nupo®

Clinical Studies Overview

Studies

Introduction

Nupo's VLCD (Very Low Calorie Diet) products have been used for over three decades in Denmark. The story of Nupo and our products dates back to 1981 and since then we have provided products for effective and safe weight loss. The name Nupo is a combination of the words "Nutritional Powder".

Nupo was developed at Hvidovre Hospital in Denmark by leading obesity researcher Dr. Flemming Quaade in cooperation with the company Oluf Mørk A/S, which was primarily responsible for commercialising the name.

Since the early 80's Nupo's VLCD products have been tested and approved in more than 35 clinical trials and they are being continuously developed and tested by research teams at hospitals throughout Denmark.

The present overview consist of ten clinical studies picked out from the very beginning of the creation of Nupo until present time (September, 2018). The criteria for the studies in the overview is the relevance of the different topics examined. When treating obesity it is of great importance how the weight loss affect the person regarding, a number of factors i.e. bone mass, lean body mass, fat body mass, cardiovascular risk factors, hunger etc.

Even though the composition of the Nupo's VLCD product have changed a bit since the early days: now the powder include fibres - the topics and results of the studies made at that time are still highly relevant and we conclude that the inclusion of fibres in our products would not have shown any differences in the results of the studies.

Future clinical studies

We are proud that research teams still use our VLCD products for an effective and safe weight loss for their studies.

Nina RW Geiker has further developed, the latest clinical study in the overview: *The effect of weight loss in obese patients with heart failure – a pilot study,* in a Ph.D. thesis. Her thesis: *Optimizing patient nutrition* includes it as; *Paper III: Weight loss by LED improves physical performance and car-diovascular risk markers in obese patients with heart failure*. The defence of this Ph.D. thesis was in March 2013.

In present time, our products are used in a voluminous study with 200 participants at Copenhagen University: *The Effect of Protein and Calcium in Weight Management and Plasma Lipid Profiles*. The preliminary results show great effect on the initial weight loss for the 97 persons already treated. A significant weight loss, positive effect on the plasma lipid profiles and reduction of several risk markers for developing cardiovascular diseases and diabetes. We are looking very much forward to including this study when terminated in the future.

We hope you will find our **Clinical Studies Overview** interesting and enjoyable to read. If you have any questions after reading, we will be happy to help you with the answer.

Best regards,

Nupo ApS

Study 1:

Gastroplasty Preceded by Very-low-calorie-Diet – A Preliminary Report

- *T. Andersen, et al. (1986)*

Introduction

Gastroplasty (GP) performed in morbidly obese patients is fraught with an unavoidable perioperative hazard, and weight loss is often unsatisfactory even on a short term. On the other hand, weight maintenance is better after GP than after diet alone. In order to increase the ultimate weight loss and reduce surgical hazards, consecutive patients of the present study receive a mandatory two-step treatment: After initial very-low-calorie-diet, (VLCD) GP is performed provided a 40% reduction of overweight has been obtained by diet. GP patients selected in this way are equally assigned to vertical banded GP or to Gomez GP. Weight control and patient education is run at group meetings.

Methods

74 patients, all admitted for morbid obesity, have been included. Their median age was 34 years, their median body weight 125.1 kg and their median overweight 93% calculated according to a Scandinavian standard. They were all screened for contraindicating diseases through clinical examination, analyses of blood and urine, ECG and liver biopsy. Treatment was started simultaneously in about 35 patients at a time. The VLCD nutrition powder used, NUPO, is apportioned as five daily meals, and water is added as vehicle. Between the 8-week periods with VLCD, a 2-week 900 Kcal diet consisting of natural high-protein, low-fat and low-carbohydrate foods is prescribed.
The VLCD programme is continued as long as a substantial weight loss is obtained. Anorexic agents are not allowed. Patients are offered operation as the second step of the programme only if a 2/5 reduction of overweight has been reached during VLCD. Horizontal and vertical GP are performed as published elsewhere. Weight control is run at group meetings together with a formalised patient education programme. Patients are seen weekly until three months after opera-tion, every second week until 6th postoperative month and at least every three months thereafter.

