى الحيوانات المعاملة بالمقارنة بالضابطة٠