Indian J Physiol Pharmacol 2009; 53 (1) : 55–60

HIGH FAT DIET INDUCES OBESITY IN BRITISH ANGORA RABBIT : A MODEL FOR EXPERIMENTAL OBESITY

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(Received on September 4, 2008)

Abstract : A reliable and cost-effective animal model for human obesity with its manifested disorders is yet to be established in the context of increased morbidity and mortality due to obesity and its related problems. Therefore, an attempt was made to produce obesity in locally available British Angora Rabbits (BAR) and examine the effect on metabolic and cardiovascular parameters. Adult male BARs weighing nearly 2 kg were randomly divided into two groups, one of the groups was fed with high fat diet (HFD) *ad libitum* for 10 weeks and the control group received standard normal rabbit chow for same period. Body weight, skinfold thickness, serum cholesterol, serum glucose and resting heart rate were measured before and after the dietary regimens. After 10 weeks, HFD group of rabbits demonstrated significant ($P<0.05$) increase in body weight (+24%) and skinfold thickness (+37%). The gain in body weight was positively correlated to skinfold thickness ($r=0.61$). Serum cholesterol, serum glucose and resting heart rate were also increased by 46%, 52% and 15%, respectively. Whereas no such increases in any of these parameters were observed in control group of rabbits. Our results suggest that obesity can be produced in BARs by feeding HFD. The obesity manifests with cardiovascular and metabolic changes. It is proposed that this may serve as a valid and reliable model of experimental obesity.

Key words : obesity high fat diet british angora rabbit

INTRODUCTION

Obesity is the end result of mismatched energy intake and energy expenditure leading to excessive accumulation of fat. In human, it may be the consequence of

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improper diet intake, less physical activity, endocrine or genetic disorders. The development of obesity may be associated with metabolic diseases like dyslipidemia, type II diabetes mellitus, and cardiovascular diseases. These diseases are not only the burden of the Western world but also a great concern to the Indian subcontinent (1–4). Various animals including rabbit (5–7), mouse (8), rat (9), and dog (10) have been used for investigation of obesity related diseases. However, not all the animal models appeared consistent in exhibiting altered cardiovascular as well as other metabolic characteristics like hypertension, dyslipidemia, dysglycemia etc. that mimic manifestations of the human obese conditions. Recent report indicates that diet induced obese rabbits also may have lipid metabolism similar to obese human (11). However, all strains of rabbits after induction of obesity may not demonstrate altered cardiovascular responses, hyperglycemia and hypercholesterolemia. For example, obese female New Zealand white rabbit, frequently employed in experimental obesity studies failed to exhibit hypercholesterolemia, which is an important pathology associated with human obesity (5). To overcome the difficulty, genetically manipulated mouse model (12, 8) or an artificially bred Watanabe Heritable Hyperlipidemic (WHHL) rabbits were also developed (13, 14). However, these animal models may require expensive advanced technologies and are difficult to maintain and propagate. Therefore, considering the rapid increase in obesity related disorders in the Indian subcontinent, the present investigation was undertaken to examine whether locally available natural strain of British Angora rabbits (BARs) can serve as a convenient, cost effective and reliable animal model for diet-induced obesity.

MATERIAL AND METHODS

Fifteen adult male BARs weighing around 2 kg were housed individually in standard cages at natural light/dark condition and room temperature maintained at 26±2°C. After a week of acclimation period, they were randomly divided into two groups. One of the groups was fed with standard rabbit chow having composition of all the dietary elements appropriate for maintaining normal rabbit (15) and served as control. Another group received high fat diet (HFD) in which 10% fat (2/3 corn oil and 1/3 animal lard) was added to the standard normal rabbit chow (16). Food and water were provided *ad libitum* and their intake was monitored daily at a fixed time of the day. Weekly body weight was recorded throughout the period of 10 weeks. The skinfold thickness (SFT, lateral to umbilicus, measured in mm) was recorded at the start (0 week) and after 4th and 10th week of dietary regimen.

