Reproductive hormones profile in male infertility

A. L. Al-Malki and Taha A. Kumosani
Department of Biochemistry, Faculty of Science,
King Abdulaziz University, Saudi Arabia

ABSTRACT

Male infertility is responsible for 35% of infertile marriages. This study is concerned with the relative importance of endocrine factors among infertile males. The so-called "endocrine disruptors" may harm wildlife, aquatic life, or human health by interfering with the action of reproductive and other hormones. Other factors, which cause infertility in the males, include alcohol, vitamin deficiencies and heavy metals. Sixty three subjects were grouped into: fertile, primary infertile and secondary infertile and investigated for the level of hormones in their blood sera. The hormones studied were; testosterone, estradiol, FSH, LH, and PRL. LH showed a significant increase, ($p < 0.05$) between primary infertile compared to fertile males.

Therefore, LH determination could be used in conjugation with other seminal analysis in the diagnosis of infertility among males. It is necessary to draw a complete reproductive hormones profile for a proper laboratory diagnosis in such cases, including biologically active LH, FSH and PRL.

INTRODUCTION

Some scientists hypothesize that certain chemicals in the environment, the so-called "endocrine disruptors," may harm wildlife, aquatic life, or human health by interfering with the action of reproductive and other hormones. Evidence to support this hypothesis is generally accepted for some vertebrate animals, such as fish and alligators, exposed to high levels of some environmental contaminants, primarily in surface water, but is scanty for humans exposed to low levels of contaminants[(1)].

Male infertility is responsible for 35% of infertility among married couples; the most common causes for infertility in male are the abnormalities of the semen including the inability to produce adequate numbers of healthy sperm and insufficient sperm count[(2)]. Other factors which cause infertility in the males include alcohol, vitamin deficiencies and heavy metals[(3;4;5;6;&7)] and hormonal disturbances[(8;9;10;11&12)].

Whether hormonal disturbances are caused by endocrine disrupters or it is a cause of infertility is not yet known. The aim of this work was to study the relative importance of endocrine factors among infertile male subjects.

MATERIAL & METHODS

Subjects

All subjects included in this study were selected from two hospitals namely; King Abdulaziz University Hospital and United Doctors Hospital in Jeddah, Saudi Arabia. A total of 63 subjects were included in this study and were divided into three main groups. The first group consisted of normal healthy fertile males, whose wives had live or still birth, (n = 5). The second group consisted of primary infertile males, whose wives had no previous pregnancy for one year, (n = 43) due to causes not related to female infertility. The third group consisted of secondary infertile males with wives who had previous pregnancies although not necessarily a live birth, (n = 15). All groups were age matched.

Methods

Blood samples from all participants were collected, left to clot, then centrifuged to obtain the sera. The determination of the hormones; (estradiol, FSH, LH, PRL and testosterone) was accomplished using Boehringer Mannheim, Elecsys, Electrochemiluminescence model 2010, Japan- German combination. This is a highly innovative technology that offers distinct advantages over other measurements techniques.

Statistical Analysis

Analyses of data were performed using **SPSS** statistical package. Student t-test was used for comparing means. Differences were considered to be statistically significant if $p < 0.005$[13].

RESULTS

Figure (1) shows the mean values, (± S.D), of serum testosterone levels in the three groups. These values are 15.4 ± 4.0, 14.4 ± 8.5 and 10.4 ± 7.4 nmol/L for the healthy fertile control group, primary infertile group and secondary infertile group, respectively. There were non-significant differences between the three groups regarding testosterone level.

Figure (2) shows the mean values, (± S.D), of serum estradiol levels in the three groups. These values are 35.5 ± 2.1, 43.1 ± 18.3 and 39.7 ± 18.5 nmol/l for the healthy fertile group, primary infertile group and secondary infertile group, respectively. There were non-significant differences between the three groups regarding the estrogen level.

Figure (3) shows the mean values, (± S.D), of serum LH levels in the three groups. These values are 3.9 ± 1.0, 6.2 ± 2.1, for the normal control group and the secondary infertile group respectively. A significant higher serum LH level in primary infertile group was noted, (8.2± 2.3 as compared to 3.9 of control; ($p < 0.05$). Non- significant difference in LH level between healthy fertile and secondary infertile groups was found.

Figure (4) shows the mean values, (± S.D), of serum FSH levels in the three groups. These values are 5.8 ± 4.1; 10.2 ± 1.7, and 9.6 ± 3.7 U/l for the healthy fertile group, primary infertile group and secondary infertile group, respectively. There were non

significant differences between the three groups regarding FSH level.

