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PHOSPHATE SUPPLEMENTATION PREVENTS A DECREASE OF TRIIODOTHYRONINE AND INCREASES RESTING METABOLIC RATE DURING LOW ENERGY DIET

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Thirty overweight women participated in 8 week slimming program consisting of a self-controlled low-energy diet (4.2 MJ/day) supplemented with highly viscous fibres and mineral tablets containing calcium, potassium and sodium phosphates (Redusan Combi, Biokraft Pharma AB, Sweden). Half of the patients received in double blind manner mineral tablets during first 4 weeks and placebo (without phosphates) during next 4 weeks (group 1) while the remaining patients were treated (cross-over) with placebo first and mineral tablets in the final period (group 2). The rate of weight loss was similar in groups 1 and 2 (4.7 vs 5.2 kg during the first 4 weeks and 2.7 vs 3.0 kg in the further 4 weeks). During periods of phosphate supplementation, the resting metabolic rate (RMR) increased by approx. 12% ($p<0.05$) in group 1 and 19% ($p<0.05$) in group 2. Phosphate supplementation ameliorated also a decrease in plasma triiodothyronine level and a decrease in thyroxine to triiodothyronine ratio. There were no differences between groups in the plasma insulin, catecholamine, growth hormone, cortisol and testosterone levels. Phosphate supplementation did not affect plasma lipids or blood glucose concentration. It is concluded that phosphate supplementation in obese patients on a low-energy diet enhances RMR irrespectively of the rate of weight loss. This efect seems to be, at least partly, due to an influence of phosphates on peripheral metabolism of thyriod hormones.

Key words: *weight-reduction, phosphates, resting metabolic rate, thyriod, hormones*

INTRODUCTION

It is well known that during energy restriction the highest rate of weight loss occurs within the first few weeks on a diet, and then the effectiveness of the therapy markedly decreases. A fall in metabolic rate (by approx. 15%) has been proved to be one of the causes of the latter phenomenon (1—6). The studies of Jaedig and Henningsen (7—9) suggested that suplementation with potassium

and phosphates increases both the resting and postprandial metabolic rate in obese women, accelerates the decrease in body weight and prevents the regain of body mass after cessation of the dietary treatment. It has been also reported that muscle and total body potassium as well as serum phosphate are significantly lower in obese than in lean subjects and phosphate concentration inversely correlates with body mass (10). Furthermore, the low calorie diet is expected to aggravate this relative phosphate depletion (11) which may secondarily counteract the beneficial effect of energy restriction on glucose storage and insulin sensitivity (12). The aim of this study was to gain a deeper insight into the effect of phosphate supplementation on metabolic and endocrine changes in overweight women undergoing an eight-week program of weight reduction.

MATERIAL AND METHODS

Thirty six clinically heathly, women aged from 31 to 46 years, and with body mass index (BMI) from 29 to 45 kg m^{-2} participated in this study after giving informed consent to take part in the eight week slimming program with specified laboratory examinations. The program was approved by the Ethical Committee at Warsaw Medical Academy. The patients were engaged in sedentary proffesional work and none of them took part in any regular sport activity. According to the questionnaries filled by all participants, their diet contained approx. 45% of carbohydrate, 40% of fat and 15% of protein, and their daily energy intake ranged between 8000 and 10000 kJ when checked daily over the period of one month preceding the beginning of the study. During this period the patients' body mass fluctuactions did not exceed $\pm$ 1.5 kg. All the patients were premenopausal and none of them claimed any irregularities in the menstrual cycle.

At the beginning of the study, all the patients were given the same dietary recommendations. In general, their daily allowence of energy intake amounted to 4200 kJ (1000kcal), and they were asked to record all food consumed each day. The prescribed diet contained on average: 40—50% carbohydrates, 30—40% protein and 10—20% fat. The patients on the diet were asked to maintain their normal activity both at work and during leisure time.

The women were randomly allocated into two groups. Those from group 1 (18 patients) received phosphates during the first 4 weeks and placebo during the next weeks on the diet, whilst those from group 2 (18 patients) received first placebo and then phosphates. The patients did not have knowledge which treatment they received. The same was true for the medical personnel conducting the study (double blind). Three patients from group 1 and three patients from group 2 were excluded from the study because they were distinctly exceeding the prescribed food intake or were not taking mineral or placebo tablets regularly. There were no significant differences between the two groups in age, body mass, BMI body fat content and waist to hip ratio (*Table 1*).