The ECG was recorded in conscious restrained animal (without notable sign of discomfort) with the help of fine needle (28 G) electrode on a physiograph (Bio-devices, India) before starting the respective dietary regimen (0 week) and then after the end of 10th week of the diet schedule. The heart rate per minute was computed from averaged R-R interval in the last five minutes of a thirty minute ECG recording. In addition, blood samples from overnight fasted animals were collected in the morning (from marginal vein of ear) for estimation of serum cholesterol and glucose. Cholesterol and glucose were estimated using cholesterol-oxidase (17) and glucose-oxidase (18) methods, respectively. The estimations were done before (at zero week) the begining and after the end of 10 weeks of dietary regime. The experimental protocol of the study was approved by the Postgraduate Research and Ethical Committee, BP Koirala Institute of Health Sciences, Nepal.

Data analysis

The data for various parameters studied in both the groups were pooled to express as mean±SEM. Student's *t*-test for paired/ unpaired observations, two-way ANOVA and Tukey's multiple comparison tests were applied and mentioned in the appropriate places. A P value <0.05 was considered significant.

RESULTS

A significant increase in body weight was observed in the HFD group after 5th week of dietary treatment, as compared to the control group (P<0.05, two-way ANOVA followed by Tukey's multiple comparison test) as shown in Fig. 1A. There was nearly 24% gain in body weight in HFD group after 10 weeks. In contrast, the body weight of the control group of rabbits remained similar to the initial weight at the end of the experimental period.

The skinfold thickness (SFT) in HFD group recorded increase at 4th and 10th week, respectively. The increases were significant as compared to its initial as well as with the control group (P<0.05, two-way ANOVA followed by Tukey's multiple comparison test) as shown in Fig. 1B. The increase of SFT was positively correlated to the body weight in HFD fed rabbits (P<0.05, r=0.61) (Fig. 2).

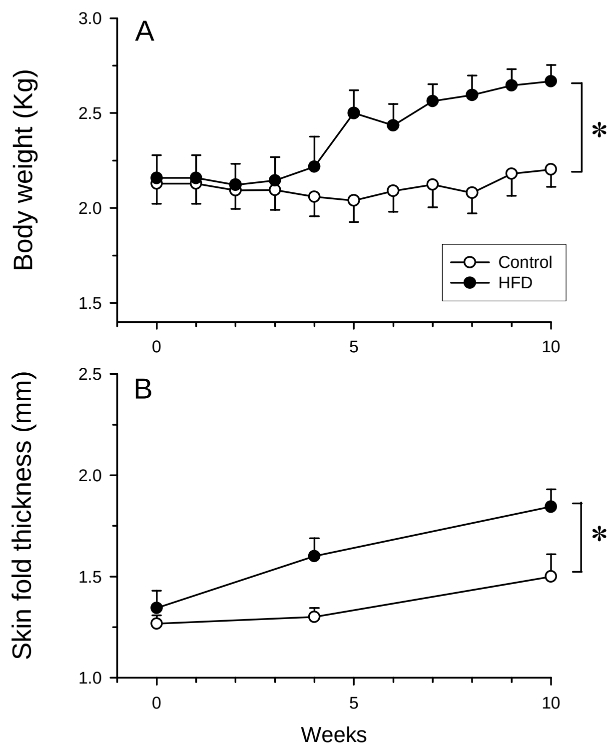

Fig. 1 : HFD fed rabbits demonstrated increased body weight and skinfold thickness. Mean±SEM values of body weight **(A)** and skinfold thickness **(B)** of control (n=6) and high fat diet (HFD) fed rabbits (n=9) during the period of 10 weeks. The basal body weight and skinfold thickness at 0 week (before the dietary regimen) are similar in both the groups. An asterisk (*) indicates P<0.05 (two way ANOVA) as compared to the control group.

Basal heart rate (HR) in control and HFD groups were similar at the beginning (Table I). In HFD group, the HR increased significantly (15%) at the end of 10th week (P<0.05, Student's *t*-test for paired observations; Table I). This was also significantly greater than the HR in the time matched control rabbits (P<0.05, Student's *t*-test for unpaired observations, Table I). No such increase in HR was seen in control rabbits.

TABLE I : Mean ± SEM values for the heart rate, serum cholesterol and serum glucose level in control (n=6) and HFD fed (n=9) rabbits, before and after 10 weeks of dietary regimen.