Results

Results are preliminary, and no comparison can yet be made between the randomised subgroups. Median weight loss after the first eight weeks of VLCD vas 17.9 kg (range, 3.6-38.4 kg, n = 74). Result of VLCD can at present be evaluated only for the treatment group first started (44 patients). Of these, 31 (70%, 95% confidence limits 55-83%) reached the limit for operation. Two patients (5% of patients otherwise available for surgery, 95% confidence limits 1-15%) failed after successful VLCD to appear for group meetings. Until now, 25 patients have had GP. Most patients have stabilised their weight 3 months after surgery. At this time median postoperative weight loss is 9.0 kg (range, 3.4-22.0 kg, n = 25) and median total weight loss from VLCD plus GP has reached 46.0 kg (range, 26.1-64.0 kg, n = 25). During VLCD, the only observed complication was one case of gout, quickly yielding to conventional treatment.

Conclusion

VLCD leads to immediate weigh losses not significantly different from those obtained by GP. Compared with VLCD, GP seems to possess a long-term effect on food intake, making regain significantly less pronounced. A comparison of therapeutic hazards is in favour of VLCD, which is safe when carried out with a nutritionally adequate formula. Combining the good elements of both treatments has led to the present protocol, investigating a two-step regimen, in which GP is preceded by VLCD. After GP, compliance with diet is essential for weight reduction and safety. Pre-treatment with VLCD offers an opportunity to test patients' ability to comply. It should be realised gastric obesity surgery will never succeed in patients not prepared to follow dietary advice. Through adjusting, the duration of VLCD weight loss can be individualised. This means that nearly all patients can reduce their overweight to less than 40%, which can be considered the lover limit of excess mortality from obesity. Preoperative weight reduction makes the operations much easier and safer and the postoperative management simpler. Accordingly, patient satisfaction is improved.

Study 2:

Formula Diet Plus Free Additional Food Choice up to 1000 Kcal (4.2 MJ) Compared with an Isoenergetic Conventional Diet in the Treatment of Obesity. A Randomised Clinical Trial.

- *H. Hey, et al. (1986)*

Introduction

The Formula diet NUPO meets all international recommendations for daily intakes of protein, essential amino and fatty acids, vitamins, minerals and trace elements within af daily intake of only 388 kcal. A very low calorie (VLCD) regimen with NUPO as sole source of nutrition for many months has caused great weight loss without risk in patients with severe obesity. If the prescribed amount of nutrition powder is taken it is justifiable to allow a free choice of additional foods, including less valuable items, as long as the energy allowance is small enough to induce weight loss. Renunciation of popular foods and beverages such as cake, sweets, wine and spirits is one major reason why many patients do not attempt to diet or, if they do, show poor compliance.
For these reasons, we felt justified in evaluating a 1000 kcal (4.2 MJ) regimen in which a fundament of formula diet is obligatory while at the same time the patients are totally free to manage the remaining energy allowance. The control group was prescribed an isoenergetic conventional slimming diet. This group was allowed diethylpropion in self-governed moderate dosage. Another purpose of the trial was to test a recently developed dietary system based on visual symbols of iso-energetic units (counters).

Methods

86 patients aged between 18 and 59 years with more than 20% overweight were assigned to one of two slimming diets. The test group had an obligatory basis (388 kcal) of a complete formula diet (NUPO) and were allowed a totally free additional choice of food and drink up to 1000 kcal including sweets and alcohol. The control group had a conventional isoenergetic diet excluding all less valuable items (“empty calories”) but were permitted to take an anorectic drug. All patients were instructed and controlled in groups, which saved resources and had psychological advantages. In both regimens dietary instructions was conducted within a new educational system based on isoenergetic, exchangeable units of every-day food and drink, visualised as illustrated symbols (counters).