For phosphate supplementation Redusan Mineral (Biokraft Pharma AB, Sweden), was used. It included: mineral tablets and high viscous fiber capsules (Redusan Fibre). Redusan mineral tablets contain: 537 mg calcium phosphate, 107 mg potassium phosphate, 25 mg sodium phosphate per tabl., and trace amounts of chromium, zinc, and magnesium salts. The subjects were instructed to take 2 Redusan mineral tables 3 times per day (after meals). Patients took also Redusan Fibre for appetite suppresing (6 capsules á 550 mg per day).

For placebo treatment the subjects received placebo tables corresponding to Redusan Mineral placebo tablets containing lactose instead of phosphate salts. The treatment was applied in double blind manner.

Table 1. Characteristics of patients ($\bar{x} \pm SE$)

Group	Age (yrs)	Height (cm)	Body mass (kg)	BMI ($kg \cdot m^2$)	Body fat* (%)	Waist (cm)	Hip (cm)	Waist to hip ratio
1 n = 15	37.9 ±0.8	164.0 ±1.6	90.1 ±2.6	33.5 ±0.8	43.0 ±0.9	91.0 ±1.8	119.8 ±2.1	0.77 ±0.02
2 n = 15	39.8 ±1.3	162.4 ±1.0	87.7 ±2.6	33.3 ±1.1	43.4 ±0.6	89.2 ±2.1	116.4 ±1.8	0.76 ±0.02

* estimated from the skin-fold thickness, according to Durnin and Womersley (1974).

Every week, throughout the study, the women attended the whole-group meetings in the Laboratory during which their body mass changes and daily records of food intake were discussed, every two weeks they took part in behavioural therapy sessions.

Before, after 4 and 8 weeks on the low-energy diet the patients' resting metabolic rate (RMR) was measured and blood samples were taken for determination of blood metabolites and hormones. Care was taken to perform the above measurements always in the follicular phase of the patients' menstrual cycle between the 5th and 10th day of the cycle. On each occasion the patients reported to the Laboratory between 8—9 h A.M. after an overnight fast, had inserted an intravenous catheter to the antecubital vein and then rested for at least 30 min under controlled thermal conditions (24—25°C, 50—60% relative humidity) before RMR measurement and blood sample withdrawal.

The metabolic rate was estimated by an open circuit system (with the mouthpiece valve) for VO_2 and VCO_2 measurements using Jaeger-Ergooxyscreen (FRG). The measurements were made for 15 min. The data were printed every 30s and then averaged.

Blood analyses

Blood glucose (BG), plasma triacylglycerol (TG), and total cholesterol concentrations were determined enzymatically using commercial kits (Boehringer Diagnostica, Mannheim, FRG). For HDL-cholesterol estimation, precipitation whith phosphotungstate acid and magnesium was applied, using Boehringer precipitant. Plasma free fatty acids (FFA) were measured enzymatically according to Shimazu et al. (13). Plasma insulin (IRI), growth hormone (hGH), total thyroxine (T_4) and triiodothyronine (T_3) levels were determined radioimmunologically using RIA-MI-96, RIA-MI-99, RIA-MI-88 and RIA-MI-86 reagent kits (Institute of Atomic Energy, Świerk, Poland), respectively. Plasma adrenaline (A) and noradrenaline (NA) concentrations were measured radioenzymatically according to DaPrada and Zurcher (14) using the tests produced by Chemapol Co. Ltd (Czech Republic). Plasma cortisol and testosterone were determined by radioimmunoassays using antibodies provided by the Institute of Animal Physiology and Nutrition, Pol. Acad. Sci., (Jablonna n. Warsaw, Poland).

A standard statistical procedure was appiled. Significance of differences within and between groups were evaluated using the paired and unpaired Student's t-test, respectively. The data are presented as means ± standard error (SE) throughout the text.

RESULTS

Changes in body mass

In both groups a higher rate of body mass reduction was found during the first 4 weeks (4.7 ± 0.5 kg in group 1 and 5.2 ± 0.4 kg in group 2) than during the further 4 weeks on the low-energy diet (2.7 ± 0.4 kg and 3.0 ± 0.3 kg, respectively). There were no significant differences between groups in body mass loss. In neither period of the study weight reduction correlated with the initial body mass or BMI.

