Journal of Experimental Research

December 2016, Vol 4 No 2
www.er-journal.com
Email: editor-in-cheif@er-journal.com

Received: August, 2016
Accepted for Publication: October, 2016

CORRELATION OF WEIGHT LOSS WITH INFERTILITY FOLLOWING SLEEP DEPRIVATION IN ALBINO RATS

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ABSTRACT

Body weight is the total mass or weight of a person or animal obtained without any external factor than the component of the body. Overweight or underweight may influence the fertility status of either animal or human as the case may be. The aim of this study is to determine whether weight loss has any correlation with male or female infertility. Twenty four Wister albino rats were sleep deprived and used in this study. The albino rats were certified healthy before sleep deprivation. Body weight of the rats were measured before and after sleep deprivation. The pre sleep deprivation body weight values of the albino rats served as control for weight loss. Serum specimen was also collected from the rats before and after sleep deprivation for the assay of some fertility hormones. The pre sleep deprivation assay results of the fertility hormones equally served as control for post sleep deprivation status of the fertility hormones. The fertility hormones assayed include follicle stimulation hormone (FSH), luteinizing hormone (LH), Prolactin, thyroid stimulating hormone (TSH), Testosterone and estradiol. The results showed a significant decrease ($P<0.05$) in body weight of albino rats after sleep deprivation when compared with the control. There were significant decreases ($P<0.05$) in testosterone, estradiol, prolactin and TSH serum levels after sleep deprivation when compared with their controls respectively, while there were no significant changes ($P>0.05$) in the serum level of FSH and LH. These results indicate that all other relevant factors being equal, body weight loss has negative effect on male and female fertility, using body weight and fertility hormone as indices.

Key Words: Sleep Deprivation, Wistar Rats, Weight Loss, Correlation

INTRODUCTION

Body weight is the total mass or weight of a person or animal in kilograms obtained without any external factor than the component of the body (Walpole et al, 2012 Owing to the fact that mass is a measure of body's inertia independent on the effect of gravity and weight is a measure of force due to gravity, ideal body weight is represented by body mass index (BMI) (WHO, 2000). BMI is obtained by body weight in kilogram divided with the value of height in meter squared. Human body weights are categorized as follows: a healthy body weight is BMI range between 18.5 and 25. BMI below 18.5 is considered underweight, BMI between 25 and 29.9 is considered over weight while beyond 30.0 is regarded as obese (WHO, 2000; WHO, 2006). A morbidity obese subject will have a BMI of 40 and above. Many factors contribute to a subject's weight. These factors include environment, family history and genetics, body metabolism and habits. The body energy is supplied primarily by food absorbed and if the amount of food absorbed is greater than the amount expended by the body, the excess is stored in tissues in form of combustible materials called carbohydrates, proteins and fats (Abraham et al, 1978). These stored materials bring about the weight of the body. The capacity of the body to store proteins and carbohydrates is limited so that further considerable storage of excess combustible energy material is accomplished by deposits of fat (Abraham et al, 1978). By these biological processes, body weight could get to either normal or abnormal body weight status.

The abnormal body weight status includes; underweight, overweight, obese weight and morbidity obese weight (DU-Bray, 1926; Pastor et al, 1996). Protein balance tends

to maintain itself spontaneously and because it contributes only a minor fraction of energy intake, it is the metabolism of carbohydrate and fat that primarily influence the regulation of body weight (Hallerstein, 1996; Hallerstein, 1999; Goodnight et al, 1982). Fat synthesis for possible overweight, obese weight and morbidity obese weight can be induced by sustained ingestion of excess carbohydrate (Hellerstein, 1996, Hellerstein, 1999, Goodnight et al, 1982).

