Effect of Progressive Muscle Relaxation Technique on Stress, Anxiety & Ovulatory Predictors Among Infertile Women Undergoing Ovulatory Induction.

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Abstract

Background: Infertility represents a pressing global health issue, exerting considerable repercussions on both the affected individuals and the broader societal context. Infertility frequently coexists with elevated stress and anxiety, resulting in a complex burden for individuals undergoing reproductive treatments. The Progressive Muscle Relaxation (PMR) method is one of the many interventions intended to address the psychological elements of infertility. Objective: To determine the effect of progressive muscle relaxation technique on stress, anxiety, & ovulatory predictors among infertile women undergoing ovulatory induction. **Setting:** The study was carried out at the infertility clinic in El-Shatby Maternity University Hospital, affiliated to Alexandria University. Subjects: A convenience sample of 80 infertile women attending the previously mentioned setting. Tools: four tools were used. Infertile women's socio-demographic and clinical data structured interview schedule & Fertility problem inventory (FPI) questionnaire & Spielberger State-Trait Anxiety Inventory (STAI) questionnaire & Ovulatory predictors assessment sheet. Results: The study showed a statistically significant difference between the study and control groups regarding the stress level at days 2, 9, & 11 after intervention

 $(p = \langle 1.010, \langle 1.001, \langle 1.010 \rangle)$, respectively. Moreover, a statistically significant difference between the study and control groups regarding the stress level at days 2, 9, & 11 after intervention (p = <1.014, <1.001, <1.001), respectively. Additionally, a statistically significant difference was observed among the study and control groups regarding E2 level at days 2, 9, and 11 from induction, where (p = 0.039* and p =0.001* & p < 0.001*) in favor of the study group. Finally, a statistically significant difference was observed among the study and control groups regarding the diameter of follicles at days 9 and 11 from induction, where $(p < 0.001^*)$ and $p < 0.001^*)$, respectively, in favor of the study group. Conclusion: Based on the findings of the present study, it can be concluded that the progressive muscle relaxation technique significantly reduced both stress and anxiety levels among infertile women who participated in the intervention. Additionally, this technique had a notable positive effect on improving the ovulation rate in this population So, the study aims and hypotheses were achieved within the framework of the present study. **Recommendations:** The progressive muscle relaxation technique should be offered as a standard component of care for women undergoing infertility treatment. This integration can help address the psychological aspects of infertility and improve overall treatment outcomes.

Keywords: Progressive muscle relaxation technique, Anxiety, Stress, Ovulatory predictors, Infertile women, Ovulatory induction.

Introduction

Motherhood is an esteemed endowment from the divine. The concept of fertility is profoundly venerated across numerous cultures, and the desire for progeny constitutes one of the most fundamental experiences human drives. The pregnancy motherhood represent and significant developmental milestones for women, which are prominently highlighted within our societal framework. When endeavors to conceive are unsuccessful, this can result in a profoundly distressing emotional experience (Taebi et al., 2021). Offspring serve as essential components for preserving familial connections facilitating the bridging of generational divides. The act of procreation is regarded as a testament to one's masculinity or femininity; it is an emblem of fecundity, and the offspring are viewed as invaluable successors tasked with perpetuating the family lineage. Consequently, infertility is perceived as a societal stigma, which exerts a detrimental impact on women's overall health (Radhi et al., 2019).

Generally speaking, infertility is defined as the inability to get pregnant after 12 months or more of consistent, unprotected sexual activity, assuming that no other factors, such as lactation or postpartum amenorrhea, are at play. Approximately 15% of couples of reproductive ages worldwide are impacted by infertility. The incidence of secondary infertility is estimated to be around 35%, whereas the prevalence of primary infertility fluctuates between 1% and 8%. Statistically, one in every eight couples encounters challenges in achieving pregnancy (Jaber et al., 2023).

Infertility can be classified into three distinct categories: primary, secondary, and unexplained infertility. Primary infertility pertains to couples who have never successfully conceived. Conversely, the inability to conceive after a prior successful pregnancy that cannot be explained is known as secondary infertility. When all currently known diagnostic tools have been

used, and no visible problem has been found to explain infertility, infertility results. The likelihood of conception is contingent upon the duration of sexual exposure, the coitus frequency, and the age of couple (Pelzman & Sandlow, 2024).

In order to achieve a successful pregnancy, both male and female partners must meet numerous prerequisites. Firstly, the female prerequisites include: the presence of normal and healthy reproductive organs; generation of a viable ovum from the ovarian tissue; the transit of the ovum into the fallopian tube within a limited time frame; fertilization of the ovum within the ampulla, alongside the subsequent implantation of the fertilized ovum and its development in a conducive location and stage within the endometrium (Bhattacharya et al., 2024).