Within both groups RMR was elevated at the end of periods of phosphate supplementation in comparison with the respective initial values and the data obtained after placebo treatment (*Fig. 1 and 2*). Comparisons between the two groups showed a significant difference in RMR after the final period of the diet ($P < 0.05$).

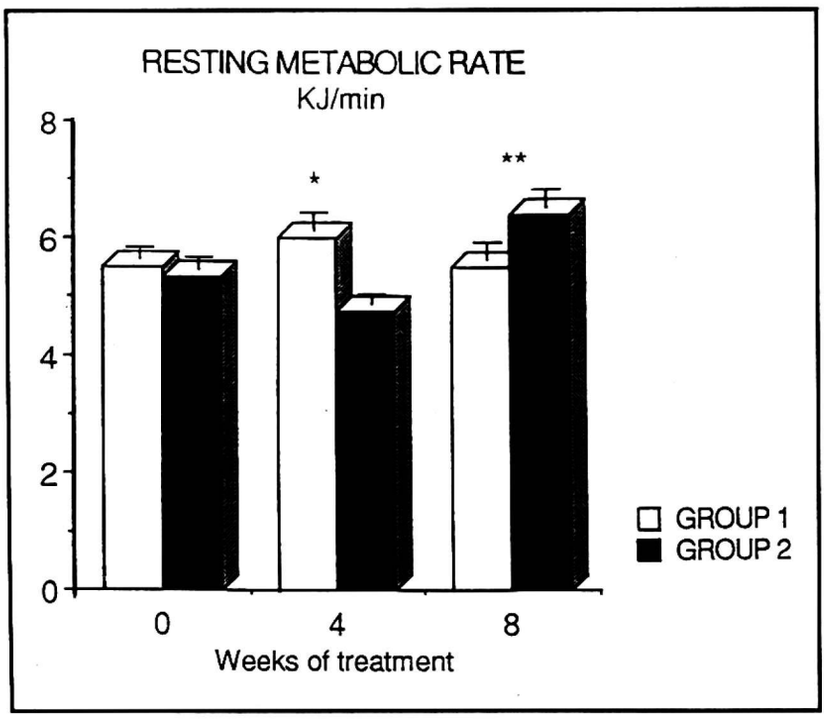

Fig. 1. Resting metabolic rate (kJ/min) before, after 4 and 8 weeks of weight reducing program in two groups of patients. Group 1 received phosphate tablets during the first 4 weeks and placebo during the final 4 weeks, whereas group 2 received placebo first and phosphates in the further period. Asterisks denote significant differences in comparison with the initial value; *$P < 0.05$, **$P < 0.01$

In both groups there was a tendency towards some decrease in the plasma total cholesterol during 8 weeks on the diet, without significant changes in the ratio of HDL to total cholesterol (*Table 2*). The plasma TG levels were decreasing in both groups with duration of the diet. Changes in the plasma FFA did not show any uniform pattern, but the values were relatively high in all stages of the treatment, particularly in group 2. In neither group any alterations in blood glucose were found.

Serum total T_4 (*Table 3*) showed marked reduction with duration of the low-energy diet. In group 1 a significant difference was ascertained already after 4 weeks, whilist in group 2 after 8 weeks of the treatment. Serum total T_3 was