Results

After 12 weeks, weight loss was insignificantly better on conventional diet (8,9 kg) than in the test group (7,5 kg). By contrast, the latter group had a better compliance, as evidenced by a significantly smaller dropout rate ($p < 0,05$). Repeated registration of energy intake showed that the consumption of “empty calories” was moderate in the test group, amounting to ab. 10%, and that excess intake was primarily due to an increased consumption of foods rich in fibre. Complaints of side effects were negligible in both groups. The counter diet system made instruction and control easy.

Conclusion

We conclude that a free qualitative food choice, made possible by the sufficiency of the formula diet as a basis, is a realistic, effective, and responsible alternative to conventional dietary treatment of obesity.

Study 3:

Initial Very Low Calorie Diet VLCD improves ultimate weight loss

- *Quaade, F. & Astrup, A. (1989)*

Introduction

Very Low Calorie Diet (VLCD) if it is of an adequate composition, especially with regard to protein, has long been a safe way of bringing about a considerable weight loss in obese persons within a reasonable time. We have used Nupo as a VLCD in the proper sense of the word, i.e. as the sole source of nutrition, for monthly periods. Furthermore, we use it as the mandatory base in diets of higher energy contents, usually 1000 kcal. One major reason for this is our experience that many patients do not follow a traditional diet instruction and, having done so, try to remedy this by eating less of the diet's valuable components. Alternatively, they try to keep within the traditional diet's overall energy frame by inserting grossly insufficient periods of total or near total starvation. In our diets the nutrition powder is supplemented with iso-energetic units of ordinary food and drink, each of about 63 kcal, and the portions are visualized as small pictures ("counters") of which there are three colours: blue for items rich in protein, green for items rich in fibre, and red for sweets, fatty items, and alcoholic beverages.
As the VLCD core of the diet covers all nutritional needs, complete freedom is allowed in the patients' choice of the 10 counters (about 630 kcal) that are allowed in the program. This regime of freedom within limits has been tested in a randomized trial and proved to reduce the dropout rate significantly. All instruction and control is done in groups, which saves resources and has obvious psychological advantages.

Methods

Thirty-eight consecutive obese persons were treated as outpatients.
The treatment commenced with VLCD formula diet Nupo (females 388 kcal, 56 g protein; males 446 kcal, 69 g protein). VLCD had no untoward effects and was continued for as long as the patient would accept. After that, the formula diet vas supplemented with ordinary items of food and drink to the level of 1000 kcal for women and 1100 kcal for men. After 5 months the data were analysed separately according to the duration of VLCD: group 1 (n=20): VLCD for less than 2 months, and group 2 (n=18): VLCD for 2 months or more. The two groups were comparable with regard to height, absolute weight and precentral overweight, but group 2 was somewhat older than group 1 (49,5 vs 38,3 years, $P \leq 0.01$).

Results

The weight losses of the two groups are very different. Group 1 who had given up VLCD early, lost much less weight, both in absolute and relative terms than group 2 who had more faithfully stuck to the initial VCLD regimen.
The differences are significant with regard to both total weight loss and weight loss on VLCD. Group 2 lost significantly more weight, both totally (17.1 kg (7.8-40.1)) and on VLCD alone (12.3 kg (4.1-28.8)), than group 1 (8.7 kg (-1.1-19.1) and 7.3 kg (0.9-18.2). Weight losses in both groups eliminated or strongly reduced the need for a wide variety of expensive drugs: antidiabetics, diuretics, antihypertensives, analgetics, etc.

Conclusion

It is concluded that VLDC is an effective and encouraging way of starting a dieting program, and that it should be continued for at least two months, as the length of the initial VLCD period related significantly to the amount of weight eventually lost.

