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Overweight and IVF – Strategies to reduce overweight before IVF

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Implications of overweight/ obese

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- Alterations in hormones

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Adiposity and sex hormones across the menstrual cycle: the BioCycle Study

Edwina H. Yeung, PhD[1], **Cuilin Zhang, MD, PhD**[1], **Paul S. Albert, PhD**[1], **Sunni L. Mumford, PhD**[1], **Aijun Ye, PhD**[1], **Neil J. Perkins, PhD**[1], **Jean Wactawski-Wende, PhD**[2,3], and **Enrique F. Schisterman, PhD**[1]

Research, Eunice
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Buffalo, New York

	Total E2	Free-E2	Progesterone	FSH	LH
A) Mean, %[†]					
Overweight	5.30% (4.6)	**15.17% (4.1)**[**]	3.35% (3.7)	**−15.60% (4.1)**[**]	**−10.12% (5.0)**[*]
Obese	1.39% (6.4)	**22.13% (5.6)**[**]	**−15.00% (5.1)**[**]	**−22.51% (5.7)**[**]	**−16.91% (6.9)**[*]
p- trend	*P=0.51*	***P<0.0001***	***P=0.04***	***P<0.0001***	***P=0.004***

nes across the
ual cycles, with up
licle-stimulating
each visit.
metry. Differences
ted models, which
level within each
, and physical
30 kg/m², n=25)
FSH (−23%,
P=0.001) and higher free E2 (+22%, p=0.001) across the cycle. To lesser magnitudes, overweight women (BMI: 25–30, n=60) also exhibited differences in the same directions for mean levels of free E2, FSH, and LH. Obese women experienced greater changes in amplitude of LH (9%, p=0.002), and FSH (8%, p=0.004), but no differences were observed among overweight women. Higher central adiposity by top compared to bottom tertile of trunk-to-leg fat ratio by DXA was

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CONFLICT OF INTEREST
The authors have no conflicts of interest to declare.

Supplementary information is available at International Journal of Obesity's website.

Implications of overweight/ obese

- Alterations in hormones
- Increased gonadotrophins required per IVF cycle

Ozekinci et al. BMC Women's Health (2015) 15:61
DOI 10.1186/s12905-015-0223-0

BMC Women's Health

RESEARCH ARTICLE Open Access

Does obesity have detrimental effects on IVF treatment outcomes?

Murat Ozekinci[1*], Ali Sever[2], Safak Olgan[1], Mehmet Sakinci[1], Ugur Keskin[2], Munire Erman Akar[1], Seyit Temel Ceyhan[2] and Ali Ergun[2]

Abstract

Background: The aim of this study was to investigate the influence of body mass index (BMI) on the in vitro fertilization (IVF) treatment outcomes in a cohort of women undergoing their first IVF, using an intracytoplasmic sperm injection (ICSI).

Methods: This retrospective cohort study included 298 cycles from women younger than 38 years old undergoing IVF-ICSI at a university infertility clinic. The treatment cycles were divided into three groups according to the BMI of the women involved: normal weight ($18.5 \leq BMI < 25$ kg/m^2, 164 cycles), overweight ($25 \leq BMI < 30$ kg/m^2, 70 cycles), and obese ($BMI \geq 30$ kg/m^2, 64 cycles). The underweight women ($BMI < 18.5$ kg/m^2) were not included in the analysis due to small sample size ($n = 22$). The patient characteristics and IVF-ICSI treatment outcomes were compared between the BMI groups.

Results: The total gonadotropin dose ($p < 0.001$) and duration of stimulation ($p = 0.008$) were significantly higher in the obese group when compared to the normal BMI group. There were no significant differences across the BMI categories for the other IVF-ICSI cycle outcomes measured, including the number of retrieved oocytes, mature oocytes, embryos suitable for transfer, proportion of oocytes fertilized, and cycle cancellation rates ($p > 0.05$ for each). Additionally, clinical pregnancy, spontaneous abortion, and the ongoing pregnancy rates per transfer were found to be comparable between the normal weight, overweight, and obese women ($p > 0.05$ for each).

Conclusion: Obese women might require a significantly higher dose of gonadotropins and longer stimulation durations, without greatly affecting the pregnancy outcomes.