Secondly, male prerequisites, such as the presence of spermatozoa or effective spermatogenesis, must be ensured in adequate quantity and quality (ranging from 200 to 400 million sperm per 2 to 4 ml); accessory glands must secrete substances that are supportive of sperm viability to constitute semen; the ductal system leading to the urethra must be unobstructed; ejaculation must result in the deposition of semen in proximity to the cervix, and coitus must occur at or in close temporal proximity to the ovulation period (Agarwal et al., 2021).

Infertile women often endure significant emotional distress as a consequence of their diagnosis. The predominant emotional distress associated infertility with encompasses stress and anxiety. Stress represents a multifaceted phenomenon distinguished by cognitive evaluations, physiological reactions, and behavioral predispositions that emerge in response to a perceived discord between situational demands and the requisite resources for effective coping mechanisms. Stressors are particular types of stimuli or events that impose significant demands on individuals, often surpassing their available resources (Rathi et al., 2024).

Conversely, anxiety represents psychological condition characterized by a pervasive sense of apprehension and concern that is often diffuse and unfocused, manifesting as an exaggerated reaction to circumstances that are subjectively interpreted as threatening. A multitude of psychological negative social consequences is associated with infertility, encompassing emotions such as frustration, depression, hopelessness, guilt, a decline in self-esteem, and an overarching sense of worthlessness in existence. On a societal scale, infertility remains correlated with social stigma across four prominent cultural contexts)(Sahraian et al., 2024). Couples encountering reproductive difficulties frequently violate established social norms and conventions. In specific cultural settings, infertility may lead to separation or divorce, social ostracism, and a perceived loss of autonomy, ultimately compromising their overall quality of life (Malhotra et al., 2024).

Relaxation techniques are essential for effectively managing stress, facilitate recuperating physiological and psychological states. Such techniques foster a sense of equilibrium, contribute to the establishment of optimal living conditions, and have been empirically validated to adverse emotional responses mitigate various medical populations among (Aulakh et al., 2024).

Within this framework, Progressive Muscle Relaxation (PMR) entails the intentional stretching and subsequent relaxation of the body's principal muscle groups, commencing with the hands and concluding with the feet. A systematic application of muscle tension administered for 5-7 seconds, and a relaxation phase lasts 10–12 seconds. Additionally, deep breathing techniques may be employed and sustained throughout the muscle tension phase of the intervention, followed by an exhalation during the

relaxation phase. Consequently, the individual will derive significant benefits from implementing deep breathing exercises (Aulakh et al., 2024).

Last but not least, maternity and psychiatric nurses play a critical role in assisting infertile patients who need precise treatment, counseling, psychological support, and health education. Emphasis on medical procedures and surgery, supporting treatment plans to carry out couples' psychological rehabilitation, and the role of the doctor and nurse should be to not only keep an eye on the patient's health but also to offer them emotional support (Imrie et al., 2023).

Aim of the Study

To determine the effect of progressive muscle relaxation technique on stress, anxiety & and ovulatory predictors among infertile women undergoing ovulatory induction.

Research hypothesis:

- H1: Infertile women undergoing ovulatory induction who practice progressive muscle relaxation technique exhibit less stress level than those who do not practice it.
- H2: Infertile women undergoing ovulatory induction who practice progressive muscle relaxation technique exhibit less anxiety level than those who do not practice it.
- H3: Infertile women undergoing ovulatory induction who practice progressive muscle relaxation technique exhibit normal ovulatory predictors than those who do not practice it.

Materials and Method

Materials

Design: A quasi-experimental research design was applied in the current research.

Setting: Our current study was conducted at the infertility clinic of El-Shatby Maternity University Hospital,

which is affiliated with Alexandria University. The aforementioned setting was selected for the study because it has a good turnover rate and because the hospital treats women from various socioeconomic backgrounds from adjacent governorates.

Subjects:

A convenience sample comprising 80 infertile women was recruited from the aforementioned facility, adhering to the following inclusion criteria: women diagnosed with primary infertility, aged between 25 and 35 years, currently undergoing ovulatory induction, experiencing moderate to high levels of stress, suffering from moderate to severe anxiety levels, and devoid of other medical conditions. The determination of the sample size was conducted utilizing a power analysis (Epi-info7) program predicated on the following parameters: a population size of 1200 every three months with an anticipated prevalence of 50%, an acceptable margin of error of 5%, and a confidence level of 95%, culminating in a minimal sample size of 79 women. Ultimately, the final sample encompassed 80 women experiencing infertility.