Study 4:

Dietary fibre added to very low calorie diet reduces hunger and alleviates constipation

- *A. Astrup, et al. (1990)*

Introduction

Very low calorie diet (VLCD) as a nutrition, powder formula diet is being widely used for the treatment of obesity, and has been documented to be effective and safe. This regimen facilitates compliance because of its simplicity combined with a rapid weight loss, which may further encourage the patient to stick to the diet. The major drawbacks are still the patients' complaints of hunger between meals, constipation and the infrequency of bowel movements.

Recently it has been shown that fibre supplementation to a conventional diet reduces hunger, increases the frequency of bowel movements and softens the consistency of the stools. The supplementation of fibre to at formula diet designed for VLCD has not hitherto been reported.

The purpose of the present investigation was to examine if the addition of fibre to a nutrition powder improves compliance by modifying hunger, satiety, stool consistency and bowel movements. As fibre may impair intestinal absorption of various divalent cations and vitamins, we also monitored plasma levels of the most important metal ions together with other relevant plasma constituents.

Methods

To examine whether supplement of dietary fibre may improve compliance to a very low calorie diet (VLCD) a nutrition powder (Nupo) providing 388 kcal/day (men: 466 kcal/day) was compared with a similar version containing plant fibre 30 g/day. Twenty-two obese patients entered the study. After a baseline habitual diet, they were randomized to two weeks of treatment in a single blind design to either VLCD with or without dietary fibre. Subsequently they were crossed over for further 2 weeks of treatment.

Results

All 22 patients completed the study without any missed appointments or other deviations from the protocol. The two groups had similar weight losses (about 10 kg/4 weeks), and dietary fibre did not improve this result. During VLCD with fibre hunger ratings were significantly lower than during VLCD without fibre.

Bowel movements decreased for 1.9/day on habitual diet to 0.7/day on VLCD without fibre, but increased to 1.0/day by fibre supplement. No effect of fibre supplementation to satiety, consistency of faeces and flatulence.
The supplement of dietary fibre did not influence plasma concentrations of divalent cations as calcium, iron or magnesium, nor did it add any lowering effect on plasma glucose, cholesterol or triglyceride to that of VLCD.

Conclusion

The supplement of dietary fibre to VLCD may improve compliance by reducing hunger and increasing the number of bowel movements, without impairment of absorption of divalent cations.

Study 5:

Effect of an energy-restrictiv diet, with or without exercise, on lean tissue mass, resting metabolic rate, cardiovascular risk factors, and bone in overweight postmenopausal women.

- *O. L. Svendsen, et al. (1993)*

Introduction

Overweight is an independent predictor of cardiovascular disease (CVD) – leading cause of death and disability in Western societies. Very little is known about the changes in overweight postmenopausal women since all studies previously have been performed in men and pre-menopausal women. Postmenopausal women are at increased risk of CVD; estrogen deficiency, an artherogenic lipid and lipoprotein profile, and fat distribution all play a role. Osteoporosis is another major cause of morbidity and mortality in this group. The consequences of weight reduction from dieting, with or without exercise, on bone in the osteoporosis are unknown. Thus, the aim was to study the effects of an energy-restrictive diet, with or without exercise, on body composition, major cadiovascular risk factors, and bone in overweight postmenopausal women.

Methods

In a longitudinal clinical study, 121 healthy, overweight postmenopausal women (age 53.8 ± 2.5 years, BMI 29.7 ± 3.1 kg/m2) were randomly assigned to 3 groups: control, a 4,200 kJ/d diet, or a 4,200 kJ/d diet with combined aerobic and anaerobic exercise. The diet consisted of an obligatory basis of the formula diet NUPO of 1.6 MJ daily (VLCD) combined with an additional energy com- sumption of up to 2.6 MJ from food freely chosen, according to a “counter diet system”. Body composition (measured by dual-energy x-ray absorptio- metry), fat distribution, resting metabolic rate, blood pressure, serum lipids and lipopro- teins, bone mineral densities, and markers of collagen and bone turnover were measured before and after 12 weeks of intervention.