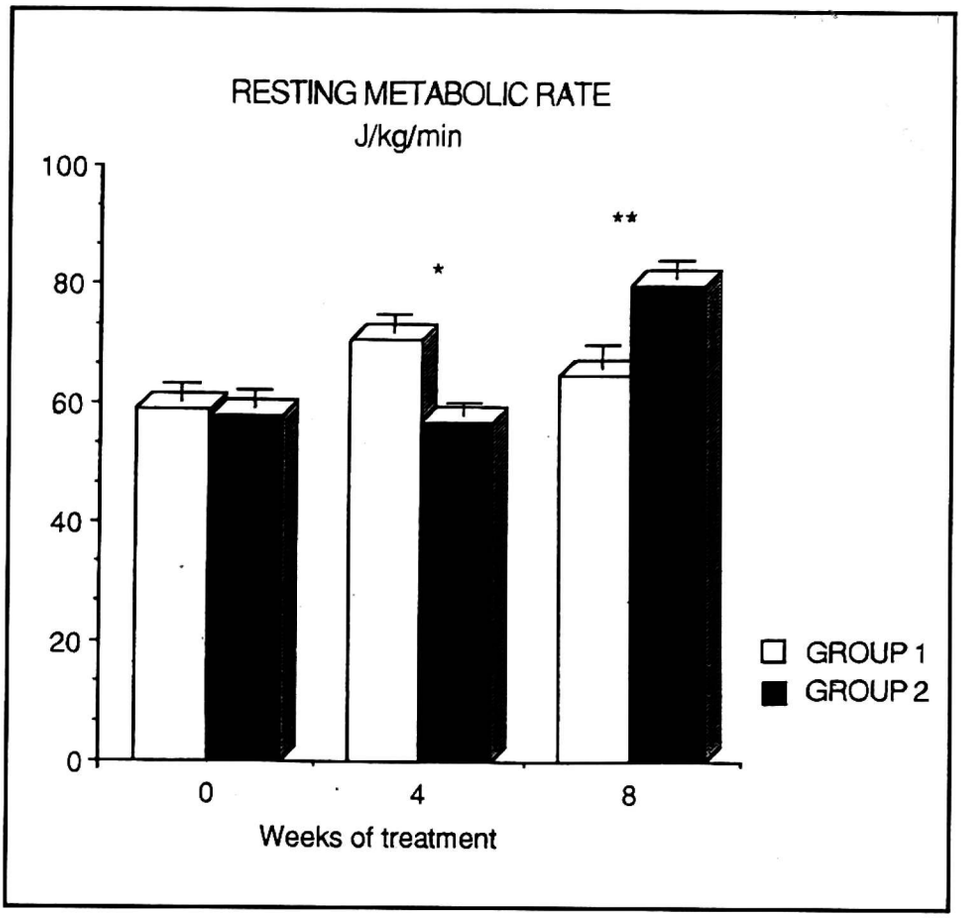

Fig. 2. Resting metabolic rate (J/kg/min) before, after 4 and 8 weeks of weight reducing program. Descriptions as in *Fig. 1.*

significantly decreased during the first 4 weeks in group 2 (placebo), whereas at the same time in group 1 (phosphate supplementation) it remained unchanged. During the next 4 weeks of the program in group 2, serum T_3 returned to initial levels and in group 1 it was reduced. The ratio of T_4 to T_3 was significantly decreased at the end of the periods of phosphate supplementation in both groups (*Fig. 3*).

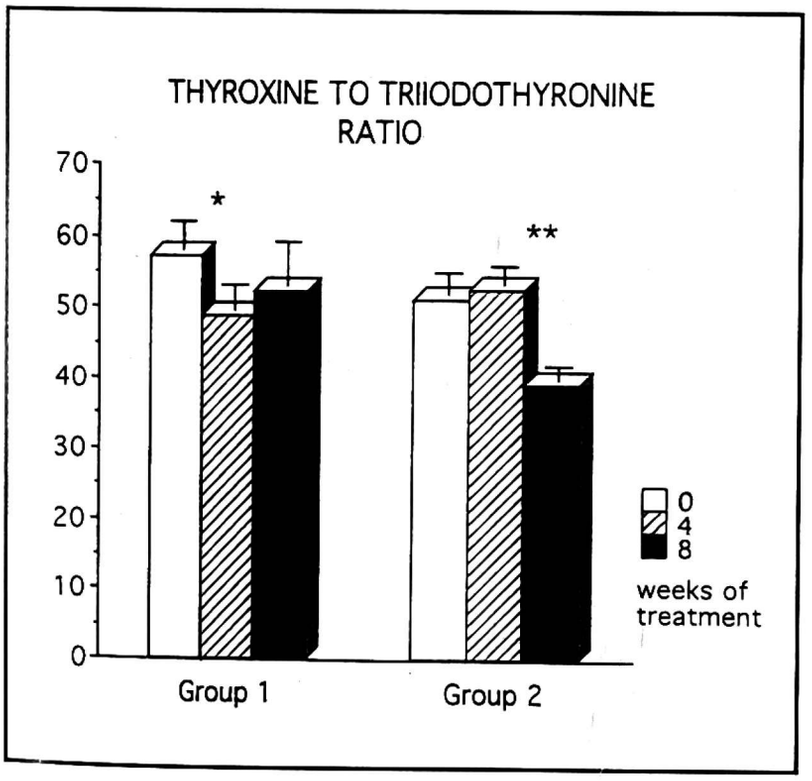

Fig. 3. The ratio of serum thyroxine to triiodothyronine concentrations before, after 4 and 8 weeks of weight reducing program. Descriptions as in *Fig. 1.*