Tools: four tools were used to collect the necessary data:

Tool one: Infertile women's sociodemographic and clinical data structured interview schedule:

The researcher developed an instrument comprising three principal components: Part (I): Part (1): Women's socio-demographic characteristics educational level, (age, occupation, monthly income, current residence, and family type). Part (2): Menstrual history, including age at menarche, cycle duration, and cycle interval, regularity of the menstrual cycle, amount of blood loss, and accompanying symptoms. Part (3): History of infertility, such as duration of the marriage, type of infertility, duration of infertility, as well as the main cause of infertility.

Tool 2: Fertility problem inventory (FPI) questionnaire: This instrument was

originally designed by Christopher Newton at the London Health Sciences Center located in Ontario, Canada (Newton et al., 1999). Subsequently, it underwent revision for thorough assessing reliability and validity by Alizadeh et al. (2005) to quantify the extent of infertilityrelated stress experienced by women. The instrument was systematically adapted and translated into Arabic, which the researcher employed during the interview process. It consisted of 46 items organized into five primary domains, delineated as follows: social concern (10 items), sexual concern (8 items), relationship concern (10 items), rejection of a childfree lifestyle (8 items), and the need for parenthood (10 items). Each item was structured on a 3-point Likert-type scale, represented by the following coding: Agree (3 points), somewhat agree (2 points), and disagree (1 point). The cumulative score for each participant ranged between 46 and 138. The perceived level of stress among participants was classified as low stress (less than 77), average stress (77 to less than 108), and high stress (ranging from 108 to 138).

Tool 3: Spielberger State-Trait Anxiety Inventory (STAI) questionnaire:

This tool was initially developed by Spielberger et al. (1983), and then it was revised for its reliability and validity by Buela-Casal and Guillén-Riquelme (2017). modified This instrument was translated into Arabic by the investigator to assess the two distinct forms of anxiety (trait and state) among women experiencing infertility. This assessment encompasses two subscales: The first part : the State Anxiety Scale (S-Anxiety) assessed the current level of anxiety by inquiring how "at this participants feel moment," employing items that evaluate subjective experiences of apprehension, tension, nervousness, worry, and the activation/ arousal of the autonomic nervous system. It consisted of 20 statements evaluated on a 4point Likert-type scale as follows: Not at all (1 point) - Somewhat (2 points)

Moderately so (3 points) - Very much so (4 points). For each participant, the cumulative score ranged from 20 to 80. Consequently, each participant's state anxiety level was categorized as follows: Low anxiety from 20-39; moderate anxiety from 40-59; severe anxiety from 60-80.

Second part: The trait anxiety scale (T-Anxiety) it can be used to evaluate the relatively constant dimensions of "anxiety proneness," encompassing overarching conditions of tranquility, self-assurance, and a sense of safety. It comprised 20 statements scored according to a 4-point Likert-like scale as follows: Almost never (1 point) - Sometimes (2 points) - Often (3 points) - Almost always (4 points). For each subject, the total score ranged between 20 and 80. Accordingly, each subject's trait anxiety level was rated as follows: Low anxiety from 20-39; moderate anxiety from 40-59; severe anxiety from 60-80. For the two subscales, stems (1, 2, 5, 8, 10, 11, 15, 16, 19, 20) on the state scale and items no. 21 (21, 26, 27, 30, 33, 36, 39) on the trait scale are positively keyed and reversely scored (1=4, 2=3, 3=2, and 4=1).

Ovulatory predictors 4: assessment: The researcher developed and used it to collect data about ovulation predictors by following the size of the follicles and the value of the follicular estradiol (E2) test. Firstly, estradiol is a form of the estrogen hormone. It's also called 17 beta-estradiol; the normal estradiol levels range between 15 and 350 pictograms per milliliter (pg/mL). Secondly, follicles are tiny fluid sacs located in the ovaries. Normally, ovulation releases the ovum from the follicle on the 14th day of menstruation. In order for the occurrence of ovulation, the average diameter of a dominant follicle should be from 22 to 24 mm.

Method

The research was accomplished according to the next steps:

Approval was secured from the Research Ethics Committee, Faculty of Nursing, Alexandria University. The researcher received certified training in applying progressive muscle relaxation techniques by a specialist from the higher authority for complementary medicine of the Arab African Union. Official correspondence from the Faculty of Nursing, Alexandria University, was directed towards the relevant authorities of the study settings to obtain permission for data collection subsequent to the elucidation of the study's objectives. The researcher developed tools (1& IV) based on an extensive review of recent, current, and relevant literature. Both tools (II & III) were adapted and translated to the Arabic language by the researcher. The tools underwent evaluation for content validity by a panel of five experts. in the field of obstetrics and gynecology. Tools are checked for reliability using the Cronbach alpha test, and the result was highly reliable (FPI =0.93 & tool three STAI = 0.91 & tool four ovulatory predictorassessment =0.90).

