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ORIGINAL ARTICLE

The role of social support for hormonal regulation for couples treated due to infertility

Rola wsparcia społecznego w regulacji hormonalnej par leczonych z powodu niepłodności

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Abstract

Introduction. From a medical point of view, hormonal balance is the most important factor in treating infertility. On the other hand, psychologists argue that the most effective way to correct hormonal imbalances is to focus on psychological stress. Therefore, this article draws attention to the potential effects of stress-reducing supportive social interactions on progesterone levels in women undergoing infertility treatment.

Materials and Method. Fifty-one heterosexual couples were randomly assigned to participate either in a group support session (experimental group) or to watch a non-emotional film (control group). Progesterone concentration was determined by solid-phase enzyme-linked immunosorbent assay (ELISA) in saliva samples collected before and after the experiment. Information on the history of infertility treatment was also collected and evaluated.

Results. The study shows a change (increase) in salivary progesterone concentration in the vast majority of women who participated in supportive social interactions, compared to the control group, where progesterone levels remained unchanged or decreased.

Conclusions There is a clear link between supportive social interaction and progesterone secretion. This may explain the positive health effects of social interactions in infertility couples treatment. The research results open a discussion on the part of social support in hormone regulation and indicate the need for further and in-depth analysis of this phenomenon.

Key words

in vitro, infertility, social support

Streszczenie

Wprowadzenie i cel pracy. Równowaga hormonalna jest z medycznego punktu widzenia najważniejszym czynnikiem w leczeniu niepłodności. Przy czym psychologowie są zgodni co do tego, że jedną z najskuteczniejszych metod na przywrócenie równowagi hormonalnej jest skupienie się na stresie psychicznym. W niniejszej pracy zwrócono uwagę na potencjalny wpływ wspierających interakcji społecznych, które – jak wcześniej wykazaliśmy – redukują stres, na poziom progesteronu u kobiet leczonych z powodu niepłodności.

Materiał i metody. Pięćdziesiąt jeden heteroseksualnych par leczonych z powodu niepłodności zostało losowo przydzielonych do udziału w grupowej sesji wsparcia (grupa eksperymentalna) lub do grupy kontrolnej, której wyświetlono obojętny emocjonalnie film. Stężenie progesteronu oznaczono za pomocą testu immunoenzymatycznego (ELISA) w próbkach śliny pobranych od kobiet przed i po eksperymencie. Zebrano również i przeanalizowano informacje dotyczące historii leczenia niepłodności pacjentów.

Wyniki. Odbycie wspierającej interakcji społecznej spowodowało wzrost stężenia progesteronu w ślinie u zdecydowanej większości kobiet. Natomiast w grupie kontrolnej poziom progesteronu pozostał na tym samym poziomie lub spadł.

Wnioski. Uzyskane wyniki wskazują na istnienie wyraźnego związku między odbyciem wspierającej interakcji społecznej a poziomem progesteronu u kobiet. Wyjaśniają ponadto, po części, pozytywny wpływ zdrowotny interakcji społecznych na leczenie niepłodności. Praca otwiera dyskusję na temat roli wsparcia społecznego w regulacji hormonalnej i wskazuje na potrzebę dalszej pogłębionej analizy tego zjawiska.

Słowa kluczowe

wsparcie społeczne, *in vitro*, niepłodność

INTRODUCTION

The strain of infertility and the fear of a childless life are an enormous challenge for a couple. Despite the widely documented psychological difficulties associated with the use of assisted reproductive technology (ART), couples struggling with difficulties in conceiving a child are increasingly turning to these methods of infertility treatment [1]. The high success rates of infertility treatment using the ART methods also support such a decision. The infertility crisis is characterized by the inability to use resources that were normally helpful in coping with stress [2, 3]. Success in coping with this

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crisis depends on the people who provide social support [4]. The various aspects of negative social evaluation of assisted reproductive technology may reinforce the sense of loss, social maladjustment, and shame that often accompanies infertility [4–7]. Reproductive success and the psychosocial consequences of infertility treatment are closely related to the social support that couples receive [8]. Perceived social support may influence not only infertility treatment but also continued family functioning [9].