However, for ideal weight to be considered, a number of other factors such as age, height, sex, chest, circumference and body build are referred(WHO, 2004).Sleep deprivation has negative effect on body weight in rats. Prolonged or complete sleep deprivation increased both food intake and energy expenditure with net effect of weight loss and ultimately death (Everson et al, 1989). In human, the reverse is the case, following the reports of some research studies (Green et al, 1988; Knusten et al, 2007; Schmid et al, 2008). The increasing prevalence of overweight, obesity and diabetes are being traced to the role of sleep loss among other factors (Knusten et al, 2007). Current data suggest that the relationship between sleep restriction, weight gain and diabetes may involve three path ways; alteration in glucose metabolism, up regulation of appetite and decrease in energy expenditure (Knusten et al, 2007)

Sleep deprivation impairs glucose homeostasis by way of engendering insulin resistance, thereby causing type 2 diabetes which subsequently affects body weight (VanHelder et al, 1993). Chronic sleep loss can reduce capacity of even young adults to perform basic metabolic functions such as processing and storing of carbohydrates or regulation of hormone secretion of endocrine system (VanHelder et al, 1993). In a research work done, food consumption of the calorie-fed rats was lower during baseline than that of protein fed group but during sleep deprivation increased to 250% of the normal without net body weight gain, implying negative energy balance and malnutrition during prolonged sleep deprivation (Everson and Wehr, 1993).

Epidemiological data confirm that obesity accounts for about 6% primary infertility and it may be surprising that body een weight loss in women accounts for 6% primary infertility (Bates and Whiteworth, 1982; Green et al, 1988). This 12% of primary infertility resulting from deviation in established bodyweight norms, can be corrected by restoring body weight to within established normal limits. More than 70% of women who are infertile as a result of body weight disorder will conceive spontaneously if the weight disorders are corrected. This is usually done through appropriate education and diet counseling; yet body weight is not often considered in an infertility evaluation (Bates and White, 1982; Green et al, 1988). It is therefore pertinent that the body weight of both partners of the infertile couple should be considered first when there is an obvious slender or obese body habitués in either partner (Green et al, 1988, Bates and Whitworth, 1982)

Following the report by Rechtschaffen and Bergmann in 1995 that sleep deprivation in rats resulted to weight loss and the responses of thyroid hormones and thyrotropin-releasing hormone during sustained sleep deprivation in rats according to Everson and Read, we chose to sleep deprive rats by single platform sleep deprivation method to avoid physical stimulation applied by Rechtschaffen and Bergmann which may have its own effect. The emphasis of their work was to ensure the sustainability of sleep deprivation and weight loss.

The aim of this work is to determine the correlation of loss of weight with infertility in albino rats (Everson and Read, 1995).

MATERIALS AND METHODS

Experimental Animals:

Twenty four (24) adult Wister albino rats (9 males and 15 females) were used in this study. The rats were fed and acclimatized at the University of Nigeria, Enugu Campus animal house for 5 days before subjecting them to sleep deprivation.

Sample Collection and Processing

Blood specimen was collected from each of the rats, before sleep deprivation. The pre sleep deprivation blood specimen served as control for the investigations. Blood samples were allowed to clot and retract, after which they were centrifuged at 3000 rpm/min to separate

the serum.

Method of Sleep Deprivation

Sleep deprivation of the rats was achieved by the single platform sleep deprivation technique (Rechtschaffen et al, 1999). This technique is based on the principle that if a sizeable adult rat is placed on 6.5 cm base of an inverted cylindrical pot with a depth of 7.5cm in a water proof rat cage and water poured at the floor of the rat cage, sleep is deprived from the rat especially in a brightly-lit non heat producing environment. (Rechtschaffen et al, 1999; Craig Lambert, 2005). Following the single platform sleep deprivation procedure the rats were respectively deprived of sleep for fourteen days. During the sleep deprivation duration, water at the floor of the rat cage was kept relatively fresh by regular replacement on daily basis.

At the end of the fourteen days sleep deprivation of the rats, the weight of the rats were measured and post sleep deprivation blood specimen was again collected from each sleep deprived rat by ocular Venipuncture for hormone assay (Van Herck, 1998). FSH, LH, prolactin, TSH and testosterone were assayed in male albino rats whereas FSH, LH, TSH, prolactin and estradiol were assayed in female albino rats in both pre- and post-sleep deprivation blood samples.

Analytical Methods:

The hormones, FSH, LH, prolactin and TSH were assayed by enzyme immuno assay method according to lequin (2005) and Uotilia et al, (1981). Testosterone and estradiol estimation were based on the enzyme-linked immunosorbent assay (ELISA) method of Tietz (1995). Statistical analysis was performed by student's t-test at 95% confidence limit and the results expressed as mean ± standard deviation (SD).