Table 2. Blood metabolite concentrations ($\bar{x} \pm SE$) in patients on low-energy diet

Variable	Group 1			Group 2		
	Initial values	4th week Phosphates	8th week Placebo	Initial values	4th week Placebo	8th week Phosphates
Total cholesterol ($mmol \cdot l^{-1}$)	4.99 ± 0.21	4.84 ± 0.21	4.84 ± 0.26	5.28 ± 0.21	4.84 ± 0.18	$4.68 \pm 0.18^{+}$
HDL ($mmol \cdot l^{-1}$)	1.24 ± 0.05	1.27 ± 0.05	$1.37 \pm 0.08^{+}$	1.27 ± 0.05	$1.19 \pm 0.05^{+}$	1.29 ± 0.04
HDL/Total cholesterol	0.25 ± 0.01	0.26 ± 0.01	0.28 ± 0.01	0.25 ± 0.01	0.25 ± 0.01	0.28 ± 0.01
Triacylglycerols	0.87 ± 0.06	0.80 ± 0.08	$0.66 \pm 0.06^{+}$	1.00 ± 0.13	0.89 ± 0.07	$0.62 \pm 0.08^{+}$
FFA $mmol \cdot l^{-1}$)	0.783 ± 0.044	0.717 ± 0.047	0.601 ± 0.061	0.725 ± 0.051	$0.923 \pm 0.076^{*}$	$0.828 \pm 0.061^{**}$
Blood glucose $mmol \cdot l^{-1}$)	5.2 ± 0.21	4.9 ± 0.09	4.9 ± 0.09	4.9 ± 0.07	5.0 ± 0.12	5.0 ± 0.09

Values significantly different from group 1 — $^{*}p < 0.05$; $^{**}p < 0.01$
Values significantly different from the initials within the groups — $^{+}p < 0.05$.

Table 3. Blood hormone concentrations ($\bar{x} \pm SE$) in patients on low-energy diet

Hormone	Group 1			Group 2		
	Initial values	4th week Phosphates	8th week Placebo	Initial values	4th week Placebo	8th week Phosphates
Insulin ($\mu U \cdot ml^{-1}$)	24.6 ± 2.6	20.07 ± 2.7	19.5 ± 1.8	21.2 ± 2.2	22.7 ± 4.0	19.5 ± 2.0
Thyroxine — T_3 ($ng \cdot ml^{-1}$)	95.3 ± 4.3	82.4^{+} ± 3.8	74.5^{++} ± 5.0	92.1 ± 7.0	89.8 ± 8.6	68.8^{+++} ± 3.3
Triiodothyronine — T_3 ($ng \cdot ml^{-1}$)	1.74 ± 0.09	1.49 ± 0.10	1.59^{+} ± 0.11	1.71 ± 0.05	1.56^{+} ± 0.06	1.75 ± 0.08
Noradrenaline ($pmol \cdot ml^{-1}$)	1.67 ± 0.13	1.55 ± 0.15	1.83 ± 0.12	1.69 ± 0.20	1.47 ± 0.19	1.41 ± 0.18
Adrenaline ($pmol \cdot ml^{-1}$)	0.13 ± 0.01	0.17 ± 0.03	0.20 ± 0.02	0.22 ± 0.04	0.17 ± 0.03	0.17 ± 0.04
Cortisol ($ng \cdot ml^{-1}$)	69.2 ± 8.4	49.3^{+} ± 5.0	82.6 ± 6.6	81.8 ± 8.9	58.7^{+} ± 9.1	84.5 ± 13.0
Human Growth Hormone — hGH ($ng \cdot ml^{-1}$)	3.0 ± 0.9	3.1 ± 0.5	2.3 ± 0.4	2.5 ± 0.6	2.5 ± 0.6	2.4 ± 0.6
Testosterone ($pg \cdot ml^{-1}$)	1.21 ± 0.25	1.26 ± 0.19	1.06 ± 0.24	1.75 ± 0.27	1.45 ± 0.23	1.01 ± 0.23

Values significantly different from the initials within the groups — $^{+}p < 0.05$; $^{++}p < 0.01$; $^{+++}p < 0.001$.

