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Anthropometric and Biochemical Effects of the 5 and 2 Diet: A Case Study

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Abstract

Objective: The aims of this paper were to undertake the 5 and 2 diet over a 5 week period to determine its effect on anthropometry, biochemical markers and psychological variables.

Methods: Five weeks of the 5 and 2 diet were undertaken. Intake was restricted to 600 kcal on 2 days and was unrestricted on remaining days. Pre- and post- blood tests including fasting blood glucose, fasting plasma cholesterol, LDL, HDL and triglyceride, fasting insulin and IGF-1 were performed following the same overnight fasting period. Pre- and post- Dual X-Ray Absorptiometry scans were performed, food intakes were recorded via weighed food record and Foodworks analysis was conducted to determine adequacy of macro and micronutrient intakes. Psychological variables were assessed during the trial via a modified profile of mood states questionnaire.

Results: This case study showed significant losses of lean tissue. No significant change in fat mass was observed however, a small loss of bone tissue was noted. Plasma cholesterol and LDL levels increased while plasma triglyceride, fasting insulin and IGF-1 levels decreased. No significant change in fasting blood glucose was observed. Inadequate dietary intakes of key micronutrients were identified such as calcium, magnesium and iodine. Psychological variables assessed showed increased hunger, irritability as well as decreased concentration and poorer sleep quality.

Conclusion: This indicates the need for more future research including randomised controlled trials with much larger sample sizes and longitudinal studies to determine more chronic effects. Such studies should investigate the efficacy of the 5 and 2 diet in a variety of populations before the diet can be safely prescribed to the general population.

Keywords: 5 and 2 diet; Fasting; Weight loss; Obesity; Diabetes; Cancer

Introduction

Intermittent energy restriction has been researched since the 1940's in rodents for its potential benefits in chronic disease prevention and anti-aging properties. This research covers modern day ailments including diabetes, cardiovascular disease [1], neurodegenerative disorders, cerebrovascular disease [2] and cancer [3].

Chronic or severe caloric restriction initiates a 'starvation response' in the human biological system which elicits an array of negative physiological and biochemical adaptations from malnutrition and impaired immune function to cardiac arrhythmia and ketoacidosis [4]. Reduction in overall caloric intake and metabolic rate during re-feeding are also observed in these conditions [5].

Evidence for some desirable metabolic changes due to intermittent energy restriction in rodent studies has been seen. These include increased insulin sensitivity, decreased fasting blood glucose levels [6] and increased serum HDL [7]. Decreased IGF-1 levels [8], decreased oxidative stress [9] and inflammatory markers such as C-Reactive proteins and homo-cysteine [10], increased brain derived neurotropic factor (BDNF) levels and entirely new brain cell development has been seen in fasted mice [11]. These adaptations to intermittent energy restriction have potential benefits for neurological diseases such as Alzheimer's [12].

Some evidence is starting to surface, supporting at least the weight loss effects of intermittent energy restriction in humans but to date there are limited trials under controlled conditions. The protocols used vary greatly in length and frequency of fasting/feeding times and the extent/type of energy restriction i.e. alternate day fasts, 3-4 day fasts, caloric restriction, and different specific macronutrient restrictions.

Alternate day fasting (ADF) has been investigated in randomised control trials (RCT) and shown to be an effective method of weight loss in normal [13] and overweight patients [1]. ADF is characterised by ad libitum eating alternated with calorie restriction to 25% of estimated energy requirements (EER). These are known as "feed" and "fast" days respectively. Reductions in fat mass and triacylglycerol levels have been observed under these conditions [1]. ADF has also shown to produce negative outcomes such as increased binge eating and depression scores [14]. Therefore the safety of this type of protocol must be more rigorously investigated.

The 5 and 2 diet is a modified version of ADF and was first introduced in the book "The Fast Diet". The basis for the fast diet is intermittent fasting via substantial caloric restriction on 2 non-consecutive days per week (500 kcal for females, 600 kcal for males) whilst eating ad libitum during the remaining 5 days a week. The 5 and 2 diet has not been scrutinized under RCT conditions. Anecdotal

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evidence suggests an easier protocol for patients to adhere to with similar benefits seen in ADF. These include weight loss, reductions in blood glucose levels and reductions in plasma cholesterol levels. This paper presents the results of a case study under controlled conditions into the effects of the 5 and 2 protocols.