RESULTS

The results of this research work are comparatively represented in the table shown

TABLE 1: The result of body weight and hormone activities before sleep deprivation.

Parameter	Pre-Sleep Deprivation Values
Body weight (G)	239 ± 2.1
FSH (mIU /ml)	5.5 ± 0.2
LH (mIU /ml)	4.88 ± 0.1
Prolactin (ng/ml)	12.8 ± 0.04
TSH (μIU /ml)	2.0 ± 0
Testosterone (ng/ml)	1.9 ± 0.09
Estradiol (pg/ml)	27.8 ± 0.3

TABLE 2: The result of body weight and hormone activities after sleep deprivation.

Parameter	Post SleepDeprivation Values
Body weight (G)	204± 0.09
FSH (mIU /ml)	5.4± 0.2
LH (mIU /ml)	5.3± 0.1
Prolactin (ng/ml)	5.1 ± 0.02
TSH (μIU /ml)	0.5± 0.1
Testosterone (ng/ml)	0.4± 0.03
Estradiol (pg/ml)	14.3± 0.5

TABLE 3: Table of Pre and post sleep deprivation results of body weight and hormone activities

Parameter	Pre-Sleep Deprivation Values	Post Sleep Deprivation Values	t-Test
Body weight (G)	239± 2.1	204± 0.09	P<0.05 **
FSH (mIU /ml)	5.5±0.2	5.4± 0.2	P>0.05
LH (mIU /ml)	4.88 ± 0.1	5.3± 0.1	P>0.05
Prolactin (ng/ml)	12.8 ±0.04	5.1 ±0.02	P<0.05**
TSH (?IU /ml)	2.0± 0	0.5± 0.1	P<0.05**
Testosterone (ng/ml)	1.9± 0.09	0.4± 0.03	P<0.05**
Estradiol (pg/ml)	27.8 ±0.3	14.3± 0.5	P<0.05**

DISCUSSION

The results of body weight of albino rats used in this research work as represented in the table 3, showed a significant bodyweight loss of rats after sleep deprivation (P<0.05). There were corresponding significant decreases (P<0.05) in the activities some fertility related hormones. Such fertility related hormones include testosterone, Ostradiol, Prolactin and thyroid stimulating hormones. However, the results obtained as represented in the same table also revealed that they were decreases (P>0.05) in the activities of follicle stimulating hormone and luteinizing hormone.

Testosterone, estradiol, prolactin and thyroid stimulating hormones along with follicle stimulating hormone and luteinizing hormone have been used as hormonal indices to determine either fertility of or infertility of mammals (Kaplan and Pesce, 1979). Similarly changes in body weight have been associated with either fertility or infertility of mammals (Green et al, 1988; Bates and Whiteworth, 1982). It therefore became necessary to further establish with empirical data how body weight loss is correlated with infertility. With the observation that this work is in agreement with the work of Green et al, (1988) and Whiteworth, (1982), it could be acceptably correlated that loss of weight has a negative effect on fertility.

Although follicle stimulating hormone and luteinizing hormone were not significantly affected in this work, testosterone and estradiol which are primary male and female fertility hormones respectively have corresponding significant decrease in activities with significant decrease in body weight in this research work.

Also observing the same corresponding significant decreases in the activities of Prolactin and thyroid stimulating hormones, it becomes necessary to consider weight loss status in case of infertility. It is for instance known that slender women metabolize estradiol to 2-hydroxyestrone, an anti estrogen (Bates, 1994).

By this further metabolism, serum status of estradiol is reduced while that of 2-hydroxyestrone, inactive estrogen or anti-estradiol is increased. The reaction creates a counterproductive state for estradiol which in normal body weight status would have progressively increased to a level during follicular growth to be able to induce positive feedback effect via the hypothalamus for a surging release of luteinizing hormone for ovulation to occur.

This probably could be part of the reasons why there was no significant increase in luteinizing hormone in this work. Reduction of estradiol level in male exposes the sperm cells to apoptosis on daily basis, resulting to oligospermia and infertility (Pentikainen et al, 2006). Sex steroid hormones testosterone and estradiol which are lipid soluble and accumulate in body fat (Green et al, 1988; Bates, 1996; Kressler, 2005) are thus liable to depletion by weight loss (Kressler, 2005).