Background

Obesity has become a worldwide epidemic, with approximately 1.6 billion adults being overweight and 400 million being obese [1]. Obesity has several serious consequences on health, including hypertension, diabetes mellitus, chronic heart disease, lipid disorders, uterine cancer, and breast cancer [2, 3]. Moreover, obesity has negative effects on reproductive health. It has been established that obesity is associated with decreased natural fecundity, a decreased ovulation rate, increased time until conception, and increased rates of miscarriage [4, 5]. Additionally, an increased rate of pregnancy complications, including gestational hypertension, preeclampsia, gestational diabetes, postpartum hemorrhage, and fetal macrosomia, are all associated with obesity [6, 7]. Since the incidence of obesity is continually rising, an increasing number of overweight and obese women are seeking fertility treatments through assisted reproduction technology (ART) [8]. Consequently, there is a need to understand the full impact of obesity on in vitro fertilization (IVF) treatments.

There is conflicting evidence with regard to the effects of a raised body mass index (BMI) on the outcome of ART. Although some studies have reported no adverse effects of a raised BMI on IVF outcomes [9, 10], others have linked various negative impacts, including a higher dose of gonadotropin stimulation, longer stimulation duration, lower number of retrieved and mature oocytes, and decreased embryo quality [4, 11]. The aim of this study was to investigate the influence of BMI on the

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Full list of author information is available at the end of the article

Implications of overweight/ obese

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- Alterations in hormones
- Increased gonadotrophins required per IVF cycle
- Decreased numbers of good quality (MII) oocytes, embryos transferred
- Decreased live birth rate
- Increased rates of miscarriage

Implications of overweight/ obese

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nutrients MDPI

Article

A Comprehensive Analysis of Body Mass Index Effect on *in Vitro* Fertilization Outcomes

Veronica Sarais [1], Luca Pagliardini [1,*], Giorgia Rebonato [1], Enrico Papaleo [1], Massimo Candiani [1] and Paola Viganò [2]

Variable	>18.50	18.50–24.99	25.0–29.99	≥30
Ongoing pregnancy	1.15 (0.67–1.96)	1.00	1.06 (0.68–1.66)	1.01 (0.49–2.06)
Miscarriage rate	1.37 (0.42–4.47)	1.00	2.24 (0.86–5.84)	4.75 (0.70–32.37)
Live birth	0.54 (0.17–1.79)	1.00	0.51 (0.18–1.41)	0.17 (0.02–1.31)
Gestational age (weeks)	37.89 ± 1.87	37.74 ± 3.03	37.59 ± 2.80	37.03 ± 4.41
Birth weight (g)	2887 ± 586	3053 ± 613	2932 ± 756	3131 ± 1186

Nutrients 2016, 8, 109; doi:10.3390/nu8030109 www.mdpi.com/journal/nutrients

Implications of overweight/ obese

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- Technical difficulties with egg retrieval
- Concerns for pregnancy
  - Gestational diabetes
  - Pre-eclampsia
  - Pre-term delivery
  - Macrosomia
  - Miscarriage/ still birth
  - Difficulties monitoring and delive

