

Follicular Fluid Brain Derived Neurotrophic Factor (BDNF) in unexplained infertility¹Ali Farid Mohamed Ali and Laila Ali¹Heliopolis Research Center, Cairo Egypt²Department of obstetrics and Gynecology, Faculty of Medicine, Ain Shams University Cairo Egyptelshayb1950@yahoo.com

Abstract: Unexplained infertility is diagnosed where routine investigations including semen analysis, tubal evaluation and tests for ovulation yield normal results. It has been recognized that neurotrophins known for their role in neuronal survival involved in the maturation of the ovarian follicle. These neurotrophins include nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin 4/5 (NT- 4/5), and neurotrophin 3 (NT-3) have been identified in the mammalian ovary. The aim of this work is to elucidate the role of BDNF in follicular fluid from unexplained infertility patient. Thirty patients complaining from unexplained infertility and 30 patients as control were subjected to laparoscopy. Group I for evaluation and confirmation of unexplained infertility. Group II for laparoscopic tubal sterilization. BDNF assay: follicular fluid BDNF were determined by enzyme linked immunosorbant assay. According to manufacturer protocol, follicular fluid BDNF was taken during laparoscopy done for tubal sterilization at mid-luteal phase, day 22 of menstrual cycle. There was no statistical difference between both groups regarding age and BMI but There was a statistical difference between the 2 groups regarding the follicular fluid BDNF ($P < 0.05$). BDNF is reduced in ovarian follicular fluid in unexplained infertility and this will open a new era in the treatment of unexplained infertility.

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Key words: Unexplained infertility, laparoscopy BDNF.

1. Introduction:

Unexplained infertility is diagnosed where routine investigations including semen analysis, tubal evaluation and tests for ovulation yield normal results. Most clinics now report incidences of 20-30% failure of routine tests to detect any obvious contributory factors has led clinicians to speculate about numerous factors contributing to a diagnosis of unexplained infertility^[1,2].

It has been recognized that neurotrophins known for their role in neuronal survival involved in the maturation of the ovarian follicle. These neurotrophins include nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), neurotrophin 4/5 (NT- 4/5), and neurotrophin 3 (NT-3) have been identified in the mammalian ovary.^[3]

Aim of work

The aim of this work is to elucidate the role of BDNF in follicular fluid from unexplained infertility patient.

2. Material and Method:

Thirty patients complaining from unexplained infertility and 30 patients as control were subjected to laparoscopy. Group I for evaluation and confirmation of unexplained infertility. Group II for laparoscopic tubal sterilization.

Follicular fluid study:

Follicular aspiration was performed when one or more follicles measuring greater than 17 mm diameter found during laparoscopy. Fluid was centrifuged at 1000 rpm for 10 minutes to remove the cellular component. The clear supernatant fraction was stored at -80 °C for assay of BDNF.

BDNF assay:

Follicular fluid BDNF were determined by enzyme linked immunosorbant assay. According to manufacturer protocol, follicular fluid BDNF was taken during laparoscopy done for tubal sterilization at mid-luteal phase, day 22 of menstrual cycle⁴.

Statistical analysis:

Follicular fluid BDNF are expressed in pg/ml as mean \pm SD. Statistical analysis of significance between unexplained infertility group (group I) and fertility group (group II) was calculated by t test, A P value of < 0.05 is considered statistically significant.

Ethics:

The study was performed in accordance with the guide lines in the Declaration of Helsinki and has been formally approved by the local ethical committee. Informed consent was obtained from all subjects.

3. Results:

Follicular fluid BDNF assay was done for 30 patients complaining of unexplained infertility and 30 patient as control were subjected to laparoscopy. Group 1 for evaluation and confirmation of unexplained infertility and Group 2 for laparoscopic tubal sterilization.

The results are summarized in table 1

Table (1): Represents the demographic characteristics of group I and group II, there was no statistical difference between both groups regarding age and BMI but There was a statistical difference between the 2 groups regarding the follicular fluid BDNF ($P < 0.05$).

Table (1): Represents the patients characteristics and follicular fluid BDNF in unexplained infertility group and control group.

Characteristic	Group I No. = 30	Group II No. = 30
Age	35.6±3.5	35.1±2.9
BMI	22.11±1.99	22.88±2.13
Duration of unexplained infertility	10.3±2.1	--
Previous gynecological operation	2 D&C	4 CS 1 ovarian cystectomy
follicular fluid BDNF	633.22±316.66	937.22±305.41

4. Discussion:

The world health organization estimates that one in six couples experience a delay in conception. Therefore unexplained infertility appears to represent either the lower extreme of the normal distribution of fertility or it arises from a defect in fecundity which cannot be detected by routine infertility evaluation¹.

Reports suggest subtle hormonal and endometrial defects in this condition. No report in the literature dealt with BDNF in follicular fluid in an unexplained infertility.

In this work we found statistically significant decrease in follicular fluid BDNF in unexplained group compared to control group (633.22±316.66 and 937.22±305.41 respectively) Table 1.

Brain derived neurotrophic factor is one neurotrophin, a family of soluble polypeptide growth factors³, it's role is known in the neuronal survival and neural outgrowth, these neurotrophins are found in a variety of non neuronal systems (cardiovascular, immune, endocrinal and reproductive systems).

BDNF has been identified in the mammalian ovary and have been shown to play a role in ovulation, steroid secretion and follicular development in the rodent⁵. There was evidence for the secretion of neurotrophins and the presence of their receptors in human cumulus cells, and that neurotrophin BDNF are produced within the follicle (specially by granulosa cells), the location of the neurotrophins and their receptors suggest both an autocrine (granulosa) and a paracrine (granulosa – oocyte and granulosa – granulosa function)^{6,7}.

It was demonstrated the role of BDNF in promoting first polar body extrusion of oocytes via

the presence of the Tr β receptors⁸ and the role in promoting the development of mouse zygote to blastocysts, this finding supports the concept that ovarian BDNF is vital to nuclear and cytoplasmic maturation of the mouse oocyte allowing it to progress to the blastocyst stage⁸.

It was found that BDNF may be involved in the cytoplasmic events of bovine oocyte maturation but that BDNF involvement in nuclear maturation was unlikely^{9,10}. Investigators had demonstrated the presence of BDNF in preovulatory follicles of normally cycling women^{6,10}. Also they found that BDNF production by granulosa cells *in vitro* can be stimulated by LH/HCG11, 12.

Collectively all these data represent the importance of BDNF and its role in oocyte development, meanwhile explore some of causes of unexplained infertility. So if we can reach precisely to the role of BDNF in the dynamic of oocyte development, this will help us to open a new era in infertility treatment.

Conclusion:

BDNF is reduced in ovarian follicular fluid in unexplained infertility and this will open a new era in the treatment of unexplained infertility.

Corresponding author

Ali Farid Mohamed Ali, MD

Professor, Exchairman of Obstetrics and gynecology Faculty of Medicine, Ain Shams University, Head of Heliopolis research center 13 Elmontazh street, Sednawy building, Heliopolis, Cairo, Egypt.
elshayb1950@yahoo.com

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