Results

One hundred eighteen women completed the study. The mean loss of body weight (9.5 kg versus 10.3 kg, NS) was similar in the intervention groups, but compared with the diet-only group, the diet-plus-exercise group lost more fat (7.8 kg versus 9.6 kg, $p \leq 0.001$) and no lean tissue mass (1.2 kg versus 0.0 kg, $p \leq 0.001$). The resting metabolic rate (per kg wt) was increased in the diet-plus-exercise group compared with the control group (11% versus 4%, $p \leq 0.009$). The levels of serum triglycerides, total cholesterol, low-density lipoprotein, and very-low-density lipoprotein decreased, and the ratio of high-density lipoprotein to low-density lipoprotein increased by 20% to 30% in both intervention groups compared with the control group ($p \leq 0.001$). The systolic bloodpressure dropped, and the waist-to-hip circumference ratio and abdominal-to-total body fat decreased in both intervention groups compared with the control group (10% $p \leq .003$, and 3.5%, $p \leq 0.0001$).
There were no consistent, major differences between the groups in terms of changes in total body, spinal, or forearm bone mineral densities, or in markers of collagen and bone turnover.

Conclusion

We conclude that, in overweight postmenopausal women, addition of combined aerobic and anaerobic exercise to a high protein, energy-restrictiv diet preserves lean tissue mass, promotes physical fitness, and increases the resting metabolic rate and loss of fat. The diet, with or without exercise, led to profound improvements in serum lipids and lipoproteins, blood pressure, and fat distribution. The weight loss induced by the diet, with or without exercise, does not seem to have any major detrimental effect on bone.

Study 6:

Bone Loss Accompanying Voluntary Weight Loss in Obese Humans

- L. Bjørn, et al. (1994)

Introduction

Some studies have demonstrated that a diet-induced weight loss is accompanied by a significant decrease in bone mineral density (BMD). Regional bone changes were not measured. The purpose of the present investigation was to measure changes in total and regional body composition in obese patients undergoing rapid weight loss on a low-calorie regimen.

Methods

Dual-energy x-ray absorptiometry was performed in 51 obese patients before and after 15 weeks on a low-calorie diet (Nupo, yielding 1.9 MJ for women and 2.4 MJ for men for 2 weeks. Thereafter a qualitatively free supplement of food and drink was allowed up to 4.2 MJ for women and 4.7 MJ for men). Of these patients, 39 were scanned 6 months later. Total and regional body bone mineral, fat mass, and fat free mass were measured. In the control group, 9 normal volunteers were scanned with up to 23 kg lard distributed anteriorly, and 9 volunteers were scanned with 15 kg lard posteriorly. The lard was then gradually removed to simulate the fat loss found in the patient group.

Results

In the patient group the mean weight loss was 12,273 g, the mean fat loss was 11,014 g, and the mean bone mineral loss was 171.6 g after 15 weeks. Close correlation between the fat loss and the bone loss was found and calculated to be 16.5 g bone mineral per kg fat in the patient group, in contrast with 0.5 g bone mineral per kg fat in the control group. In the control group, 15 kg lard placed posteriorly had no statistically significant effect on the bone measurements. If weight and fat were regained at the scanning time 6 months later, the bone mineral was regained as well. Patients with further weight loss continued to lose bone mineral. One patient lost 754 g bone mineral in 9 months. Her weight loss was 45 kg in that period, and the bone mineral content remained within the range for normal women at her age. Methodologic and patogenetic problems are discussed.

Conclusion

It is concluded that the observed bone loss should be regarded as physiologic normalization within acceptable limits accompanying a diet-induced weight loss in the obese.