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Blood Glucose/ Cortisol

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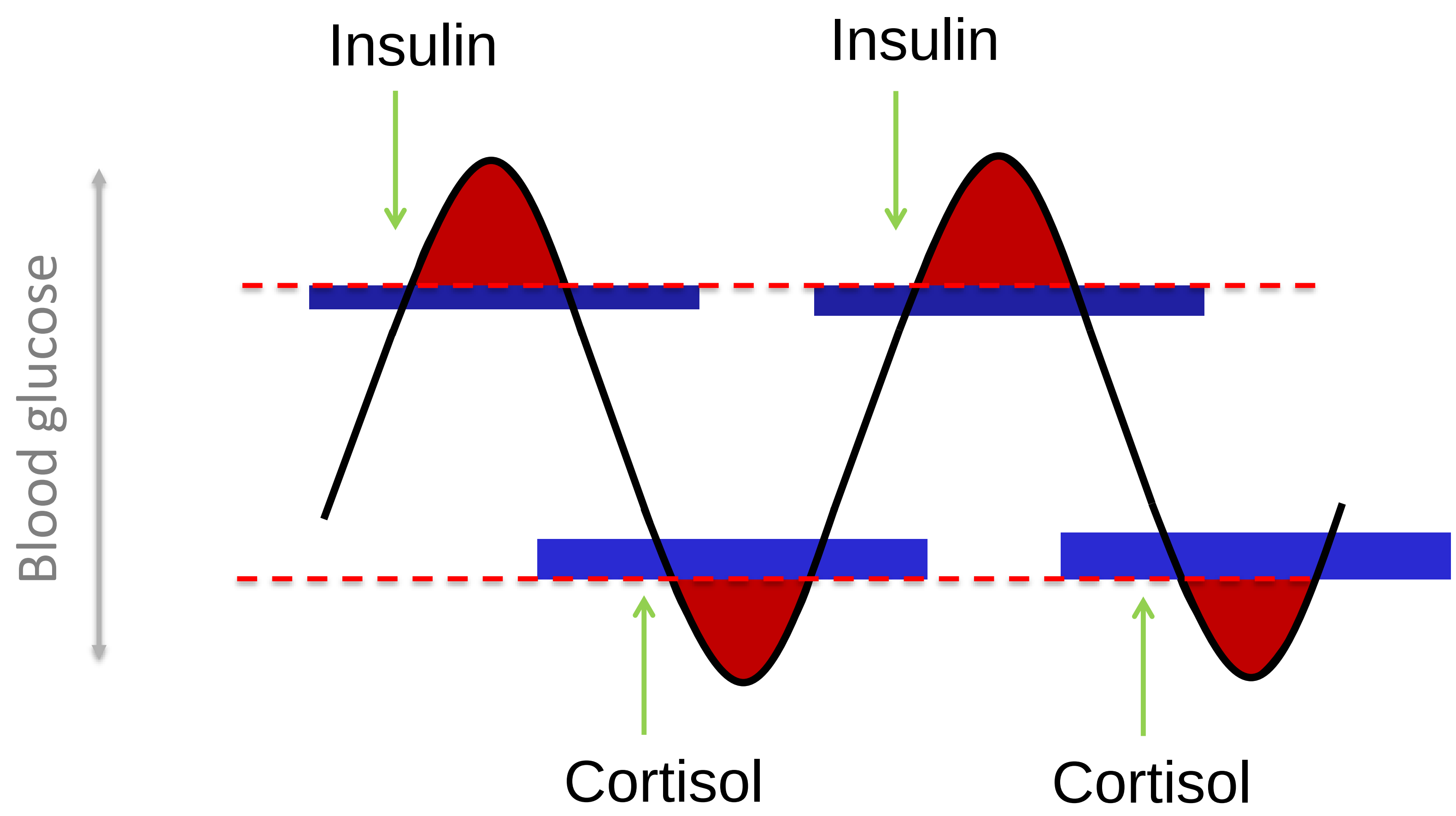