Methods

Study design

Case study

Participants

A 37 year old healthy adult male university student agreed to participate in this study. Height 186 cm, Weight 91 kg.

Inclusion/Exclusion Criteria

Inclusion criteria include: Male or female, aged 18-50 years, non-smoking.

Exclusion criteria include: Currently or dieting for the past 12 months, currently participating in any high level training regimen e.g. sport specific training, any known medical conditions or medications which may adversely affect outcomes.

Intervention

The intervention was five weeks of the fast (5:2) diet comprising two non-consecutive days (Mondays and Thursdays) of energy intake of 600 kcal on these days. An ad libitum diet was permitted on the remaining five days per week. Food intakes on both fasting and feeding days were recorded using weighed food records. Analysis of the food record was conducted to determine mean macronutrient (carbohydrate, fat, protein and fibre) and micronutrient (calcium, magnesium, phosphorous, iodine, folate and vitamin E) profiles and overall energy intake (Xyris software Foodworks 7 Professional version: 7.0.3016). The participant was asked not to change the current level of physical activity.

Outcome measures

Biochemical assessments were conducted 1 day prior to the start of the study (Pre-trial) and 1 day following the conclusion of the study (Post-trial). All measures were taken in the fasted state and included blood glucose (glucose oxidase rate reaction) total plasma cholesterol (spectrophotometry, coefficient of variation (CV 3.0%), triglyceride concentrations (spectrophotometry, CV 5.3%), plasma high density lipoprotein (HDL, ultracentrifugation and electrophoresis, CV 6.0%), low density lipoprotein (LDL, CV 4.4%, calculated by Friedewald equation) [15], insulin like growth factor (IGF-1 determined by the Abott Architect Meia method, CV 5.6%) and insulin (measured by the IDS-SYS method, CV 1.8%) [16,17]. The biochemical tests were performed in a public hospital Biochemistry and Endocrinology departments.

Body composition measures of the head, legs, arms and trunk were assessed using Dual X-Ray Absorptiometry (DXA- Hologic QDR 2000) and included: fat mass, fat-free mass, lean mass, total body mass, bone mineral content (BMC) and bone mineral density (BMD). Stature was measured in triplicate using a stadiometer (Seca 213 portable stadiometer).

Psychological variables of mood were assessed at the same time of day on fast days using a modified Profile of Mood States (POMS) self-administered questionnaire [18]. The mood states included: sleep quality, concentration, productivity, alertness, irritability, hunger and fatigue.

Results

Foods consumed

A typical fast day intake is shown in a detailed Foodworks analysis in Appendix 1. A typical day of unrestricted intake (also known as 'feed day') is shown in a detailed Foodworks analysis in Appendix 2. Types of foods did not vary greatly between fast days. Similar fast day meals were consumed on most days for breakfast and dinner. These usually consisted of 4 egg whites and 2 slices of whole meal toast for breakfast. While dinner usually consisted of approximately 200 g lean chicken breast and 200 g (raw) stir fried vegetables such as broccoli, carrot, celery and/or capsicum. Feed days were more varied and unrestricted. Approximate energy intake was around 3500 kcal. No alcohol was consumed for the duration of the study.

Calories and nutrients

A total of 10 feed days and ten fast days were recorded as weighed food records and analysed in Foodworks. Results are presented in tables. Energy intakes on feed days were significantly different from the overall feed day mean intakes (3469.1 kcal) in weeks one, two and three p=<0.008. This effect was moderated towards the end of the study as feed day intakes were not significantly different from overall feed day means in weeks four and five. Feed day intakes were significantly different from the weekly mean intakes for all weeks studied. Fast day intakes were significantly different from the overall fast day means (564 kcal) in weeks two, four and five p=<0.0001.