Study 7:

Twenty-four-hour plasma tryptophan concentrations and ratios are below normal in obese subjects and are not nor-malized by substantial weight reduction

- *L. Breum, et al. (2003)*

Introduction

Plasma tryptophan concentrations and the ratio of tryptophan to other large neutral amino acids (plasma tryptophan ratio) are reportedly low in obese subjects. The plasma tryptophan ratio predicts brain tryptophan uptake and serotonin production. If this is low in obese subjects, serotonin function may also be low. Serotonin neurons in the brain participate in the control of appetite. In general, serotonin neurons function in neuronal circuits that diminish food intake. Plasma tryptophan concentrations and ratios have been measured only at single time points in obese subjects; it is not known whether low values for these two variables persist throughout a 24-h period. The objective of the study was to determine whether plasma tryptophan concentrations and ratios in obese subjects are lower than those in normal-weight subjects throughout a 24-h period and whether they increase when body weight is reduced.

Methods

The original group consisted of 18 obese patients and 18 sex- and age-matched nonobese subjects. 9 obese patients completed the weight-loss program and their age- and sex-matched nonobese counterparts formed the groups examined in the study. The obese subjects participated of structured, outpatient weight-loss program to achieve ideal body weight. During the initial phase of the program, the subjects consumed a very-low-energi-diet (Nupo). When body weight had decreased to ≈ 130% of ideal body weight (6-17 mo) the patients were instructed to discontinue the VLCD and begin consuming a 5 MJ/d diet of normal food items. When ideal body weight was achieved or when no further weight could be lost, the patients were instructed to begin consuming a basic 8 MJ/d diet. Sampling in post-obese patients was performed after body weight had remained stable (±1.5 kg) for ≥ 1 mo after switching to the last diet program.

Plasma tryptophan concentrations and ratios were examined in obese subjects before, after weight loss, and in nonobese control subjects. Blood samples were drawn frequently throughout the 24-h period. An insulin tolerance test was also used to demine whether weight loss altered the ability of insulin to modify plasma concentrations of tryptophan and of the other large neutral amino acids.

Results

Plasma tryptophan concentrations and ratios in obese subjects were low at all times; these effects persisted after weight reduction. Plasma concentrations of all the large neutral amino acids decreased during insulin infusion in all the groups.

Conclusion

In relation to the present findings, such results predict that when serotonin transmission is low, appetite will be stimulated. The persistently lower plasma tryptophan ratios observed throughout the day and night in the obese subjects than in the normal-weight control subjects support the notion that brain tryptophan uptake and serotonin synthesis in obese subjects may be abnormally low. The fact that the plasma tryptophan ratio remains persistently low after weight reduction further suggests that the formerly obese may struggle against a biochemical signal oriented toward increased appetite and food intake. We conclude that the low 24-h plasma tryptophan ratios in obese and formerly obese subjects suggest that brain tryptophan uptake may be continuously diminished and may remain below normal despite weight reduction.

Study 8:

Comparable reduction of the visceral adipose tissue depot after a diet-induced weight loss with or without aerobic exercise in obese subjects: a 12-weeks randomised intervention study

- *T. Christiansen, et al. (2009)*

Introduction

Obesity, in particular excess visceral adipose tissue (VAT), is associated with the metabolic syndrome resulting in increased morbidity and mortality. By contrast, accumulation of body fat in the subcutaneous gluteal-femoral adipose tissue (GFAT) is generally less associated with health problems or may even mediate some protection against cardiovascular diseases. These findings suggest that fat distribution and particularly the ratio between VAT and GFAT may be of importance for the obesity-related health complications. Weight loss with preferential effect on the visceral adipose tissue (VAT) depot could have important clinical benefits. In this study, we investigated the independent and combined effect of regular exercise and diet induced weight loss on body fat distribution.