Figure (5) shows the mean values, (± S.D), of serum PRL levels in the three groups. These values are 16.4 ± 6, 13.3 ± 10.3 and 11.9 ± 6.7 nmol/L for the healthy fertile group, primary infertile group and secondary infertile group, respectively. There were non-significant differences between the three groups regarding prolactin level.

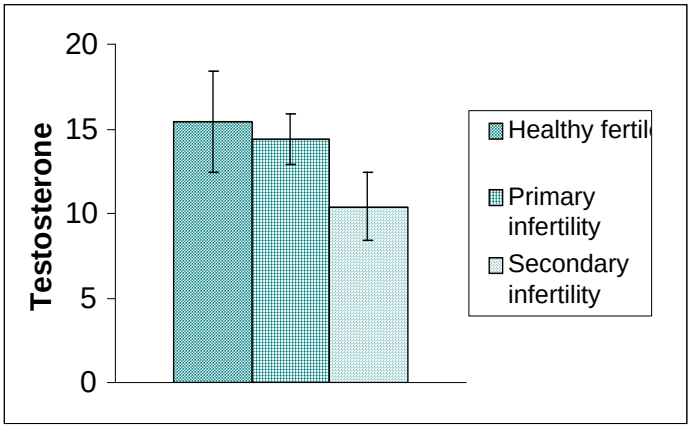

Figure 1: Mean serum testosterone in the three groups; healthy fertile, primary infertile and secondary infertile males.

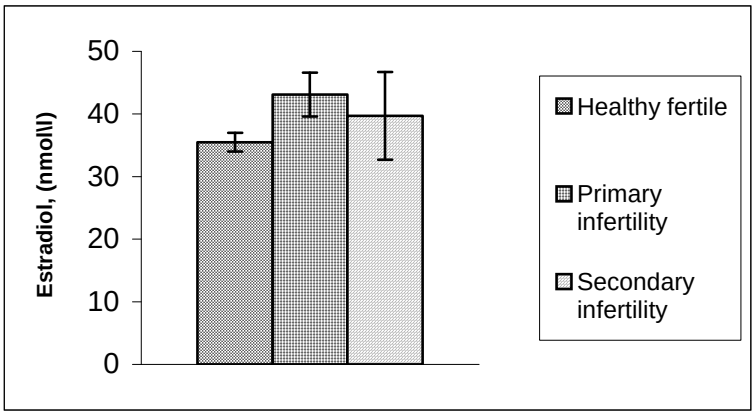

Figure 2: Mean serum estradiol in the three groups; Healthy fertile, primary infertile and secondary infertile males.

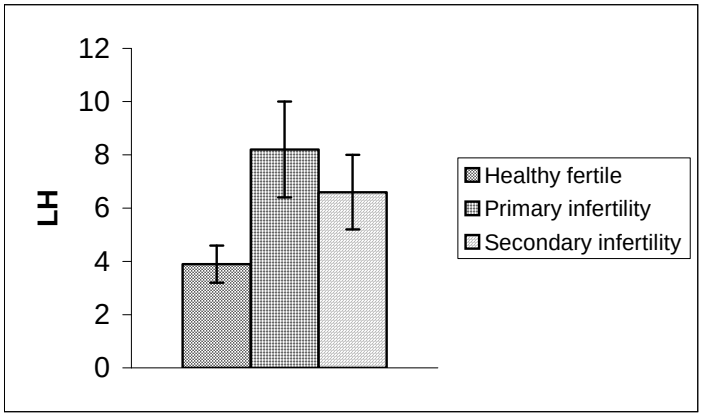

Figure 3: Mean serum LH in the three groups;
healthy fertile, primary infertile and secondary infertile males.

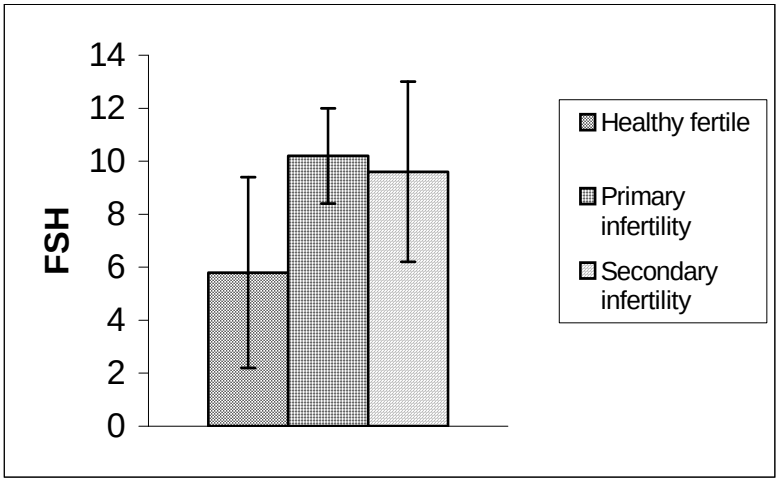

Figure 4: Mean serum FSH in the three groups;
healthy fertile, primary infertile and secondary infertile males.