Figure 1 shows the weekly decrease in body mass in comparison to weekly caloric intakes. There was a significant decrease in body mass overall (3.7%). Weekly decreases were consistent and showed no significant difference from week to week p=0.004.

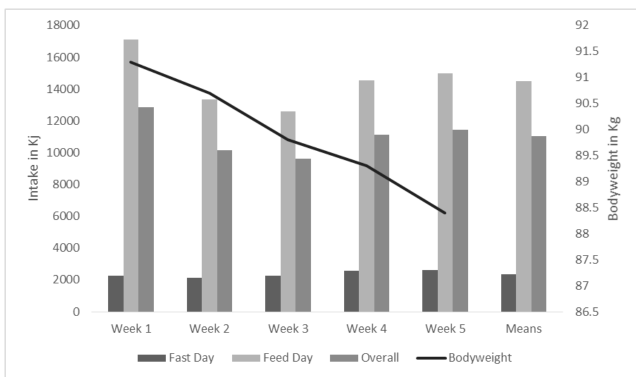

Figure 1: Weekly fast days, feed days and total (all days) energy intake and weekly body mass.

Mean macronutrient and micronutrient intakes for both feed and fast days are shown in Table 1. Mean macro- and micronutrient profiles on fasting days were significantly different to those on feeding

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days. Protein intake on fast days contributed a higher percentage of overall intakes than feed days (46% vs. 22% of total energy). Intakes of fat and carbohydrate were lower than feed days (8% vs. 19% and 34% vs. 53% of total energy respectively). Mean feed day intakes of dietary cholesterol were 459.2 mg. Mean fast day intakes were 196 mg. Mean fast day intakes for saturated fats were (2.2 g or 25% of total fat intake). Mean intakes of saturated fats for feed days were (39.2 g or 38% of total fat intake).

	Week 1		Week 2		Week 3		Week 4		Week 5		Total	
Macro nutrients	Fast days	Feed days	Fast days	Feed days	Fast days	Feed days	Fast days	Feed days	Fast days	Feed days	Mean intake fast days	Mean intake feed days
Protien (g)	59.4	174.1	50.4	161	67	137.5	71.2	156.4	62.5	157.2	62.1	157.2
Fat (g)	12.9	168.3	9.7	118.2	7.2	111.9	11.3	137.9	15	139.7	11.2	135.2
CHO (g)	38.5	449.7	47	354.3	42.9	323.7	46.6	380.7	50.6	404	45.1	382.5
Fibre (g)	16.3	48	13.5	38.8	17.3	33	15.7	42.2	17.4	42.3	16	40.9
CHO = Carbohydrate, % = Percentage												

Table 1: Macronutrient intake comparison on feed and fast days.

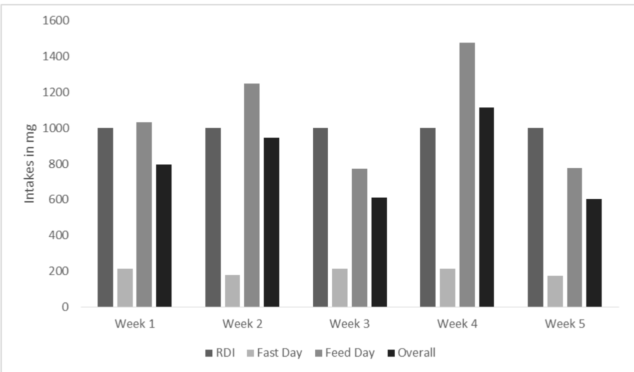

Figure 2a: Calcium intakes on feed, fast days and overall (compared to RDI).

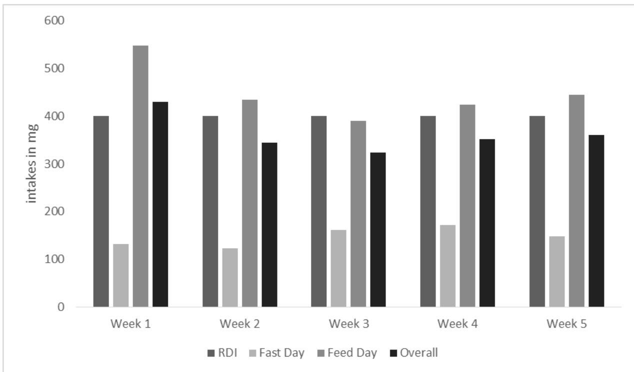

Figure 2c: Magnesium intakes on fast, feed days and overall (compared to RDI).