Studies suggest that social support not only reduces the level of stress experienced, but may also reduce the negative effects of stress on reproductive success [10, 11]. Stress is not only an emotional state, but also a biological process that affects most physiological processes in the human body. Infertility-related stress arises in the personal and marital domains [12]. Previous studies have shown that women describe experiencing greater overall stress than men, and higher specific stress related to social and sexual concerns and the desire for parenthood [13, 14]. Social, sexual, and relationship concerns related to infertility are effective predictors of depression and marital dissatisfaction [15,16]. Research has found that infertility-related stress predicts treatment outcome one year after treatment initiation in both men and women. Fertility stress has been associated with poorer treatment outcome in both genders [12].

Stress also has a negative impact on fertility treatment [17], affecting both reproductive potential (ovulation) and the course of pregnancy – severe stress and the hormones it releases can pose a risk to the developing foetus and lead to miscarriage [18–20]. Chronic stress also affects sexual activity in women, i.e. sexual desire and genital arousal [21, 22]. During the menstrual cycle, several hormones interact in a complex during ovulation and menstruation. One of the most important hormones is progesterone. Studies indicate the importance of progesterone in the treatment of infertility and its relationship with the psychological well-being of patients [23]. Its concentration is determined to control ovulation and the course of pregnancy, or to determine the causes of conception problems. Progesterone is responsible for preparing the female body for the fertilization process and the continued maintenance of pregnancy. Progesterone is produced by the ovaries not only in the luteal phase but also in the follicular phase of the menstrual cycle [24]. Progesterone is absolutely necessary for the successful implantation of the embryo and maintenance of pregnancy. After fertilization, it triggers changes in the endometrium that allow successful implantation of the fertilized egg. Therefore, insufficient levels of this hormone lead to infertility [25]. Progesterone levels increase in response to stimulation of the hypothalamic-pituitary-adrenal (HPA) axis [10]. Among the various mechanisms that activate the HPA axis, stress appears to be the most important. Progesterone levels have been shown to increase in response to a stressor in laboratory animals [26]. Therefore, it is not surprising that glucocorticoids (cortisol) and progesterone should remain in precise balance during both pregnancy and the childbearing period. Even a minor disturbance of this balance can have significant consequences for the course of pregnancy and foetal development [27]. Of particular importance is its function in the regulation of sexual behaviour and libido. A rapid drop in progesterone concentration after delivery is currently considered to be one of the causes of postpartum depression [28].

Understanding the correlation between social support and hormone levels and neuroendocrine mechanisms of stress management in women struggling with infertility may be useful for treatment.

OBJECTIVE

The aim of this study was to investigate how supportive social interactions involving the sharing of experiences, psychological needs, or personal beliefs affect women›s progesterone levels. The proposed research procedure was intended to confirm the hypothesis that supportive social interactions positively affect hormonal changes that contribute to the efficacy of infertility therapy with ART. Therefore, the current study predicts that participation in supportive social interaction increases progesterone levels in women.

MATERIALS AND METHOD

The participants comprised a systematic sample of 51 women from infertile couples recruited by a gynaecologist. Infertility is defined by the WHO as a condition of the male or female reproductive system characterized by failure to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse [29]. All participants reported being in good health and had no history of mental disorders. Approval to perform the study was obtained from the Bioethics Committee of the Nicolaus Copernicus University in Toruń? Casimir the Great University in Bydgoszcz? before participants were recruited. Participation was anonymous and voluntary. Informed consent was obtained from all volunteers before the start of the study and the objective of the study was described as the psychological aspects of infertility.

The age of the participants ranged from 23–40 years, mean age – 31 years (SD =3.55). The majority of women were eligible for their first *in vitro* procedure (40), and less than half (17) of them underwent the insemination procedure. Full information on descriptive statistics is presented in Table 1. Data from 3 of the 51 women whose saliva was discarded because of visible blood contamination or whose salivary progesterone levels exceeded the sensitivity of the kit used, were excluded from the study.

Table 1. Descriptive statistics for quantitative variables in the studied sample

Variable (n=48)	Min	Max	M	SD
Age (years)	23	40	31	3.55
Length of relationship (years)	3	20	9	4.35
Time since diagnosis of infertility (months)	6	180	37	34
After how many *in vitro* procedures	3	0	0.7	0.74
After how many inseminations	4	0	0.9	1.42

