

# Effects of obesity and rapid diet induced weight loss on testicular and erectile function (EF), sexual desire (SD), and lower urinary tract symptoms (LUTS)

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## Introduction

- Abnormalities in sexual and lower urinary tract function in men are rarely included in lists of obesity related co-morbidities.
- Prospective observational studies have in general demonstrated a relationship between obesity and low plasma androgen levels (1) and erectile dysfunction (2).
- We have previously reported age independent associations between obesity and low plasma testosterone, erectile dysfunction, reduced sexual desire and increased lower urinary tract symptoms (LUTS) of an irritative nature (3) in men.
- Although weight loss intervention studies have been shown to result in improvements in androgen levels, erectile function and LUTS, less is known about effects on sexual desire. It is also not clear whether it is weight loss per se, the improvements in metabolic state and endothelial function, or the overall effects of the lifestyle intervention that are responsible for the improvements in androgen levels, sexual and lower urinary tract symptoms.
- The novel peptide hormone insulin-like peptide 3 (INSL3) is a major secretory product of the Leydig cells of the testis, and in adult men secreted into the blood which we have shown to be an independent measure of Leydig cell function (quality and number), independent of acute control via the HPG axis. Although we have not shown an independent relationship between obesity (4) and BMI the effect of weight loss on INSL3 as a marker of testicular function is not known.

## Aims

To determine the effect of obesity and aggressive diet induced weight loss on:

- Erectile function, sexual desire and lower urinary tract symptoms
- Plasma testosterone and INSL3

## Methods

### Subjects

- Thirty five obese men gave informed consent for the study which was approved by the Human Ethics Research Committee of the Royal Adelaide Hospital.
- Age: (mean  $\pm$  SEM), 43.3  $\pm$  9.9 yrs
- BMI: 37.1  $\pm$  4.6 kg/m<sup>2</sup>
- Waist circ: 111.2  $\pm$  12.6cm
- No known disease, non-smokers, no prescription medication.
- Four men had a BP  $\geq$  140/90;
- Fasting plasma glucose was elevated in two.

### Weight loss protocol

- Induced using 3 sachets of KicStart (450 Kcal) (Pharmacy Solutions, Sydney), and one low energy density carbohydrate free meal (~400 Kcal) over 8 weeks.
- Participants were reviewed 2 weekly.
- Primary outcomes measures were assessed prior to commencement of the diet and at week 8.

### Outcome measures

#### Questionnaires

- Erectile function (EF) (international index of erectile function (IIEF))
- Sexual desire (SD) (sexual desire inventory 2 (SDI-2))
- Lower urinary tract symptoms (LUTS) (international prostate symptom scale (IPSS)).

#### Plasma Assays (drawn fasting 08.00-09.00hrs)

- Total testosterone (TT), S
- Sex hormone binding globulin (SHBG),
- Calculated free T (cFT)
- INSL3
- Glucose, insulin and lipids

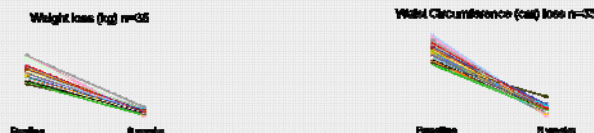
### Analysis

Data was analysed by paired T tests and ANOVA. Bivariate Correlations were performed using Pearson Correlation Coefficients with 2-tailed significance. SPSS v14 software package was used.

## Results

The study was completed without incident and there were no significant adverse effects. One participant dropped out and was excluded from analysis.

**Weight Loss (Fig 1):** All other men completed the 8 weeks without adverse events. All lost weight. Weight loss (mean  $\pm$  SEM) was 13.1  $\pm$  4.78 kg ( $p < 0.01$ ). The reduction in waist circumference (mean  $\pm$  SEM) was 14.4  $\pm$  4.5 cm, (range 5.0 – 20.5 cm),  $P < 0.001$ .