A tendency towards a decrease in the plasma IRI and testosterone with duration of the weight-reducing program was noted in both groups, whilist no changes were found in the plasma catecholamines and hGH. The plasma cortisol decreased significantly after 4 weeks on the diet, and then increased in the further period both in group 1 and 2.

DISCUSSION

The study showed a significant increase in RMR at the end of the periods of phosphate treatment in overweight women on low calorie regimen. These data are in agreement with those of Jaedig and Henningsen (7, 8) who showed an increase in RMR during 12 weeks of caloric restriction in overweight women receiving supplement of potassium and magnesium phosphates. In the present study, the elevations of RMR occurred irrespectively of the rate of body weight reduction, the latter being similar in both groups. The reason for the lack of difference between groups in body mass changes in spite of enhancement in RMR in phosphate treated women is not apparent. However, since food intake was checked only on the basis of patients' daily records, it could not have been excluded that there was a small compensatory increase in food intake that counterbalanced the enhanced energy ependiture. Furthermore, much longer period of observation is probably required to show and verify the possible impact of small changes in energy expenditure on measurable changes in body mass.

Inorganic phosphate plays an important role in the control many energy yielding processes. Moreover, it was shown that phosphates increase the concentration of 2, 3 diphosphoglycerate (2, 3 DPG) in erytrocytes, promoting disociation of oxyhemoglobin, and thus improving tissue oxygenation (16). This may enhance fat combustion, and subsequently increase metabolic rate. However, in our study no change in the respiratory quotient were noted in the patients treated with phosphates, so the increased oxidation of fat was not confirmed.

On the other hand, supplementation with phosphates was found to increase maximal oxygen uptake (VO_2 max), the increase being correlated to the simultaneous increase of 2, 3 DPG in the red blood cells (17). Similarly (18), it was reported that maximal and submaximal run performance were influenced by elevations in serum phosphates elicting an increase of VO_2 max, and ventilatory anaerobic threshold. According to Briedle et al. (19) supplementation with phosphates is causing the greater arteriovenous O_2 difference which is not correlated with any changes in erythrocyte 2, 3 DPG and suggest a peripheral effect of phosphates that increases O_2 extraction (20). The absence of lowering RQ in our study was not expected in view of well

known RQ decrease associated with energy restrictions and dependent on the increased availability and oxidation of FFA. However, it can be speculated that parallel increase of glucose utilisation could counterbalance the lowering of RQ. Tsobui and Fukunaga (21) found that inorganic phosphates enhance glucose utilisation by the activation of phosphofructokinase. According to Rose et al. (22) the enhancement of glucose metabolism could depend on activation of hexokinase, the phosphate modulating the inhibitory effect of glucose-6-phosphate on the enzyme activity. In line with these findings is the observation that phosphates are enhancing the breakdown of glycogen stores in skeletal muscles (23). DeFronzo and Lang (12) showed that a decreased tissue insulin sensitivity, caused by hypophosphatemia, is leading to an inhibition of some energy consuming processes, such as glycogen synthesis. The enhancement of insulin sensitivity and glucose metabolism can also prevent the normally observed increase of the concentration of reverse triiodothyronine (rT_3) occurring in the course of low calorie diet and dependent mostly on the lowered carbohydrate intake (24).

The present data suggest that phosphate supplementation during low energy diet may also affect metabolic rate through the changes in thyroid hormone action. Triiodothyronine has been accepted to by primary regular of RMR. Reduced energy availability caused by restriced dietary intake (6) or increased energy expenditure (25) results in the lowered rate of deiodination of T_4 to T_3, manifesting itself by a fall of the plasma T_3 concentration and increased ratio of T_4 to T_3. The present study demonstrated that the decrease in circulating T_3 occurred in dieting women on placebo while during phosphate supplementation the level of this hormone was even increased and the ratio of T_4 to T_3 was lowered. This effect somehow resembles that occurring when the subjects were on a low energy diet but containing mainly carbohydrates (26).

The possible explanation of our finding is that phosphate supplementation reverses a block in the conversion of T_4 to T_3. This conversion requires NADPH which is produced in the process of glucose degradation *via* penthose cycle. Thus, one can assume that it relays not only on the continous supply of glucose but also phosphates.