Source: own data

The study was conducted in an experimental model in 2 independent groups. The women were randomly divided into an experimental group (26 participants) and a control group (25 participants). In the first phase of the study procedure, a saliva sample was collected from all

women (from both the experimental and control groups) to determine progesterone levels. In the second phase of the experiment (immediately after the samples were taken from all volunteer participants), participants in the control group watched a 3 hour video on human embryology (non-emotional factor). At the same time, the experimental group participated in a supportive social interaction, defined by the author as a group interaction involving talking or listening in an informal and non-judgemental environment, leading to the reduction of stress. For more details see [30]. The interaction was conducted in groups of 10–12 participants. The psychologist who moderated the discussion did not participate in the conversation, but asked additional questions about the participants› feelings about infertility treatment. The participants spoke individually and spontaneously. The interaction was based on the needs of the participating couples. The supportive social interaction lasted 3–5 hours, depending on the participants› needs and willingness. Participants were encouraged but not forced to speak. In all 5 groups, all participants spoke with varying frequency.

After the introduction of the experimental and control condition, a second collection of saliva samples was performed (third phase). Demographic data and medical history related to fertility were also collected. After the experiment, the couples were interviewed and fully informed about the aim of the study.

Immunoenzimatic assay. Saliva was collected from the participants into pure polypropylene tubes. Three separate samples were collected before and after the introduction of the experimental factor. The saliva samples were sent to the laboratory in a cool box (2–8°C). Progesterone levels in the samples were determined by solid-phase enzyme-linked immunosorbent assay (ELISA) from Demeditec Diagnostics GmbH (Kiel, Germany; Cat. No. DES6633) with a detection limit of 0.1 ng/ml. Colourimetric changes were detected using a Synergy HT Multi-Mode Microplate Reader (BioTek Instruments, USA). All samples were analyzed individually and in duplicate according to the manufacturer›s instructions. Because food may contain significant amounts of steroid hormones, samples were preferably collected during fasting. Samples with visible blood contamination were discarded. Samples with progesterone levels that exceeded the sensitivity of the kit were also discarded. Appropriate control samples were examined to ensure the correct performance of each kit used in the experiment as a quality control. The determination of progesterone in saliva combines a highly sensitive technique with non-invasive sampling and represents the concentration of metabolically active free progesterone.

All procedures were approved by the Bioethics Committee of Nicolaus Copernicus University in Toruń functioning at the Collegium Medicum in Bydgoszcz (Permission No. KB 343/2018).

RESULTS

Because progesterone levels change according to the phase of the menstrual cycle, the concentration of this hormone were measured for each participant before and after the introduction of the experimental or control condition. The values are therefore expressed as delta progesterone levels. False positives (values strongly above the expected value) were excluded. Of the 20 women in the control group, progesterone salivary concentration remained unchanged in 6 women, increased significantly in 6, and decreased in 11 (Fig. 2B). At the same time, progesterone concentration increased in 17 women in the experimental group, decreased in 5, and remained unchanged in 3 (Fig. 1B). This clearly indicates that supportive social interaction led to an increase in progesterone concentration in the vast majority of cases.

The observed changes in salivary progesterone concentration accompanying social interaction in the experimental group were weakly positively correlated with age (r = 0.089), relationship duration (r = 0.095), time since infertility diagnosis (r = 0.097), number of IVF procedures performed (r = 0.148), and number of inseminations performed (r = 0.124) (Fig. 3A). In contrast, in the control group, delta progesterone levels were negatively correlated with age (r = -0.229) and relationship duration (r = -0.133) of the participants (Fig. 3). Accordingly, a weak positive correlation was found with other variables: time since infertility diagnosis (r = 0.023), number of IVF procedures performed (r = 0.078), and number of inseminations performed (r = 0.1632) (Fig. 3).