Parameters	*Control*		*HFD*	
	Before	*After*	*Before*	*After*
Heart rate (beats/min)	248±8.97	239±5.66	256±10.60	295±13.06*@
Serum Cholesterol (mg/dl)	47.80±6.07	44.13±3.53	50.83±3.22	74.17±8.65*@
Serum glucose (mg/dl)	86.11±4.78	88.95±3.97	78.32±2.35	119.18±3.25*@

*P<0.05 as compared to before values in HFD group (Student's *t*-test for paired observations)
@P<0.05 as compared to after values in control group (Student's *t*-test for unpaired observations)

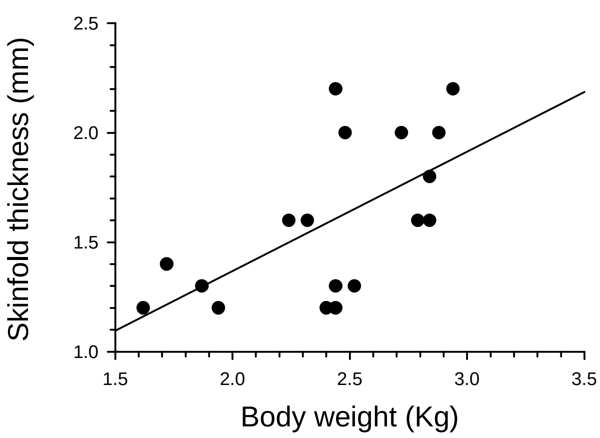

Fig. 2 : Linear regression analysis showing the relationship between the skinfold thickness and body weight in HFD fed rabbits. The skinfold thickness exhibited positive correlation with the body weight/v–. (*P<0.05, r=0.61).

The results regarding changes in serum cholesterol and serum glucose are shown in Table I. Overall, there was a significant increase in serum cholesterol (46%) and glucose (52%) in HFD group after 10 weeks (P<0.05, Student's *t*-test for paired observations). The control group of rabbits did not show any remarkable changes (Table I).

DISCUSSION

The present study demonstrated that feeding of high fat diet to British Angora rabbits, can produce obesity with manifestations like hypercholesterolemia, hyperglycemia and increased heart rate. The metabolic and cardiovascular alterations observed in these rabbits are similar to human obesity. A number of studies used diet-induced obesity in different animal models including rat (19), rabbit (5) and dog (10) and were considered promising models for the investigation of obesity-related cardiovascular dysfunction. However, an important limitation of the above studies was inconsistency in producing major obesity-related metabolic changes that observed in human obesity. In this context, it may be observed that, female New Zealand White rabbits used in diet-induced obesity demonstrated alterations in hemodynamic and neurohumoral status reflecting human-like obesity associated changes, but failed to show an increase in serum cholesterol level (5) which is an important independent risk factor for coronary heart disease, a major consequence of human obesity. In the present study, the BARs fed with HFD developed significant hypercholesterolemia and high fasting blood glucose level. The hyperglycemia observed in the present study could be attributed to increased insulin resistance in obese rabbits as speculated earlier (5) and closely comparable to biochemical manifestations of human obesity.

A significant increase in body weight observed in the HFD group after 10 weeks of feeding indicate that obesity can be produced within a reasonable period of time in BARs. Another interesting observation of the present investigation is that SFT showed a significant positive correlation (Fig 2) with body weight that corresponds with the obesity in human (20). Therefore, SFT might serve as a good indicator for obesity in animal models too.

In the present study, an increase in heart rate was observed in obese rabbits and thus confirms the obesity-induced resting heart rate changes as documented in earlier studies on human obesity (21) as well as studies in obese rabbits (5, 7). Although the mechanisms underlying the metabolic and cardiovascular changes can not be ascertained from the present investigations but their similarity with of human obesity may be speculated. A recent study confirmed the speculation, as the lipid metabolism in diet-induced obese rabbits and that in obese human are similar (11). The other advantages of BARs that may attract the experimental researchers on obesity are their easy availability and documented husbandry (22, 23). Thus, BARs appear to be reliable model for investigation of obesity related metabolic as well as cardiovascular changes similar to that observed in human.

In conclusion, it can be observed that obesity developed in these rabbits is comparable to human obesity in terms of major physical, biochemical and cardiovascular markers such as changes in body weight, skinfold thickness, serum cholesterol and serum glucose levels. Therefore, the BARs can be used as a reliable and valid animal model for obesity-related studies.

ACKNOWLEDGEMENTS

This study was supported by the Postgraduate Research Grant of BPKIHS. We also acknowledge the contributions of Dr. Madhab Lamsal and Mr. Amrendra Jha of Department of Biochemistry, BPKIHS for their help in analysis of biochemical parameters.

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