Methods

Randomized control design of i) exercise-only (EXO; 12 weeks of exercise without diet-restriction), ii) hypocaloric diet (DIO; 8 weeks of very low energy diet (VLED 600 kcal/day (Nupo)) followed by 4-weeks weight maintenance diet) and iii) hypocaloric-diet and exercise (DEX; 8 weeks VLED 800 kcal/day (Nupo

+ supplement of 150-200 kcal) + a 4-week weight maintenance diet combined with exercise throughout the 12 weeks). Seventy-nine obese males and females were included.

Body fat distribution was quantified by magnetic resonance imaging (MRI)-technology.

Results

In the EXO group, the weight loss (3.5 kg) and the relative reduction in VAT (18%) was significantly lower compared with the weight losses in the DIO and DEX groups (12.3 kg; P≤0.01) and to the reduction in VAT (30-37%; P≤0.001). In all the three groups, the relative reduction of VAT was higher as compared with the reduction in fat mass (FM; combining all fat depots determined by MRI; P≤0.01 for all comparisons). The changes in VAT were associated with changes in FM and related to the initial VAT/FM ratio (r2=0.72; P≤0.01).

Conclusion

Exercise has no additional effects in reduction of the VAT depot, compared with the major effects of hypocaloric diet alone. In addition, the effects of exercise per se on VAT are relatively limited. The effects on the VAT depot are closely associated with changes in total FM.

Study 9:

Investigations of the Endocannabinoid System[1] in Adipose Tissue. Study III: No indications of hyperactivity of the endocanna-binoid system in subcutaneous adipose tissue in the obese state. Investigations in lean subjects and in obese subjects before and after weight loss.

- *Bennetzen, M. F. (2011)*

Introduction

The study aimed to establish whether 10% weight loss would affect components of the ECS (Endocannabinoid System) in AT (adipose tissue) in humans and to establish whether hyperactivity of the ECS in adipose tissue is present in the obese state.

Methods

The obese study participants underwent a 12 weeks diet regimen resulting in 10-12% weight loss. The weight loss was achieved by very low calorie diet (NUPO) including 200 grams of fruit and vegetables daily and weekly moti-vation sessios with a dietician. All study participants underwent fasting blood samples and AT biopsies from abdomen and gluteal region, the obese subjects both before and after weight loss. Setting and participants: A total of 21 healthy obese individuals (10 men/11 women, age 39.5 ± 1.6 years, body mass index (BMI): 37.5 ± 0.8 kg m(-2)) and 21 age- and gender-matched lean subjects (BMI: 23.8 ± 0.4 kg m(-2)) were studied. Main outcome measures: The activity of ECS in AT was determined by measuring arachidonoyl glycerol (2-AG) and N-arachidonoylethanolamine/anandamide in AT by mass spectrometry and gene expressions of enzymes and receptors involved in the ECS.

Results

The EC, 2-AG was reduced in obese individuals in the gluteal AT depot ($P<0.01$). Moreover, 2-AG increased in both depots in the obese subjects following weight loss ($P<0.05$). The gene expression of the CB1 was either not affected by the obese state (in the gluteal AT depot) or reduced (in the abdominal depot, $P<0.05$) and significantly affected by weight loss. The expression of the degrading enzymes FAAH, FAAH2, MGL and MGL2 was differently affected by obesity, AT depot and weight loss.

Conclusion

We found reduced levels of 2-AG in subcutaneous AT in obesity, which increased after weight loss. In abdominal AT, the low CB1 expression was normalised after weight loss, whereas in gluteal AT the CB1 expression was reduced after weight loss. These findings support the concept of a dysregulated ECS in AT in association with obesity. Thus, both one of the important endogenous ligands, 2-AG, and the main EC receptor were down regulated in the obese state, indicating that simple obesity is not associated with ECS hyperactivity in subcutaneous AT.