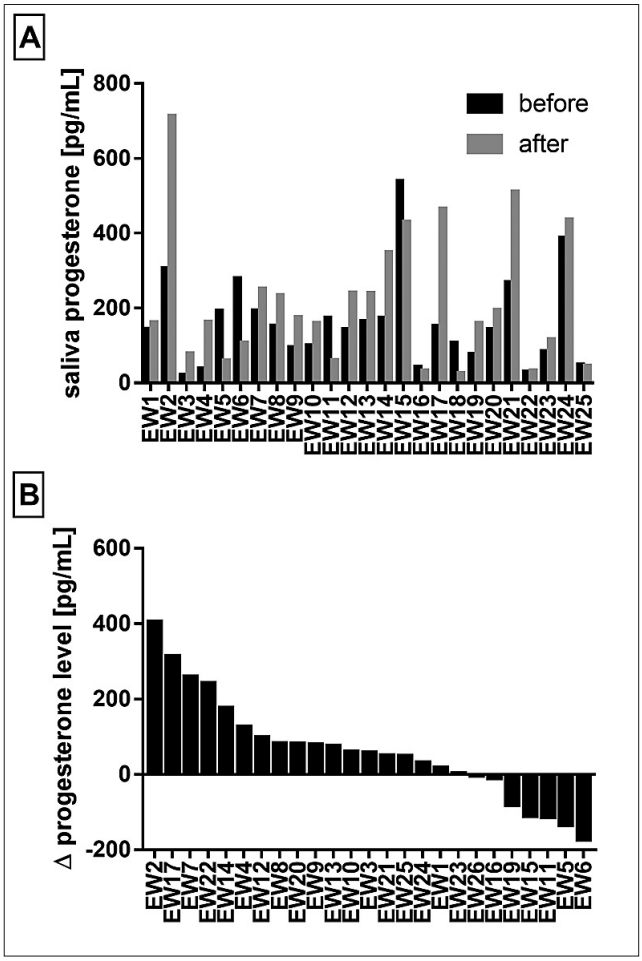

Figure 1. Salivary progesterone levels of women in the experimental group. Panel A shows salivary progesterone levels of women from the experimental group before (black bars) and after (grey bars) supportive social interaction. Numbers EW1–25 denote individual women in a group. Panel B shows the changes in progesterone concentration in women, calculated as the difference between progesterone levels before and after the introduction of the experimental conditions. Subjects were ranked by decreasing delta progesterone levels

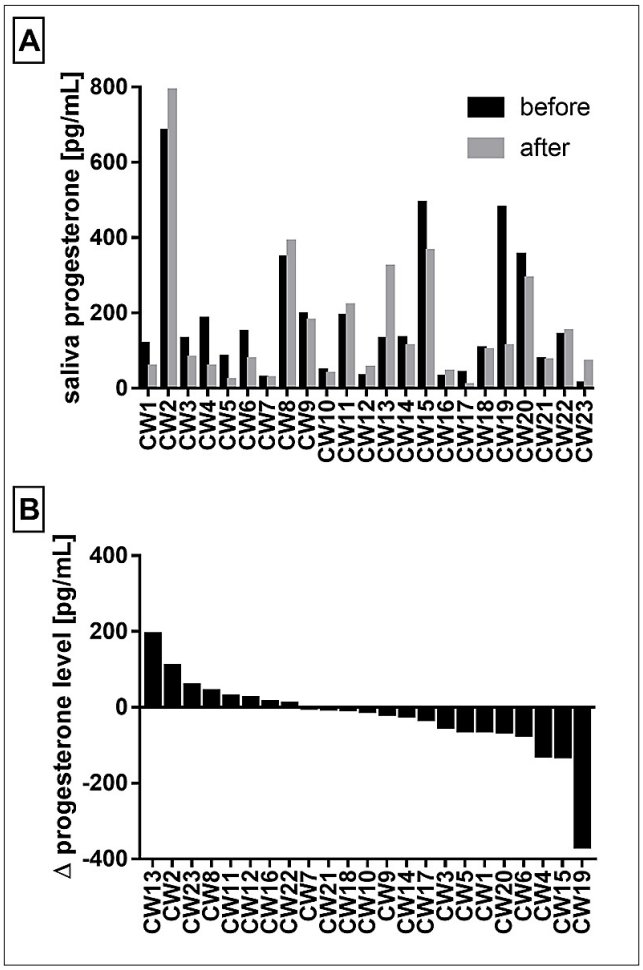

Figure 2. Salivary progesterone levels in women from the control group.
Panel A shows salivary progesterone levels in women from the control group before (black bars) and after (grey bars) introduction of the non-emotional control factor. Numbers CW1–23 denote individual women in a group. Panel B shows the changes in progesterone concentration in women, calculated as the difference between progesterone levels before and after the introduction of the control conditions. Volunteers were ranked by decreasing delta progesterone levels

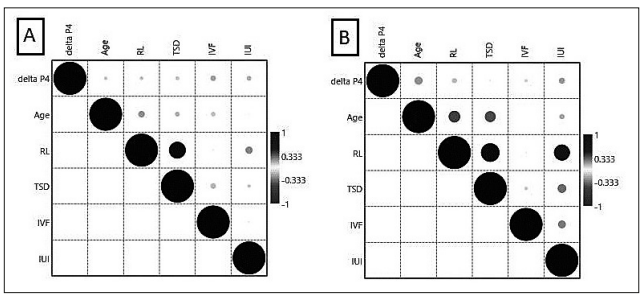

Figure 3. Correlation matrix.
The correlation matrix shows the relationship between the changes in salivary progesterone (delta P4) in the experimental group (panel A) and in the control group (panel B).
Variables: Age – participant's age; RL – relationship duration; TSD – time since infertility diagnosis; IVF – number of IVF procedures performed; IUI – number of insemination procedures performed.
Source: data presented in Table 2

