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Correlation between leptin content and sperm retrieval in cases of functional azoospermia

Merihan Mahmoud Shehata Ellithy [a,*], Osama Kamal Zaki Shaeer [b], Khadiga Mohammed Gaafar [a]

[a] *Department of Zoology, Faculty of Science, Cairo University, Giza, Egypt*
[b] *Department of Andrology, Kasr El Aini School of Medicine, Cairo University, Giza, Egypt*

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KEYWORDS

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Abstract *Introduction:* Testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI) became the preferable techniques for solving the problem of azoospermic men. Non-invasive techniques are needed to predict sperm retrieval chance before TESE to avoid the psychological and physiological problems that may be developed.

Aim: To investigate the correlation between serum, seminal and testicular leptin levels and sperm retrieval in functional azoospermic men.

Methods: The study included 61 men classified into 4 groups; normozoospermia (NOR), obstructive azoospermia (OA), positive non-obstructive azoospermia (NOA (+)) and negative non-obstructive azoospermia (NOA (−)). Blood FSH, LH, Prolactin, Free and Total testosterone levels plus serum and seminal leptin levels were measured for all groups. For azoospermic groups, TESE and testicular leptin level were applied.

Main outcome measures: Both OA and NOR groups were used as control groups. The prediction accuracy for FSH and serum, seminal and testicular leptin was compared by receiver operating characteristic (ROC) curve analysis.

Results: There were no significant differences in serum leptin levels among the four groups. Azoospermic groups showed higher seminal leptin levels than the NOR group. Seminal and Testicular leptin levels of NOA (−) men were significantly increased in comparison with OA and NOA (+) men. There was a significant negative correlation between serum leptin and total testosterone concentrations, and a significant positive correlation between testicular and seminal leptin concentrations. In ROC curve; for differentiation between positive and negative NOA, areas under

* Corresponding author. Tel.: +20 1003202171.
E-mail address: merihan_ellithy@hotmail.com (M.M.S. Ellithy).
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the curve (AUC) of testicular and seminal leptin were greater than that of serum leptin. The combination of seminal leptin with FSH gave AUC greater than that of FSH alone.

Conclusion: There is a role for leptin in spermatogenesis, and seminal leptin can be used as a good assistant marker to increase the prediction accuracy for sperm retrieval in NOA men especially in combination with FSH.

Introduction

Azoospermia is a medical condition of males having total absence of spermatozoa from the ejaculate. It is found in 1–3% of the male population and approximately 10% of infertile males (Jarow et al., 1989). Azoospermia is classified according to etiology into OA and NOA. Obstructive azoospermia is failure of sperm transport due to the presence of obstruction in the seminal ducts, thus spermatogenesis is normal, while NOA is failure of sperm production or maturation by the testis, thus there is deficient spermatogenesis (NOA (+)) or absent spermatogenesis (NOA (−)) (Ginsburg and Racowsky, 2012). In early 1990s, testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI) were introduced for the treatment of OA, later these techniques are applied on NOA (Gardner et al., 2011), where it was reported that sperm retrieval chance for each biopsy is 20–50% in the NOA patients (von Eckardstein et al., 1999).

Many predictive markers that could predict the presence of sperm in testicular tissue were proposed. It was reported that follicular stimulating hormone (FSH) and testicular volume constitute the best options to make such a prediction (Toulis et al., 2010), in addition to serum Inhibin B (Inh-B) level (Ballesca et al., 2000; Bohring et al., 2002; Bailly et al., 2003), seminal Inh-B level (Nagata et al., 2005), serum and seminal levels of anti-Müllerian hormone (AMH), detection of round spermatids in seminal fluid (Amer et al., 2001), as well as the testicular histopathological findings (Su et al., 1999; Abdel Raheem et al., 2013). None of the aforementioned markers has gained universal acceptance (Isikoglu et al., 2006; Mostafa et al., 2007; Duvilla et al., 2008; Mitchell et al., 2010; Toulis et al., 2010), and with regard to taking diagnostic testicular biopsies, it is an invasive procedure. Therefore the search for a better spermatogenic non-invasive marker and more accurate method of predicting TESE outcome is still in process (Vernaeve et al., 2002; Ma et al., 2010).

Leptin is an adipocytokine, synthesized as a 167-amino acid hormonal protein and it is the product of the obesity gene. Zhang et al. have reported that leptin was originally discovered in 1994 by Jeffrey M. Friedman and colleagues. They also reported that mature leptin is 146 amino acids in length, with a molecular weight of approximately 16 kDa (Zhang et al., 1994). Originally leptin was defined in association with satiety and energy balance and claimed to be an anti-obesity factor that functioned via a feedback effect from adipocytes to hypothalamus. In addition it was found to play a role in the regulation of metabolism, sexual development, angiogenesis, hematopoiesis, immunity, gastrointestinal functions, sympathetic activation, and reproduction (Ziylan et al., 2009).

Previously, some studies have linked leptin and male reproduction; puberty, spermatogenesis, functional regulation of the male gonadal axis, sperm maturation, sperm capacitation and sperm motility (El-Hefnawy et al., 2000; Kiess et al., 2000; Kratzsch et al., 2000; Glander et al., 2002; Tena-Sempere and Barreiro, 2002; Aquila et al., 2005; Cervero et al., 2006; Ishikawa et al., 2007; Zorn et al., 2007; Haron et al., 2009; Nicopoulou et al., 2009). Only a handful of studies have dealt with leptin association with azoospermia (Steinman et al., 2001; Zorn et al., 2007; Ma et al., 2010; Gao et al., 2011). Very few studies have focused on the use of leptin to increase the prediction accuracy for sperm retrieval in azoospermic men; Ma et al. (2010) studied the use of seminal leptin as a marker to differentiate between sperm negative and sperm positive NOA patients and Gao et al. (2011) studied the use of both serum and seminal leptin concentrations for the differential diagnosis of OA and NOA.

In this study we investigated the correlation between serum, seminal and testicular levels of leptin and sperm retrieval in functional azoospermic men.

Materials and method

Patients

The research included four groups of 61 men with mean age 33.557 ± 0.626 (24–48 years). Group 1 (n = 6) was NOR, group 2 (n = 15) was OA, group 3 (n = 11) was non-obstructive azoospermic men with positive TESE (NOA (+)) and group 4 (n = 29) was non-obstructive azoospermic men with negative TESE (NOA (−)). Both OA and NOR groups were used as control groups (n = 21).

Group 1 was subjected to history taking, full examination, determination of body mass index (BMI), measurements of blood sugar level, semen analysis, hormonal evaluation; including FSH, LH, Prolactin, Free and Total testosterone, and measurement of leptin level in serum and seminal plasma. The same protocol was applied to other groups in addition to scrotal duplex, karyotyping, TESE, measurement of leptin level in the testicular tissue.

Patients with genetic abnormality, varicocele or any other known cause for azoospermia, as well as patients with diabetes or an abnormal BMI were excluded.

Ethical approval

All patients signed a consent form before proceeding with procedures. The Research Ethical Committee (REC) at the Department of Andrology, Cairo University, Egypt has approved this research.