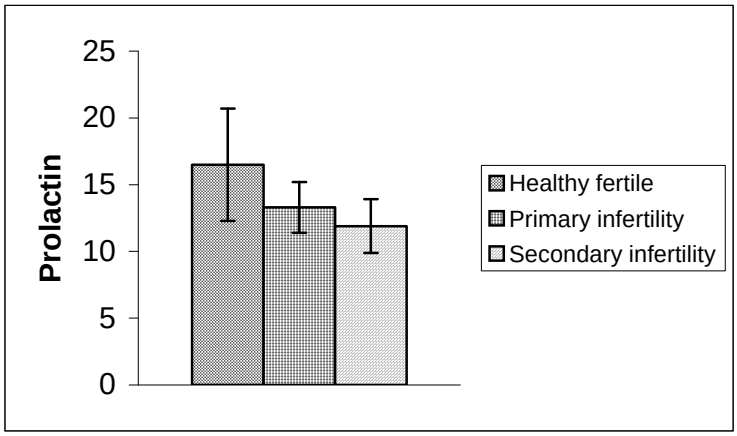

Figure 5: Mean serum PRL in the three groups; healthy fertile, primary infertile and secondary infertile males.

DISCUSSION

The main objective of this work was to study the serum levels of some reproductive hormones; (testosterone, estradiol, LH, FSH, and PRL), in normal fertile and infertile subjects in a trial to access the relative importance of such endocrine factors.

Literatures showed the role of some hormones in male infertility. In a recent study, 257 males were studied, in 3.5% of them, the cause of infertility was defined as pretesticular, and that included hypothalamic and pituitary endocrine causes, [11]. Hyperprolactinaemia was studied as a cause of male infertility in "Ibadan, Nigeria"[14]. Hyperprolactinemia influence spermatogenesis and steroidgenesis in infertile male patients[15]. Both hyperprolactinemia and overproduction of growth hormone and IGF-1 seem to be involved in testicular dysfunction[16]. Prolactinomas may cause male-factor infertility by producing hypogonadism[17].

This study showed non-significant differences between the three groups regarding serum testosterone, estradiol, FSH and PRL, while there was a statistically significant increase between primary infertile and healthy fertile control subjects, ($p < 0.05$) regarding serum LH.

In humans, increased LH secretion occurs in infertility, often concomitant with adrenocortical dysfunction. Chronically elevated serum LH, augmented by enhanced prolactin production induces functional LH receptor expression in adrenal cortex, leading to elevated, LH-dependent, corticosterone production[18]. It is of utmost importance to consider biologically vs. immunologically active LH. The hormone might show

normal or increaded serum levels but rather being not biologically active.

Serum levels of biologically active LH should be used as the marker for a number of pathological conditions including male infertility instead of other many methods like RIA, IRMA, and ELISA, which are employed to a large extent. Such procedures, suffer from the drawback that they depend on the immuno reactive and not the bioactive part of the hormone[19].

REFERENCES

1. **Colbum, Theo, Dianne Dumanoski, and John Peterson Myers (1996):** Our Stolen Future: Are we threatening our fertility, intelligence, and survival? A scientific detective story. New York: Penguin. 316 p.
2. **Jouathan, S., Eli, Y., Paula, A. (1996):** Infertility. *Gynecology, Twelfth Edition*. *Chap*. 27: 915-952.
3. **Holland, M. and White, I., (1980):** Heavy metals and spermatozoa-1-inhibition of the motility and metabolism of spermatozoa by metals related to copper. *Fertile Steril*, 34:483-9.
4. **Benoff, S., Cooper, G., Centola G., Jacob, A., Hurley, I. (2000):** Metal ions and human sperm mannose receptors. *Andrologia*, 32:317-29.
5. **Kanwar, U., Chadha, S., Batla, A., Sanyal, S., Sandlu, R. (2000):** Effect of selected metal ions on the motility and carbolydrate metabolism of ejaculated human spermatozoa. *Indian J Physiol Pharmacol*, 32:195-201.
6. **Telisman, S., Cvitkovic, P., Jurasovic, J., Pizent, A., Gavella, M., Rocic, B. (2000):** Seemen quality and reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc, and copper in men. *Environ Health Perspect*, 108:45-53.
7. **Huang , Y., Tseng ,W., Lin, T. (2001):** In vitro effects of metal ions (Fe^{2+}, Mn^{2+}, Pb^{2+}) on sperm motility and lipid perixodation in human semen. *J Toxicol Environ Health*, 62:259-67.
8. **Gladkova, A., Vasilatii, S., Sidorova, I. (1989):** The role of prolactin in the pathogenesis of male sterility. *Urol Nefrol*, 5:38-41.
9. **Hess, R., Buniek, D., Lee, K., Bahr, J., Taylor, J., Korach K., Lubahn, D. (1997):** A role for oestrogens in the male reproductive system. *Nature*, 390:509-12.
10. **Ramirez, M., Carrera, A., Zambrana, M., (2000):** High incidence of hyperestrogenemia and dyslipidemia in a group of infertile men. *Ginecol obstet mex*, 68:224-9.
11. **Devoto, E., Madariage, M., Lioi, X. (2000):** Causes of male infertility. The contribution of the endocrine factor. *Rev Med Chil*, 128:184-92.
12. **Pavlovich ,C., King, P., Goldstein, M., Schlegel, P., (2001):** Evidence of a treatable endoerinopathy in infertile men. *J Urol*, 165:837-41.
13. **Marija, J. N. (1985):** SPSS/PC+ for IBM PC/XT/AT. SPSS INC. *Chicago. USA.*