DISCUSSION

The study examined changes in progesterone levels in women who participated in supportive social interactions during psychological intervention in the treatment of infertile patients. It shows a change (increase) in progesterone levels

Table 2. Table shows the Pearson correlation coefficients between the different variables shown in Figure 3

Pearson correlation coefficients calculated for data shown in Fig 3A						
	delta P4	Age	RL	TSD	IFV	IUI
delta P4	X	0.089	0.095	0.097	0.148	0.124
Age		X	0.179	0.123	-0.119	-0.018
RL			X	0.500	-0.024	0.201
TSD				X	-0.146	0.089
IFV					X	0.031
IUI						X

Pearson correlation coefficients calculated for data shown in Fig 3B						
	delta P4	Age	RL	TSD	IFV	IUI
delta P4	X	-0.229	-0.133	0.028	0.078	0.163
Age		X	0.342	0.318	-0.017	0.137
RL			X	0.554	-0.029	0.475
TSD				X	0.086	0.248
IFV					X	0.219
IUI						X

Delta P4 – changes in saliva progesterone.; Age – age of participant; RL – relationship length; TSD – Time since the diagnosis of infertility; IVF – number of IVF procedures performed; IUI – number of insemination procedures performed

in the vast majority of women who participated in supportive social interactions. The results of the study open a discussion on the role of social support in the hormonal regulation of infertile women and show the need for an in-depth analysis of this phenomenon.

Scientific studies prove that prolonged exposure to stressors leads to serious disorders [31], including ovarian dysfunction [20]. Chronic stress can lead to the production of the so-called aggressive mucus, which immobilizes spermatozoa, and to a decrease in the level of progesterone which is necessary for embryo implantation. Chronic stress can disrupt normal ovulation and menstrual flow, which negatively affects the chance of becoming pregnant [32]. The protective mechanism triggered by stress signalizes that the body is not yet ready for pregnancy, resulting in a temporary inability to conceive a baby.

The role of progesterone in the menstrual cycle and early pregnancy has been studied for many years. In the era of the development of assisted reproductive technology, more questions have arisen about progesterone. Considering the role of progesterone in fertilization, more studies should focus on its role in the treatment of infertile couples. Combining the two fields of psychology and medicine also involves behavioral determinants and their effects on changes in the endocrine system.

The finding of higher levels of progesterone in the saliva of participants who experienced supportive social interactions could be due to at least 2 mechanisms. First, progesterone is an indicator of stress response activation [33], and is a precursor in cortisol biosynthesis. It can be assumed that the higher the level of circulating progesterone, the more cortisol is synthesized [34]. If this were the case, one might also expect that progesterone and cortisol would increase simultaneously in the experimental group, but this was not the case (data not published). The second possibility is that progesterone is part of the neuroendocrine basis of social bonding, and increases in response to manipulations of social proximity [35, 36].

The results obtained are of great importance and need to be shared with a wider audience. The study contributes to the understanding of the importance of social support in the success of infertility treatment. Identifying non-professionals and informal support groups (friends, family members, other infertile couples) as important sources of support contributes to the discussion on the possibility of improving the quality of life of infertile couples.

CONCLUSIONS

The use of biomarkers in this study falls within the trend of growing interest in human behavioural endocrinology. The relationship between stress, social interactions, HPA axis activation, cortisol, and progesterone release is still not fully understood. Since the relationships between stress response, progesterone, and neuro-hormonal secretion may explain the positive health effects of social interactions and play a positive role in the treatment of couples with infertility, it is necessary to investigate these relationships to further define their interactions.

Limitations of the study. Some limitations should be mentioned. Unfortunately, no information was collected on the day of the menstrual cycle the women participating in the study were experiencing. The impact of the influence of menstrual phase may be significant. Therefore, when planning future studies to assess progesterone levels and other hormones in women participating in supportive social interactions, this factor will be controlled, as well as the pharmacologic (hormonal) supplementation.

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