Cortisol increases during fasting

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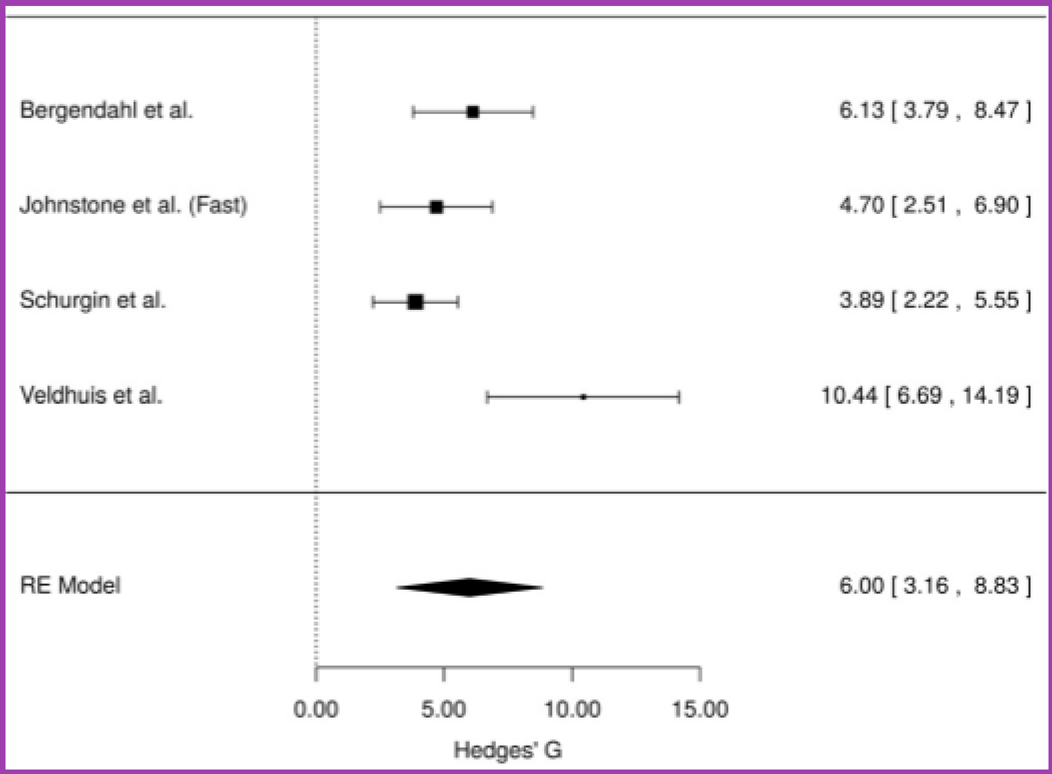

STRESS

Stress, 2016; 19(2): 151–157

Taylor & Francis
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ORIGINAL RESEARCH REPORT

Systematic review and meta-analysis reveals acutely elevated plasma cortisol following fasting but not less severe calorie restriction

Yuko Nakamura[1], Brian R. Walker[2], and Toshikazu Ikuta[3]

[1]The John B. Pierce Laboratory, New Haven, CT, USA, [2]BHF Centre for Cardiovascular Science, Queen's Medical Research Institute, University of Edinburgh, Scotland, UK, and [3]Department of Communication Sciences and Disorders, School of Applied Sciences, University of Mississippi, University, MS, USA

Abstract

Elevated plasma cortisol has been reported following caloric restriction, and may contribute to adverse effects including stress-induced overeating, but results from published studies are inconsistent. To clarify the effects of caloric restriction on plasma cortisol, and to assess cortisol as an indicator of stress during caloric restriction, we conducted a systematic review and meta-analysis of published studies in which cortisol was measured following caloric restriction without other manipulations in humans. We further compared effects of fasting, very low caloric diet (VLCD), and other less intense low caloric diet (LCD), as well as the duration of caloric restriction by meta-regression. Overall, caloric restriction significantly increased serum cortisol level in 13 studies (157 total participants). Fasting showed a very strong effect in increasing serum cortisol, while VLCD and LCD did not show significant increases. The meta-regression analysis showed a negative association between the serum cortisol level and the duration of caloric restriction, indicating serum cortisol is increased in the initial period of caloric restriction but decreased to the baseline level after several weeks. These results suggest that severe caloric restriction causes activation of the hypothalamic-pituitary-adrenal axis, which may be transient, but results in elevated cortisol which could mediate effects of starvation on brain and metabolic function as well as ameliorate weight loss.

Keywords

Caloric restriction, cortisol, diet, endocrinology, hypothalamic–pituitary-adrenal axis, meta-analysis, stress, weight control

History

Received 12 June 2015
Revised 22 October 2015
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Introduction

Adverse effects of dietary restrictions are a significant public health concern (Dirks & Leeuwenburgh, 2006). While obesity itself is a health risk, attempts to reduce body weight can increase stress and result in adverse effects, including stress-induced overeating (Pankevich et al., 2010) and cognitive dysfunction (Hutchinson, 2011; Rolland-Cachera et al., 2006; Vedhara et al., 2000). Increased stress responses, both psychological and physiological, after dietary restrictions have been reported (Epel et al., 2001). There have been attempts to assess the increased stress after dietary restriction by measuring serum cortisol levels. In humans, cortisol can be reliably measured in saliva, blood and urine and is elevated by chronic stress (Nater et al., 2013; Staufenbiel et al., 2013). Elevated cortisol can stimulate appetite, alter mood and memory and alter peripheral metabolism in favor of weight gain, all of which might be disadvantageous during caloric restriction.