Among factors influencing metabolic rate the sympatho-adrenal system plays an important role since activation of this system increases heat production under various conditions, e.g. cold exposure, physical exercise, psychological stress. However, contribution of catecholamines to the control of basal or resting metabolic rate is not quite obvious. The data concerning the catacholamine response to reduced energy intake are inconsistent. Some authors found a decrease of circulating catecholamines with caloric restriction (27—29) whilst the others failed to demonstrate any changes (30, 31). In the present study energy restriction was not associated with significant altreations

in the plasma adrenaline or noradrenaline levels, and no effect of phosphate supplementation on plasma catacholamine concentration was found. Thus, it seems unlikely that this treatment affects RMR in dieting women through modifications of the sympatho-adrenal system.

The other hormones, i.e. insulin, hGH, cortisol, and testosterone did not show any changes related to phosphate supplementation. It should be mentioned that in both groups the plasma cortisol level decreased after 4 weeks on the low energy diet, and then returned to basal values after 8 weeks. A decrease in the urinary excretion of corticosteroids during weight reduction has been described before (32), but no data were reported on the reversibility of the decrease in spite of continuation of the low energy diet. Zelissen et al. (33), demonstrated that a marked loss of body mass (by approx. 18%) does not influence cortisol production rate, which indicates that decreased cortisol secretion during weight reduction is a transient phenomenon.

In summary — the present study demonstrated an enhancement of RMR in obese women undergoing the weight-reducing program while supplementing the diet with inorganic phosphates (Redusan). Since it was shown that the decrease in the plasma T_3 level was ameliorated and the ratio of T_4 to T_3 decreased during phosphate treatment it is suggested that the observed elevation in RMR is casually connected with changes in the rate of thyroxine deiodination most probably associated with enhancement of glucose utilisation and production of NADPH induced by addition of inorganic phosphates.

REFERENCES

1. Apfelbaum M, Bostsarrou J, Lacatis D. Effect of caloric restriction and excessive caloric intake on energy expenditure. *Am J Clin Nutr* 1971; 24: 405—409.
2. Warnold J, Carlgen G, Krotkiewski M. Energy expenditure and body composition during weight reduction in hyperplastic obese women. *Am J Clin Nutr* 1983; 38: 680—693.
3. Barrows K, Snook JT. Effect of high protein, neru low calorie diet on resting metabolism, thyroid hormones, and energy expenditure of obese middle-aged women. *Am J Clin Nutr* 1987; 45: 391—398.
4. Ravussin E, Burnand B, Schutz V, Jequier E. Twenty-four hour energy expenditure and resting metabolic rate in obese, moderately obese and control subjects. *Am J Clin Nutr* 1982; 35: 566—573.
5. Velle SL. Amatrude M, Forbes GB, Lockwood DA. Resting metabolic rates of obese women after rapid weight loss. *J Clin Endocrinol Metab* 1984; 59: 41—44.
6. Krotkiewski M, Tross L, Bjorntorp P, Holm G. The effect of very-low calorie diet with and without chronic exercise on thyroid and sex hormones, plasma proteins, oxygen uptake, insulin and C-peptide concentrations in obese women. *Int J Obesity* 1981; 5: 281—293.
7. Jaedig S, Henningsen NC. Prevention of increasing body weight after weight reducing program by use of K^+, HPO_4 supplement. In The 1st European Congress of Obesity. Abstract Book. Stockholm, 1988, p. 202.