Decrease in serum level of testosterone as seen in this work obviously in agreement with other such previous results that affect normal libido in both male and female, clitoral engorgement and penile erectile frequency (Metha et al, 2008). Low level of testosterone makes it difficult for genes of sertoli cells to be

activated for promotion of normal differentiation and development of spermagonia (Zhou et al, 2001).

Decrease in prolactin level affects fertility since optimal prolactin level promotes orgasm, proliferation of oligodendrocytes precursor cells, proliferation of corporal lutea and stimulation of progesterone secretion (Abraham et al, 1978). Low level of TSH is associated with hypothyroidism which is invariably associated with infertility (Amada-Dias et al, 2001). Further work is needed to establish why TSH is significantly lowered in this weight loss. Thyroid hormones regulate the metabolic processes of the body. In cases where the T_3 and T_4 are low, the hypothalamus signals the pituitary gland to produce TSH through the action of TRH . TSH therefore stimulates the thyroid gland to produce sufficient T_3 and T_4 to meet up with the metabolic needs of the body. When T_3 and T_4 become raised, they signal the hypothalamus and pituitary gland to discontinue TSH production through the feedback mechanism(Abraham et al, 1987; Nussey and Whitehead, 2009). Therefore, low TSH as seen in this work raises speculations on whether weight loss has effects on the hypothalamus, pituitary gland or thyroid gland.

It is pertinent to note that this research is in consonance with the report in American society of reproductive medicine which stated that loss of body weight contributed 6% to the 12%, said to have been contributed by abnormal body weight to primary infertility (Bates GW, 1994). Experimental results have shown that infertility due to weight disorder could be reversed if the body weight disorder is corrected (Bates and Whiteworth, 1982; Bates, 1996). Intense exercise lowers testosterone level which in turn affects male fertility (Harkney, 1998; Arce, 1993; Green et al, 1988). This is obvious as it is partly stored in fat which is broken down by intense exercise (Green et al, 1988, Bates, 1996; Kresssler, 2005). Following the observations and data in this research work, we therefore tend to conclude that bodyweight loss is significantly correlated to both male and female infertility.

REFERENCES

Abraham W, Handler P, Emil S, Robert H, Lehman R. (1978). Major processes that provide and conserve in cells. In Principles of Biochemistry,6th Ed.1296-1299.

Amada-Dias L, Canvalho TJ, Breitenbach MMD, Francis CR, Maura EG. (2001). Infertility in hypothyroidism. *Braz. J Med. Biol Res.* 34: 1209-1215.

Arce J. (1993). Subclinical alterations in hormone and semen profile in athletes. *Fertile Steril.* 59(2): 398-404.

Bates GW. (1994). Body weight Loss and estradiol. American Society of reproduction Medicine.

Bates GW. (1996). Body weight and Reproduction. In seebel MM (ed.), Infertility: A comprehensive text. Appleton-Century-Crofts. New York.

Bates GW, Whitworth NS. (1982). Effect of Body Reproduction on Plasma Androgens in Obese Infertile Woman. *Fertile Sterile*. 38:406 -407.

Cianflone K. (1993). Nutritional and training strategies to maximize fat burning. *Int. J. Obos. Relat. Metab. Disord*.17: (3): 32-36.

Craig L. (2005). Deep into sleep. *Harvard Magazine*. July – Aug.

Du-Bray ES. (1926). Excess of body energy storage as fats. *Can. Med. Assoc. J*. 16 (1): January, 64-66.

Everson CA, Read HL. (1995). Pituitary and peripheral hormone during sustained sleep deprivation in freely moving rats. *Endocrmol.* 136: 1426-1434.

Everson CA, Bergmann BM, Rechtschaffen A. (1989). Sleep deprivation in rats: Total sleep deprivation. *Sleep*.12 (1):13-21.

Everson CA, Wehr TA. (1993). Nutritional and metabolic adaptations to prolonged sleep deprivation in rate. *Am. J. Physiol. Regul. Integer. Comp. Physiol.* 264:376-387.