Previous studies suggest that caloric restriction increases cortisol levels (Dubuc et al., 1998; Pasiakos et al., 2011; Tomiyama et al., 2010), but results are inconsistent. While fasting has been consistently shown to increase cortisol level, it is unclear whether lesser degrees of caloric restriction, such as those which are relevant during weight loss diets, cause elevated cortisol.

We therefore undertook a systematic review and meta-analysis of published studies to establish whether plasma cortisol is elevated during caloric restriction. We further studied the effects of graded caloric restriction (fasting, very low caloric diet (VLCD) and low caloric diet (LCD)). Finally, we used meta-regression to assess the influence of duration of caloric restriction on cortisol levels. In order to maximize the sample homogeneity (Andrew et al., 1998), only studies with serum cortisol, but not saliva or urine cortisol, were included in the meta-analysis.

Methods

In order to determine eligible studies for the meta-analysis, a MEDLINE search was performed for publications available on 7 November 2014. The following search term was used [cortisol AND ((((caloric restriction) OR food restriction) OR dietary restriction) OR diet restriction)]. Searches in Google scholar and Cochrane Library databases were also conducted to supplement the MEDLINE search.

Nonhuman studies were first excluded and then human studies that did not include cortisol assessment or caloric

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Cortisol increases during fasting

‘caloric restriction overall significantly increased serum cortisol, an effect which is attributable to fasting’


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ORIGINAL RESEARCH REPORT

Systematic review and meta-analysis reveals acutely elevated plasma cortisol following fasting but not less severe calorie restriction

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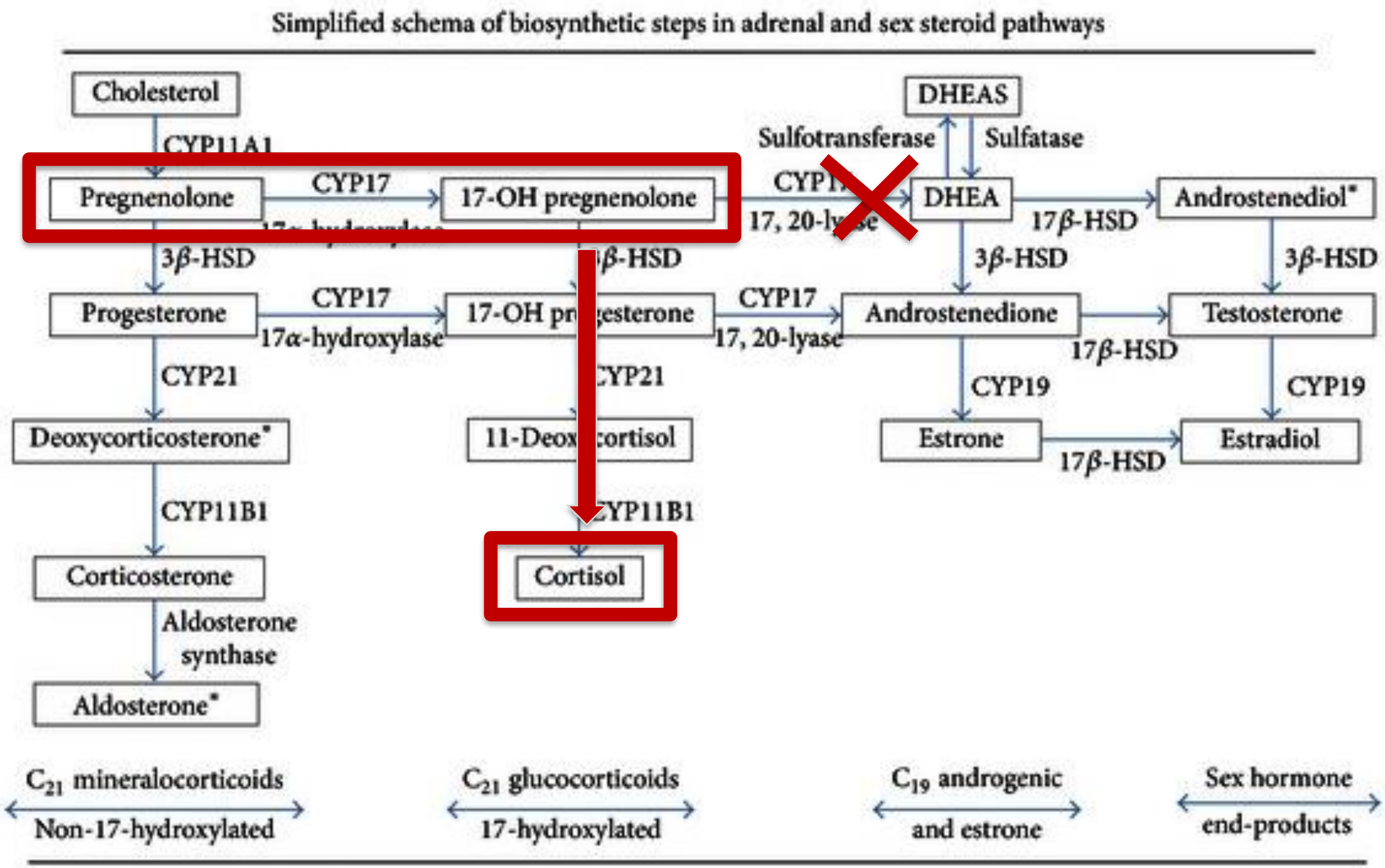
Methods