14. Adejuwon, C. A., Ilesanmi, A. O. and Ode, E. O. (1999) Hyperprolactinaemia as a cause of male infertility in Ibadan. *West Afr. J. Med*., 18(1): 17-9.

15. Nishimura, K., Matsumiya, K., Tsuboniwa, N., Yamanaka, M., Koga, M., Miura, H., Tsujimura, A.,Uchida, K., Kondoh, N., Kitamura, M. and Okuyama, A. (1999): Bromocriptine for infertile males with mild hyperprolactinemia: hormonal and spermatogenic effects. *Arch. Androl*., 43(3): 207-13.

16. Schuppe, H. C., Neumann, N. J., Schock-Skasa, G., Hoppner, W. and Feldkamp, J. (1999): Secondary infertility as early symptom in a man with multiple endocrine neoplasia-type 1. *Hum. Reprod*., 14(1): 252-4.

17. Biller, B. M. (1999): Hyperprolactinemia. *Int. J. Fertil. Womens Med*., 44(2): 74-7.

18. Kero, J., Poutanen, M., Zhang, F. P., Rahman, N., McNicol, A. M., Nilson, J. H., Keri, R. A. and Huhtaniemi, I. T. (2000): Elevated luteinizing hormone induces expression of its receptor and promotes steroidogenesis in the adrenal cortex. *J. Clin. Invest*., 105(5): 633-41.

19. Stadler, U. Rovan, E. Aulitzky, W. Frick, J. Adam, H. and Kalla, N., (1989): Bioassay for determination of human serum luteinizing hormone (LH): a routine *Andrologia*;21(6):580-3.

ملخص باللغة العربية

يعتبر عقم الرجال مسؤلا عن ٣٥ % من حالات عدم الأنجاب فى الزيجات. وهذه الدراسة معنية بالأهمية النسبية للعوامل المتعلقة بالغدد الجنسية فى الذكور العقيمين. فمن المعروف أن ما يسمى بمدمرات الغدد التناسلية يمكنها أن تضربكافة مكونات الحياه البرية والبحرية وبصحة الأنسان عن طريق التدخل فى تأثيرات الهرمونات التناسلية وغيرها من الهرمونات. ومن العوامل الأخرى التى تسبب عقم الذكور تعاطى الكحول ونقص الفيتامينات والتلوث بالمعادن الثقيلة.

أشتملت هذه الدراسة على ٦٣ من الذكور من ثلاثة مجموعات : ذكور يتمتعون بالخصوبة وذكور عقيمين لأسباب أولية وآخرين عقيمين لأسباب ثانوية وتمت قياسات أهم الهرمونات التناسلية فى أمصال دماءهم وهى هرمونات "تستوستيرون" و"أستراديول" و"ألفا أتش" و "ألفا أس أتش" و"البرولاكتين".

وقد ظهر فرق أحصائى معنوى فى تركيزات هرمون "ألفا أتش" بين الذكور الطبيعيون وبين الذكور الذين يعانون من العقم لأسباب أولية.

وعلى ذلك فأنه من الواجب أجراء تقدير لهذا الهرمون الى جانب تحليلات السائل المنوى الأخرى فى حالات تشخيص عقم الذكور . بل من اللازم معرفة صورة كاملة عن الهرمونات التناسية بما فيها الصور النشطة بيولوجيا من هذه الهرمونات.