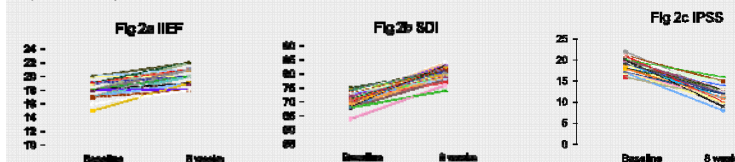
**Changes in testicular function, androgens, metabolic status and blood pressure (Table 1):** The changes (Mean SD) in TT, FT, INSL3, lipids, glucose and blood pressure are shown in Table 1. TT but not cFT or INSL3 increased. Systolic and diastolic BP, total and LDL cholesterol, triglycerides, insulin and glucose decreased.

Table: mean  $\pm$  std. error mean

	Baseline	8 weeks	p
Systolic BP (mmHg)	134.0 $\pm$ 2.7	122.9 $\pm$ 1.8	0.000
Diastolic BP (mmHg)	81.4 $\pm$ 1.5	77.3 $\pm$ 1.4	0.023
Glucose (mmol/L)	5.8 $\pm$ 0.3	5.2 $\pm$ 0.14	0.045
Insulin (mU/L)	16.8 $\pm$ 2.0	9.8 $\pm$ 1.6	0.000
Total Triglycerides (mmol/L)	1.9 $\pm$ 0.17	1.3 $\pm$ 0.12	0.001
Total Cholesterol (mmol/L)	5.0 $\pm$ 0.18	4.4 $\pm$ 0.17	0.002
HDL Cholesterol (mmol/L)	1.0 $\pm$ 0.04	1.0 $\pm$ 0.03	0.867
LDL Cholesterol (mmol/L)	3.1 $\pm$ 0.15	2.8 $\pm$ 0.14	0.023
Testosterone (mmol/L)	26.1 $\pm$ 1.6	30.7 $\pm$ 2.0	0.005
SHBG (mmol/L)	19.7 $\pm$ 1.5	27.3 $\pm$ 1.9	0.000
cFT (mmol/L)	0.8 $\pm$ 0.05	0.8 $\pm$ 0.05	0.431
INSL3 (mU/L)	0.4 $\pm$ 0.03	0.5 $\pm$ 0.03	0.435

### Changes in sexual function and LUTS

Erectile Function (Fig 2a): IIEF improved in 31 men -17.91  $\pm$  1.15 a to 20.0  $\pm$  1.19,  $P < 0.0001$ . Sexual Desire (Fig 2b): SDI improved in all - 71.46  $\pm$  2.45 to 80.54  $\pm$  2.19,  $P < 0.0001$ . LUTS (Fig 2c): IPSS improved in all - 18.86  $\pm$  1.44 to 12.14.0  $\pm$  1.74,  $P < 0.0001$ .



- Decreases in weight were positively associated with decreases in plasma insulin ( $P = 0.007$ ), triglycerides ( $P = 0.034$ ) and LDL cholesterol ( $P = 0.033$ ).
- There was a significant relationship between a decrease in obesity and increase in SHBG ( $P = 0.014$ ) and INSL3 ( $P = 0.007$ ) but not with total or calculated free plasma testosterone, and there were no significant relationship relationships between changes in weight or waist circumference and erectile function, sexual desire or LUTS.
- Improvements in erectile function were associated with increases in plasma T ( $P = 0.051$ ), cFT ( $P = 0.038$ ) and INSL3 ( $P = 0.043$ ) (and also with flow mediated dilatation – data not shown).
- Improvements in sexual desire and LUTS were associated with each other ( $P = 0.011$ ) but not with changes in any other parameter.

## Conclusion

Rapid, diet induced weight loss, improved EF and LUTS, and sexual desire without being directly related to the amount of weight loss or changes in metabolic state in this group of men without hypertension or significant abnormalities in metabolic state at baseline.

#### References:

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**Acknowledgements:** KicStart was supplied by Pharmacy Solutions, Sydney NSW. Funding was provided by the Royal Adelaide Hospital