Cortisol affects sex hormones



Cortisol affects sex hormones

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'longer average menstrual cycle length'

'affected luteinising hormone dynamics'

behavioral sciences

MDPI

Review

Potential Benefits and Harms of Intermittent Energy Restriction and Intermittent Fasting Amongst Obese, Overweight and Normal Weight Subjects—A Narrative Review of Human and Animal Evidence

Michelle Harvie * and Anthony Howell

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Academic Editors: Amanda Sainsbury and Felipe Luz
Received: 28 September 2016; Accepted: 13 December 2016; Published: 19 January 2017

Abstract: Intermittent energy restriction (IER) has become popular as a means of weight control amongst people who are overweight and obese, and is also undertaken by normal weight people hoping spells of marked energy restriction will optimise their health. This review summarises randomised comparisons of intermittent and isoenergetic continuous energy restriction for weight loss to manage overweight and obesity. It also summarises the potential beneficial or adverse effects of IER on body composition, adipose stores and metabolic effects from human studies, including studies amongst normal weight subjects and relevant animal experimentation. Six small short term (<6 month) studies amongst overweight or obese individuals indicate that intermittent energy restriction is equal to continuous restriction for weight loss, with one study reporting greater reductions in body fat, and two studies reporting greater reductions in HOMA insulin resistance in response to IER, with no obvious evidence of harm. Studies amongst normal weight subjects and different animal models highlight the potential beneficial and adverse effects of intermittent compared to continuous energy restriction on ectopic and visceral fat stores, adipocyte size, insulin resistance, and metabolic flexibility. The longer term benefits or harms of IER amongst people who are overweight or obese, and particularly amongst normal weight subjects, is not known and is a priority for further investigation.

Keywords: intermittent energy restriction; fasting; weight loss; weight gain

1. Introduction

Excess energy intake, weight gain and subsequent adiposity are consistently linked to illness, disability and mortality [1–3]. Randomised trials demonstrate that intentional weight loss reduces type 2 diabetes [4], all-cause mortality [5] and increases cognitive [6] and physical function [7]. The health benefits of weight loss and energy restriction in these human clinical trials are supported by a century of laboratory research in rodents, which has established that energy restriction (ER) prevents age-related disease including tumours, cardiovascular disease, diabetes and dementia; retards aging-related functional decline; and increases lifespan [8].

Most human and animal studies on weight loss have involved continuous energy restriction (CER) administered on a daily basis. More recently, interest has focussed on intermittent energy restriction (IER) defined as periods of energy restriction interspersed with normal energy intake.