8. Jaedig S, Henningsen NC. Increased resting metabolic rate during caloric restriction in $K^+/Mg^{++}-HPO_4$ treated obese women. In The 1st European Congress of Obesity. Abstract Book. Stockholm, 1988, p. 214.
9. Jaedig S, Henningsen NC. Increased metabolic rate in obese women after ingestion of potassium, magnesium and phosphate-enriched orange juice or injection of ephedrine. *Int J Obesity* 1990; 14: 429—436.
10. Lindgarde F, Tress E. Serum inorganic phosphate in middle aged men: An inverse relation to body weight. *Acta Med Scand* 1977; 202: 307—311.
11. Keller V, Berger W. Prevention of hypophosphatemia by phosphate infusion during treatment of diabetic ketoacidosis and hyperonkotic coma. *Diabetes* 1980; 29: 87—95.
12. DeFronzo RA, Lang R. Hypophosphatemia and glucose intolerance: Evidence for tissue insensitivity to insulin. *N Engl J Med* 1980; 303: 1259—1263.
13. Shimazu S, Inoue Y, Tani Y, Yamada H. Entzymatic micro-determination of serum free fatty acids. *Analyt Biochem* 1979; 98: 341—345.
14. DaPrada M, Zurcher G. Radioenzymatic assay of plasma and urinary catecholamine in men and various animal species: Physiological and pharmacological applications. In Radioimmunoassay of Drugs and Hormones in Cardiovascular Medicine, Albertini, Da Prada, and Pescar (eds.). Amsterdam, Elsevier North Holland, 1979, pp. 112—119.
15. Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness measurements of 481 men and women aged from 16 to 72 years. *Br J Nutr* 1974; 32: 77—97.
16. Benesch R, Benesch RE. Intracellular organic phosphates as regulators of oxygen release by haemoglobin. *Nature* 1969; 221: 618.
17. Code R, Coute M, Zauner Ch. Effects of phosphate loading on 2, 3 diphosphoglycerate and maximal oxygen uptake. *Med Sci Sports Exerc* 1984; 16: 263—266.
18. Kreider RP, Miller GW, Melvin H. Effect of phosphate loading on oxygen uptake, ventilatory, anaerobic threshold and performance. *Med Sci Sporta Exerc* 1990; 22: 250—256.
19. Briedle DL, Stager JM, Brechne NF, Farber MO. Phosphate supplementation, cardiovascular function, and exercise performance in humans. *J Appl Physiol* 1988; 65: 1821—1826.
20. Bark H, Nizri M, Tarsiuk A, Heimer D. Effects of hyperphosphatemia on diaphragmatic strenght and endurance. *J Appl Physiol* 1992; 73: 82—87.
21. Tsuboi KK, Fukunaga K. Inorganic phosphate and enhanced glucose degradation by the intact erythrocyte. *J Biol Chem* 1965; 240: 2806—2810.
22. Rose JA, Warms JVB, O'Connell L. Role of inorganic phosphate in stumulating the glucose utilization of human red blood cells. *Bioch Biophys Res Comm* 1964; 15: 33—37.
23. Chastiotis D. The regulation of glycogen phosphorylase and glycogen break-down in human skeletal muscle. *Acta Physiol Scand* 1983; suppl. 18.
24. Danforth E Jr, Burger Ag. The impact of nutrition on thyroid hormone physiology and action. *Ann Rev Nutr* 1989; 9: 201—227.
25. Loucks AB, Callister R. Induction and prevention of low — T_3 syndrome in exercising women. *Am J Physiol* 1993; 264: R924—R930.
26. Matzen LE, Kvetny J. The influence of caloric deprivation and food composition on TSH, thyroid hormones and nuclear binding of T_3 in mononuclear blood cells in obese women. *Metabolism* 1989; 38: 555—561.
27. Fagerberg B, Andersson OK, Isaksson B, Bjorntorp P. Blood pressure control during weight reduction in obese hypertensive men: separate effects of sodium and energy restriction. *Br Med J* 1984; 288: 1—14.
28. Sowers JR, Nyby M, Stern N et al. Blood pressure and hormone changes associated with weight reduction ion the obese. *Hypertension* 1982; 4: 686—691.

29. Scherrer U, Nussberger J, Torriani S et al. Effect of weight reduction of moderately overweight patients on recorded ambulatory blood pressure and free cytosolic platelet calcium. *Circulation* 1991; 83: 552—558.
30. Anderssson B, Wallin G, Hedner T, Ahlberg A-Ch, Andersson O. Acute effects of short-term fasting on blood pressure, circulating noradrenaline and efferent sympathetic nerve activity. *Int J Obesity* 1989; 13 (Suppl. 1): 50—92.
31. Weinsier RL, James LD, Darnell BE, Dustan HP, Birch R, Hunter GR. Obesity related hypertension: evaluation of the separate effects of energy restriction and weight reduction on hemodynamic and neuroendocrine status. *Am J Med* 1991; 90: 460—468.
32. Krotkiewski M, Butruk E, Lembrowska L. L'influence d'un regime hypocalorique a 44% de lipides et de l'amalgrissement sur l'excretion urinaire des corticosteroids chez les obeses. *Le Diabete* 1966; 14: 253—256.
33. Zelissen PN, Koppeschaar HP, Erkelens DW, Thijssen JH. Beta-endorphin and adrenocortical function in obesity. *Clin Endocrinol* 1991; 35: 369—372.

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