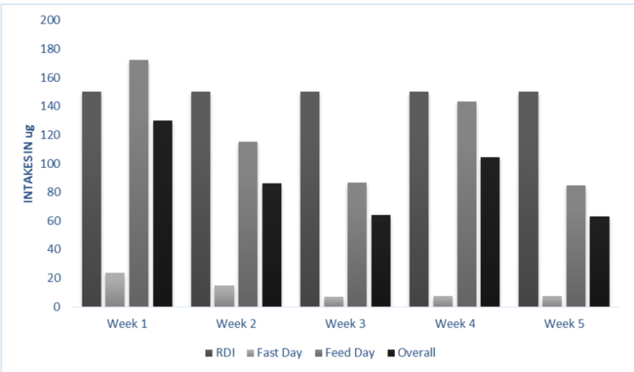

Figure 2b: Iodine intakes on feed, fast days and overall (compared to RDI).

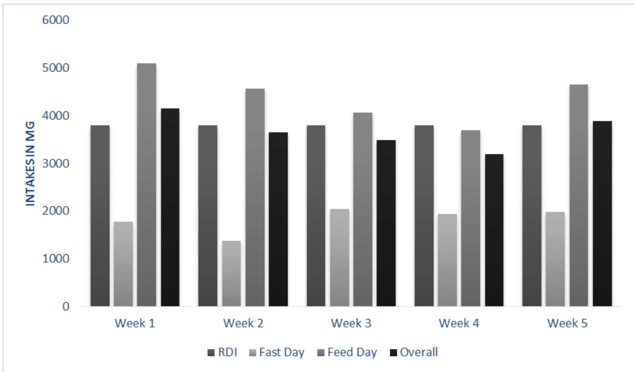

Figure 2d: Potassium intakes on fast, feed days and overall (compared to RDI).

Micronutrient intakes were low compared to acceptable daily intakes (AI) and recommended daily intake (RDI) requirements on

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fast days. Inadequacies in some micronutrient intakes were seen on these days. Intakes for thiamine, niacin, phosphorous and vitamins A and C were all acceptable according to recommendations and are therefore not shown here. Requirements of calcium, iodine and magnesium are shown in Figures 2a-2c. Weekly averages for these micronutrients did not meet requirements on most occasions. Other micronutrients that failed to meet RDI levels in weekly averages were folate (not shown here) and potassium (Figure 2d) on 60% of occasions, vitamin E on 40% of occasions (not shown here). Although inadequate on fast days (3.7 mg/day or 46% RDI). Mean daily iron intakes (not shown here) were high overall (12.3 mg/day or 154%) RDI.

Biochemistry

Pre and post fasting blood parameter concentrations are summarised below in Table 2. Blood glucose levels increased by 2%, however this was insignificant. A significant decrease (56%) in fasting blood insulin was observed. Fasting plasma cholesterol levels significantly increased (0.9 mmol/L or 19%), LDL (1.00 mmol/L or 40%). HDL cholesterol also increased (0.07 mmol/L or 4%) although this was insignificant. Plasma triglyceride levels exhibited the greatest change from baseline. A significant decrease in this measure was observed (0.7 mmol/L or 47%). These measures remained within normal reference values. Fasting plasma IGF-1 recorded a significant reduction of (18 mmol/L or 25%).