IER is of potential interest to manage obesity and its metabolic sequelae and also for normal weight subjects hoping to optimise their health independent of weight loss for two main reasons: firstly, IER only requires the individual to focus on ER for defined days during the week which is potentially

Behav. Sci. 2017, *7*, 4; doi:10.3390/bs7010004 www.mdpi.com/journal/behavsci

Cortisol affects sex hormones

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‘longer average menstrual cycle length’

‘affected luteinising hormone dynamics’

‘ increased feelings of hunger, worse mood, heightened irritability, difficulties concentrating, increased fatigue, eating-related thoughts, fear of loss of control and over eating during non-restricted days’

behavioral sciences

MDPI

Review

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Michelle Harvie * and Anthony Howell

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Cortisol Measurement via Saliva

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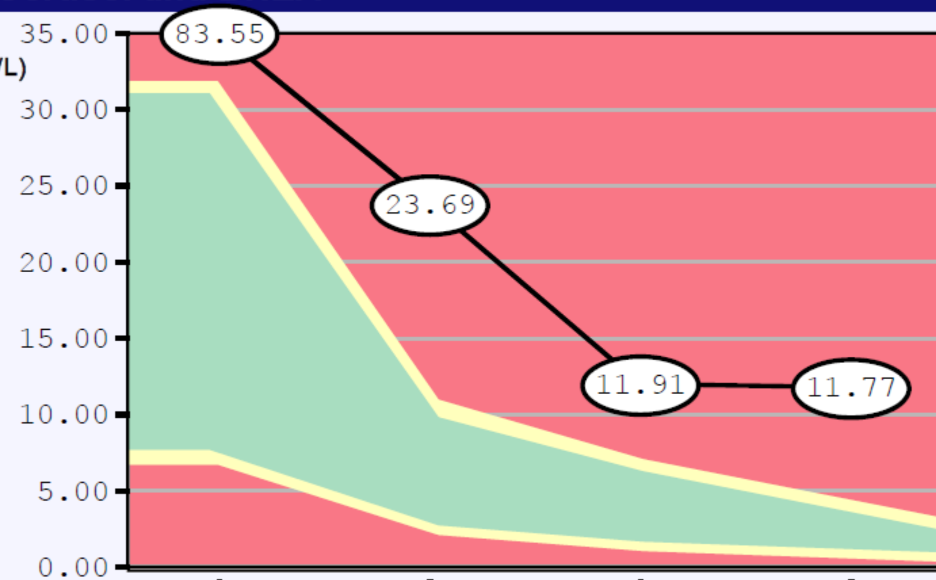
Salivary Cortisol and DHEA

Cortisol Levels

			Reference Range (nmol/L)
Sample 1 Post Awakening	83.55	H	7.45-32.56
Sample 2 (+ 4 - 5 Hours)	23.69	H	2.76-11.31
Sample 3 (+ 4 - 5 Hours)	11.91	H	1.38-7.45
Sample 4 (Prior to Sleep)	11.77	H	0.83-3.86
Sum of Cortisol	130.9		