1) The endocannabinoid system (ECS) is one of the signalling systems that control feeding behaviour. The ECS is implicated in many functions, such as pain, memory, addiction, inflammation, and feeding, and could be considered a stress recovery sy-stem. It also seems to integrate nutrient intake, metabolism and storage maintaining homeostatic balance. The ECS is a recently discovered system, and research indicates hyperactivity in obesity. The aim of this thesis is to elaborate on the relationships of this widespread system and its elements in adipose tissue in obesity.

Study 10:

The effect of weight loss in obese patients with heart failure – a pilot study

- *Mikkelsen, M. G. (2011)*

Introduction

Dietary recommendations in heart failure management are contradictory to findings established by the obesity paradox. The objective of this study was to investigate if a weight reduction could reduce symptoms of heart failure; thus resulting in an improvement of body composition, plasma lipid profile and functional status and thereby positively affect cardiac function.

Methods

We enrolled 26 obese patients with heart failure and NYHA II or III. They were randomly assigned to adhere to a low calorie diet (Nupo VLCD: 700 kcal/day + 100 kcal of supplementary food) or a conventional diet for 12 weeks. The study, we assessed body weight and -composition, plasma lipid profile, NT-proBNP, functional status and quality of life.

Results

Of the 26 patients, 18 completed the study (11 in the intervention group and 7 in the control group). The mean weight loss with the low calorie diet (LCD) was 11.3% of initial body weight and the difference in mean weight loss between the low calorie diet group and conventional diet group was 11.7 kg at the end of the study (95% CI: 6.8, 16.6, p<0.0001). Patients following the low calorie diet significantly reduced their body mass index (p<0.0001, 95% CI: 2.3, 5.3), waist circumference (p<0.0001, 95% CI: 5.9, 15.3) and hip circumference (p<0.0010, 95% CI: 5, 15.2,) compared to the patients following the conventional diet. The walking distance significantly improved between baseline and week 12, between-group difference amounted to 172m after 12 weeks p<0.0005. There was a significant mean difference for cholesterol- (p<0.0006), triglyceride- (p<0.0100) and low-density lipoprotein (p=0.0265) concentrations between baseline and week 8. Mean differences in plasma lipid levels were not significant at week 12.

Conclusion

In this small pilot study, a low calorie diet led to a significant improvement in body weight and -composition and functional status in patients with heart failure. Larger studies need to confirm these preliminary findings.

Study 11:

Effect of low energy diet for eight weeks to adults with overweight or obesity on folate, retinol, vitamin B_{12}, D and E status and the degree of inflammation: a post hoc analysis of a randomized intervention trial

- *N. R. W. Geiker, et al. (2018)*

Introduction

Obesity is associated with vitamin insufficiency and low-grade inflammation. The purpose of this study was to investigate the effect of weight loss on folate, retinol, vitamin B12, D and E status and the degree of inflammation..

Methods

Out of 110, 85 individuals (75% women) aged 39 ± 11 years with a mean ± SD BMI of 33 ± 4 kg/m2, completed an eight-week low energy diet (LED). Serum concentration of folate, retinol, B12, D and E and C-reactive protein and homocysteine (Hcy) were measured at baseline and at end of the LED

Results

At baseline, 8% of the participants were deficient in folate, 13% in vitamin B12, 2% in retinol, 28% in vitamin D (72% were insufficient in vitamin D), and none were deficient in vitamin E. At baseline, BMI was inversely associated with retinol ($P < 0.05$) as was total and abdominal fat percentage with folate ($P < 0.05$); further BMI and measures of adiposity were positively associated with CRP ($P < 0.01$) and Hcy ($P < 0.05$). Homocysteine was inversely associated with all vitamins but retinol ($P < 0.001$). After the LED, the participants lost a mean [95% confidence intervals] of 12.3 [− 13.1,-11.6] kg. The serum concentration of folate, vitamin B12 and D were

Conclusion

Eight-weeks LED resulted in 13% weight loss and an increase in the serum concentrations of folate, vitamin B12 and D. Baseline adiposity was inversely associated with folate and retinol, and positively associated with markers of inflammation.