Test	Units	Ref Range	Pre Trail	Post Trail	Change
Glucose	mmol/L	3.0 – 5.4	4.6	4.7	0.1(2%)
Cholesterol	mmol/L	<=5.2	4.8	5.7*	0.9(19%)
Triglyceride	mmol/L	<=2.5	1.5	0.8	0.7(47%)
HDL	mmol/L	1.00 – 2.50	1.64	1.71	0.07(4%)
LDL	mmol/l	<=3.5	2.5	3.6*	1.1(40%)
IGF-1	nmol/L	9.6 – 28.4	25.2	18.8	6.4 (-25%)
Insulin	pmol/L	10 - 96	32	14	18(-56%)
*Denotes exceeds normal reference range					

Table 2: Baseline and post diet biochemistries.

Body Composition

Pre- and post-trial DEXA results are shown in Table 3. A significant reduction (-3.37 kg) in total body mass was observed. Reductions in lean tissue measured 3.35 kg. Bone mineral content decreased by 0.05 kg and fat mass increased by +0.03 kg. This small increase in fat mass (0.6%) is insignificant when considered relative to losses in lean tissue.

Total body bone mineral density decreased from 1.26 $g.cm^{-2}$ to 1.25 $g.cm^{-2}$ although this remained within the normal range. Central abdominal fat decreased from 0.43 kg to 0.38 kg and remained in the low risk category. Resting Metabolic Rate decreased approximately 3.7% from week 1 (2223 kcal/day) to week 5 (2148 kcal/day). This is due to the decrease in body mass (3.4%) as RMR is a function of gender, age, height and body mass.

Psychological Symptoms

Table 4 shows psychological data gathered during fast days. In Table 4 the lower score indicates a poorer result i.e. concentration, productivity and alertness all increased throughout the trial. In Table 5 a lower score indicates a better result i.e. irritability, hunger and fatigue decreased as the trial progressed.

Region	Bone mineral content (g)			Fat mass (g)			Lean mass (g)			Fat free mass (g)			Total mass (g)			Fat %		
	Pre	Post	% change	Pre	Post	% change	Pre	Post	% change	Pre	Post	% change	Pre	Post	% change	Pre	Post	% change
L Arm	235.06	230.33	-2.1%	637.2	637.7	+0.08%	5088.2	4981.5	-2.1%	5323.2	5211.8	-2.1%	5960.5	5849.5	-1.9%	10.7	10.9	+0.2%
R Arm	263.49	251.56	-4.6%	600.5	591.9	-1.4%	5205.2	5087.0	-2.3%	5468.7	5338.5	-2.4%	6069.2	5930.4	-2.3%	9.9	10.0	+0.1%
Trunk	775.85	776.86	+0.1%	5256.6	4740.2	-9.8%	36293.8	34149.5	-5.9%	37069.7	34926.3	-5.8%	42326.3	39666.6	-6.2%	12.4	12.0	-0.4%
L Leg	512.71	496.12	-3.2%	2573.2	3267.6	+26.7%	12326.8	11601.4	-5.9%	12839.5	12097.6	-5.8%	15412.7	15365.1	-0.3%	16.7	21.3	+4.6%

R Leg	503.78	511.30	+1.5%	2842.4	2760.4	-2.9%	12277.2	12246.0	-0.3%	12781.0	12757.3	-0.2%	15623.4	15517.7	-.01%	18.2	17.8	-0.4%
Head	758.82	730.68	-3.7%	1171.5	1112.6	-5%	4060.5	3836.2	-5.5%	4819.3	4566.9	-5.2%	5990.8	5679.4	-5.2%	19.6	19.6	No change
Total	3049.71	2996.86	-1.7%	13081.4	13110.4	+0.2%	75251.7	71901.5	-4.5%	78301.4	74898.4	-4.3%	91382.8	88008.7	-3.7%	14.3	14.9	+0.6%

Table 3: Pre and Post Trial Body composition parameters measured by Dual X-Ray absorptiometry.

Discussion

The results of this 5 week trial of the 5:2 diet produced some positive and negative changes to biochemical and physiological measures. Total body mass decreased by 3.7% over the 5 weeks, however, the majority of this decrease was muscle tissue which was associated with a drop in resting metabolic rate. Biochemical changes were also seen and provided some unexpected results with increases in total cholesterol and LDL and a decrease in triglycerides. Fasting blood sugar concentrations showed little change and fasting insulin levels dropped significantly.