Sample 1	Sample 2	Sample 3	Sample 4
7.45-32.56	2.76-11.31	1.38-7.45	0.83-3.86

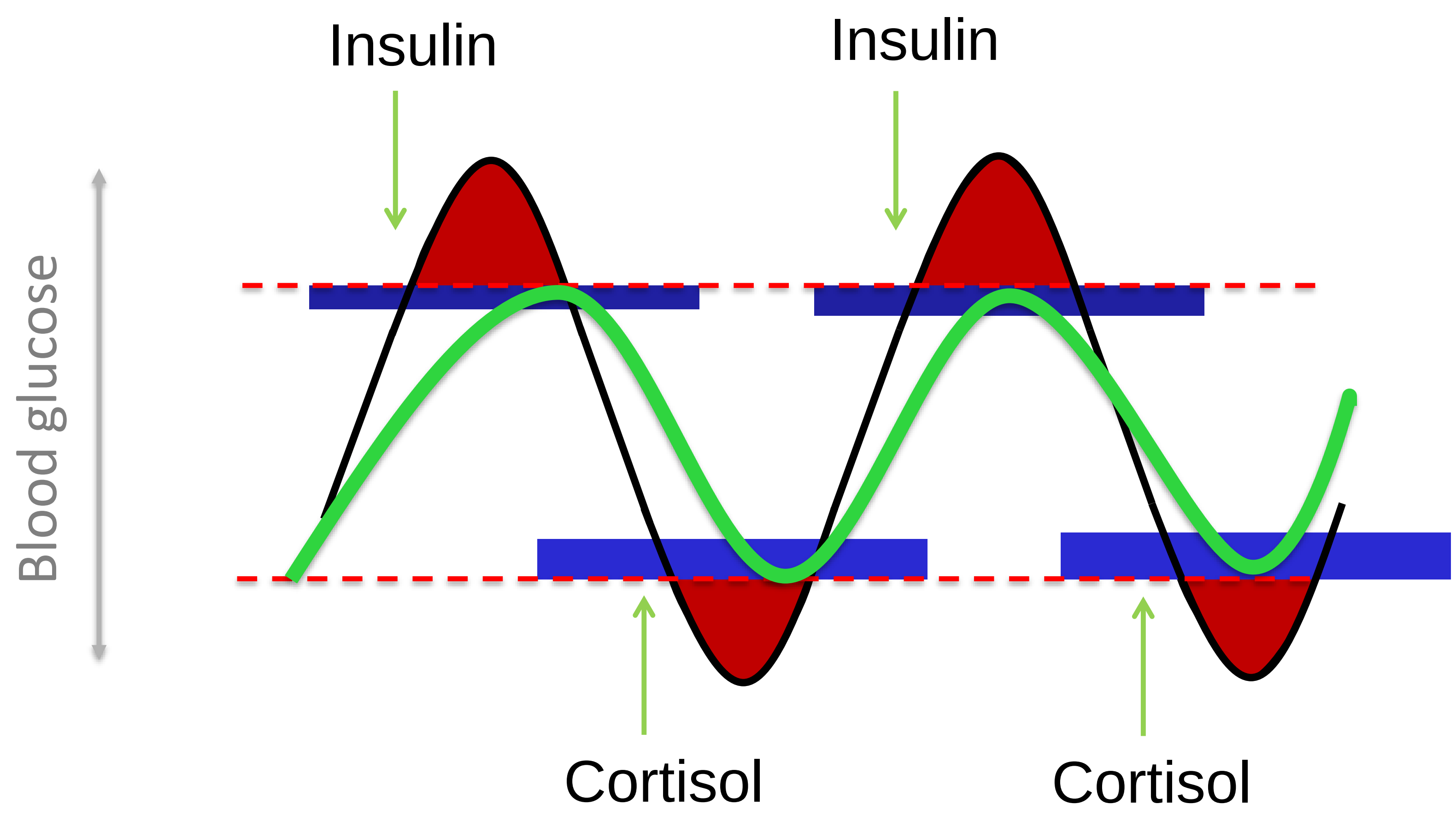
Cortisol Reference Limits - nmol/L

DHEA Levels

DHEA Mean	0.34		
DHEA : Cortisol Ratio	0.007	L	0.015-0.150

Hormones		Reference Range (nmol/L)
DHEA Sample 1 (am)	0.55	0.25-2.22
DHEA Sample 3 (pm)	0.12	0.25-2.22

Blood Glucose/ Cortisol



Blood Glucose/ Cortisol

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- Eating little and often
- Slow- release wholegrain carbohydrates
- Paired with protein and/or healthy fat
- Including healthy snacks
- Restricting carbohydrates in the evening

Mediterranean Diet

- Wholegrains
- Plenty of fresh fruit and vegetables
- Nuts and seeds
- Pulses
- Reduced red meat
- Increased intake of fish

Support

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- Focus on what you can have instead of what you can't
- Practical support
- Ongoing support and feedback
- Encouragement, positive re-enforcement

Recommendations

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- Avoid extreme caloric restriction and fasting
- Slow steady weight loss
- Incorporate exercise
- Slow release energy, small meals throughout the day
- Nutrient dense meals to support fertility
  - High in antioxidants, minerals, omega-3
- Support your patients through weight loss

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