Goodnight S, Harris W, Connor W, Illingworth DR. (1982). Polyunsaturated Fatty Acids, hyperlipidemia and thrombosis. *Arteriosclerosis*. 2:87-113.

Green BB, Weiss NB, Darling JR. (1988). Risk of Ovulatory Infertility in Relation to Body weight. *Fertile Steril*. 50:721.

Haslam DW, James WP. (2005). Obesity. *Lancet*. 9492:1197-1209.

Hackney A. (1998). Testosterone and Reproductive Dysfunction in Endurance-Trained Men. *Encyclopedia of Sports Medicine and Science.* 20 Sept.

Hellerstein MK. (1996). Regulation of hepatic denovo Lipogenesis in humans. *Annu. Rev. Nutr.* 16(52):523-557.

Hellerstein MK. (1999). Denovo lipogenesis in humans: metabolic and energy regulatory aspects. *Eur. J. chin. Nutr.* 53:53-65.

Kaplan LA, Pesce AJ. (1989). The Gonado. In Clinical Chemistry, Theory, analysis and correlation. 2nd Ed, 651-662.

Knusten KL, Spiegel K, Penev P, Vancouver E. (2007). Metabolic consequences of sleep deprivation. *Sleep Med. Rev.* 11(3): 163-178.

Kresster H. (2005). Determination of fat oxidation during exercise. *J. Appl. Physiol*. 98(1): 160-167.

Leguin R. (2005). Enzyme Immunoassay EIA/Enzyme immunosorbert Assay (ELISA). *Clin. Chem.* 52 (12) 2415-2418.

Metha PH, Jones AE, Joseph RA. (2008). The social endocrinology of dominance: basal testosterone predicts cortisol changes and behaviour following victory and defeats. *J. Pers, Soc Psycho*. 94(6):1078-1093.

Nussey S, Whitehead S. (2001). Endocrinology: An Integrated Approvach. Oxford BIOS Science Publishers. 3:1-44.

Pastor DR, Fisher M, Fredman SB. (1996). Abnormalities in weight in weight status, eating attitudes and eating behaviours, among Urban High School Students: Correlation with self esteem and anxiety. *J. Adolsce Health*. 18(5): 312-319.

Pentikainen V, Erkkila K, Suomalainen L, Parvinen M, Dinkel L. (2006). Extradiol as a germ cell survival factor in human testis invitro. *J. Clin. Endocrinol. Metab*. 85:2057-2067.

Rechtschaffen and Bergmann BM, Gilliland MA, Bauer K. (1999). Effect of method dilation and sleep stage on rebounds from sleep deprivation in rats. *Sleep*. 22(1):11-31.

Schmids SM, Hall-Schimid M, Jauch-chara K, Born J, Schultes B. (2008). A single night of sleep deprivation increases Ghrelin level and feeling of hunger in normal-weight healthy men. *J. Sleep. Res.* 17:31-334.

Tietz NW. (1995). Clinical Guide to Laboratory Tests. 3rd Ed; W.B Saunders & Co. Philadelphia. 578-580.

Votila M, Ruoslaht E, Engvav E. (1981). Enzyme immunoassay. *J. Immunol Methods*. 42:11.

VanHerck H. (1998): Orbital Sinus blood sampling in rats as performed by different technicians. The influence of technique and expertise. *Lab. Animals*. 32:377-386.

VanHelder T, Symons JD, Radomski MW. (1993). Effect of sleep deprivation and exercise on Glucose Tolerance. *Aviate Space Environ. Med.* 64:487-492.

Walpole A. (2012). The Weight of Nations: An estimation of adult human biomass. *BMC Public Health*, 12(1): 439-440.

White A, Handler P, Emil S, Robert H, Lehman R. (1978). Gonadotropic hormones. In principles of Biochemistry. 6th Ed. pp1221-1224.

World Health Organization Report. (2000): Bodyweight pp.16.

World Health Organization Report. (2006): Bodyweight pp.16.

Zhou Q, Clarke L, NIC R, Carnes K, Lai LW, Lien YHH, Merkman A, et al (2001). Estrogen Action and male fertility: Roles of sodium Hydrogen Exchanger – 3 and fluid reabsorption. In reproductive tract function. *Proc. Natl. Acad. Sci. USA.* 98(24): 14132-14137.