Protein intakes during the trial were inadequate and micronutrient deficiencies were seen in calcium, magnesium, iodine and potassium. Other nutrients such as folate and vitamin E also failed to meet RDI requirements on all occasions. Iron intakes were significantly higher than RDI. This is a significant observation as iron has been identified as a potential carcinogen through oxidative pathways associated with excess serum levels [19,20]. However, it has been suggested that adequate dietary iron may play a role in prevention of neurodegenerative pathways associated with conditions such as Alzheimer's [21]. This is one of the focal points of the rationale for ADF and similar protocols such as the 5 and 2.

Changes in biochemical markers form a large part of the rationale for fasting [6,10]. Five weeks is likely too short a period to elicit any significant changes in blood glucose measures particularly when measures are within normal ranges pre-trial. Fasting insulin changes were substantial with implications for insulin sensitivity in individuals with insulin resistance as well as significant implications for diabetes treatment and management.

Date	Sleep Quality	Concentration	Productivity	Alertness	Irritability	Hunger	Fatigue
15/4	1	1	1	2	2	5	4
18/4	1	1	1	2	3	5	4
22/4	1	1	1	3	2	5	3
25/4	1	1	1	3	3	5	4
29/4	1	3	3	3	4	4	3
2/5	3	2	2	3	4	4	3
5/5	1	3	3	4	3	4	3
8/5	3	3	3	3	3	3	4
12/5	1	3	3	4	3	4	3
15/5	3	3	3	4	2	3	3

Table 4: Modified POMS scores on fast days.

This loss of lean tissue could be due to a number of issues. The most likely scenario would be inadequate protein intakes on fast days equating to 0.68 g/kg bodyweight which does not meet RDI (0.8 g/kg). Secondly there is a potential confounder to the loss in lean tissue with regards to the first two weeks of the study. Physical activity levels decreased significantly in this period [22]. As the weight loss was not significantly greater in the first two weeks the effect of this was likely to be minimal. RCT trials into ADF have produced weight loss results of between 2.5 kg over a 3 week trial to 5.7 kg over a 10 week period [23]. Anecdotally weight reduction of up to 9 kg over 10 [24] weeks has been observed. Results such as these indicate there is potential for this method to be implemented with obese or overweight populations with low to normal levels of muscle tissue and higher than normal ranges of fat mass.

Losses in bone mineral content although small, are likely to be the result of inadequate intakes and reflect the difficulty in meeting calcium requirements. The most likely scenario was inadequate calcium intakes on fast days and lower levels of physical activity during weeks 1 and 2. However as the subjects exercise regime doesn't include high impact work which is known to be the greatest stimulus for new bone formation [25] the extent of this impact would be minimal. This result shows why several at risk populations requiring higher than normal calcium intakes such as pregnant women, children and the elderly must be advised against following such methods. As females have been shown to decrease bone mass more significantly than males during weight loss [26] it would be useful to compare gender groups in future research.

Date	Sleep quality	Concentration	Productivity	Alertness	Irritability	Hunger	Fatigue
16/4	3	3	3	4	1	4	3
19/4	3	4	3	4	2	3	3
23/4	3	3	4	3	1	3	2
26/4	4	3	3	4	3	3	3
30/4	4	4	4	3	2	3	2
3/5	3	3	3	3	2	4	2
6/5	4	4	4	4	2	2	2
9/5	4	3	3	3	2	2	2
13/5	4	4	4	4	1	3	3
16/5	3	4	4	3	1	2	2

Table 5: Modified POMS scores on feed days.

Changes in plasma LDL and cholesterol values are of concern as both increases were significant enough to move the total values beyond the reference range for normal values. Mean daily cholesterol intake was low 145 mg/1000 kcal which would indicate it is unlikely the increased serum cholesterol levels could be attributed to this. Mean feed day intakes of saturated fats were low (2.2 g). However, they represented a higher than recommended proportion of total fat intake (25%). Feed day intakes of saturated fat (39.2 g) represented an even higher proportion of total intakes (38%). This may have contributed to increased serum cholesterol levels as dietary saturated fat consumption has been shown to increase serum cholesterol levels [27].

The timing of the post- trial blood collection for cholesterol may have also affected results. The measure was taken immediately following a fast day which meant that only 600 kcal had been consumed in around 36 hours [28]. It has been shown that in cases of prolonged fasting in normal adults plasma cholesterol rises over the initial 3 days [29,30]. This rise is usually around 20% overall but free fatty acid concentrations can rise by 2 to 3 times their initial values. This is assumed to be a function of hormonal responses to fasting such as increased glucagon and growth hormone with concurrent drop in circulating insulin as seen in the insulin results here. These effects result in increased mobilization of stored cholesterol in adipose tissue with a concurrent reduction in excretion of labile cholesterol creating higher circulating plasma values [31].

Decreases in plasma IGF-1 were larger than expected given the short time frame, but remained within the normal range. These are consistent with changes seen in previous case studies (50% reduction) when the difference in time frame is accounted for.

Inadequate micronutrient intakes may be able to be compensated for in a normal population via increased intakes on feed days, however, these results highlight the need for dietary education strategies to be employed with anyone wishing to undertake the 5:2 diet. Serious concerns are raised for at risk populations with higher nutritional requirements for certain nutrients such as calcium and folate.

Sleep quality was poor for the majority of the study and this was closely related to the sensations of hunger. Productivity and concentration were very poor initially but improved during the study. Irritability was higher throughout the study on fast days than feed days. Greater alertness on fast days with an overall improvement in mood and sense of well-being have been seen anecdotally, despite experiencing sensations of hunger on fast days. Mattson et al. liken this feeling to the effects of anti-depressant drugs and observed that in rodent trials the effects of fasting are greater than that of anti-depressants on mood [32].

Limitations to this case study therefore results must be interpreted with caution. As the sample size is n=1 any results cannot be reliably extrapolated to the entire population. In addition to this there are certain other considerations which must be taken into account. Firstly the gender difference that exists between males and females with regards to weight loss and the respective anthropometric changes. Men have been shown to lose weight at a greater rate initially to women (the first 2 months) upon implementing dietary restrictions. This however has been shown to even out over a 6 month period [28]. Additionally they have been shown to lose a greater proportion of fat free mass in the early stages of weight loss [28]. This may also help to explain the loss of lean tissue observed in this study. The study length of 5 weeks is probably too brief to elicit certain physiological responses. A number of confounders existed which although unavoidable were not ideal. Changes in physical activity levels may have exerted an influence on results and ideally subjects would maintain normal physical activity levels for the duration of the study. The timing of the post-trial blood tests created further potential for confounding to the results and in future studies would be wise not to run these tests immediately after a fasting day.

In conclusion this study showed a reduction in body mass of 3.38 kg or 3.7% over the 5 week period. The majority of this reduction in mass was attributed to a loss of lean tissue of 3.35 kg or 4.5%. A small loss of bone tissue was also observed (-0.0528 kg). Biochemical results showed significant decreases in fasting insulin (-18 pmol/L or -56%) and IGF-1

(-6.4 nmol/L or -25%) levels while no change in fasting blood glucose was observed. Plasma cholesterol, HDL and LDL levels were all elevated from pre to post (0.9 mmol/L, 0.07 mmol/L and 1.1 mmol/L respectively). Plasma triglycerides decreased (0.7 mmol/L).

This study highlights the need for more rigorous research into the effects of intermittent fasting in humans in order to determine the efficacy before the population can be reliably advised to undertake such measures safely. Specifically there needs to be both short term randomised control trials and longitudinal studies investigating not only the efficacy but also the safety of intermittent fasting and the 5:2 diet. These studies should include control groups consuming a eucaloric diet. Such studies should focus on evaluating potential micronutrient deficiencies of the intervention as well as body composition changes with careful attention paid to the make-up and percentages of types of tissue lost. Specifically these trials need to be conducted in populations from obese to healthy weight and include male and female gender comparisons.

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