A pilot study was conducted on eight infertile women (excluded from the study subjects) to evaluate the practicality of the study and to ascertain the clarity and applicability of the tools, in addition to calculating the time required for their completion.

Data collection covered 6 months, from the middle of January till the middle of July 2022, 2 days/week: 1-2 infertile women /day.

Data collection:

Data was collected through the following phases:

1 Assessment- Phase

- Each infertile woman undergoing ovulatory induction who attends the infertility clinic was informed about the aim of the study in order to obtain her informed consent from the researcher.

- Each infertile woman was individually interviewed for approximately 20 minutes based on the pilot study to collect the basic data by using tools 1, II, and III to assess their anxiety and stress level to select those who fulfill the inclusion study criteria.
- The first 40 women who met the inclusion criteria within the study cohort were recruited as the control group. The researcher initiated procedures with the subjects in the control group to preclude any contamination of the study sample. The subsequent 40 women were allocated to the study group, after which the study's purpose, design, and the role of the subjects were thoroughly elucidated.
- **2- Preparation Phase:** the researcher conducted the following preparations:

Content preparation (theoretical component): this comprised a presentation (demonstration) elucidating the progressive muscle relaxation technique (definition, objectives, categories of relaxation therapy, and application methods).

Environment preparation: The researcher ensured that the research setting was characterized by safety, cleanliness, and tranquility as well as the needed equipment, such as chairs and mattresses.

3-Implementation Phase:

Study group: Each woman was trained individually by the researcher as follows: Theoretical part: the researcher explained the definition, aim, benefits, steps, frequency, and duration of progressive muscle relaxation technique for each woman in the study group through a PowerPoint presentation.

Clinical training techniques for progressive muscle relaxation techniques:

It aimed to achieve a balance between being alert and energetic, yet staying calm and relaxed. After introducing the infertile woman to the clinical training environment. The relaxation training was done as follows:

Relaxing music played as a resource to improve motivation

Both the lighting and temperature were controlled during the training.

- The researcher commenced the session and posed the following inquiries to each woman:
- After emptying her bladder, sit comfortably on the chair
- Engage in diaphragmatic breathing (inhaling deeply through the nasal passages, consciously perceiving the elevation of the abdominal region as one fills the body with air, followed by a gradual exhalation through the oral cavity), and subsequently repeat this process 3 to 5 times in succession.
- Contract the facial musculature, creating furrows in the forehead, furrowing the nasal region, tightly closing the eyelids, pursing the lips together, and maintaining this contraction for a duration of 5 to 7 seconds, followed by a gradual release of the tension while counting to 10 seconds.
- Engage the musculature of the hands, forearms, and biceps in a state of contraction.
- Form a clenched fist with the hands, transition to the biceps by elevating the forearm towards the shoulder, and then gradually relax the contraction while counting from 1 to 10, followed by a repetition of this process on the left arm.
- Rotate the head in a deliberate manner until a mild stretch is perceived, maintaining this position for five seconds, and subsequently allowing the head to descend to its maximum comfortable extent.

Draw in the abdominal region as far as feasible while supporting it with the hands, maintaining this contraction for 5 to 7 seconds, and then slowly release while counting from 1 to 10 seconds.

- Contract the gluteal musculature by adducting them, sustaining the contraction for 5 to 7 seconds, and then progressively releasing while counting from 1 to 10 seconds.
- Engage the leg muscles by elevating the leg off the ground, extending the knee, and orienting the toes towards the head; maintain this position for 5 seconds, then gradually release while counting from 1 to 10 seconds, and replicate the process with the opposite leg.
- Home-based intervention: The researcher directed the participant to execute the progressive muscle relaxation technique three times daily (specifically in the morning, evening, and night). The researcher maintained contact with the participant via telephone.
- The relaxation training is implemented in 3 sessions according to the specialist instructions, as follows:
- First sessions on the 2nd day of menstruation before receiving ovulatory induction.
- Second session on the 9th day of menstruation after receiving ovulatory induction.
- Third session at the 11th day of menstruation after receiving ovulatory induction.
- Each session lasted 15-20 minutes under the supervision of the researcher. The control group received routine care from the clinic.

4-Evaluation Phase:

- Tools (II, III) used by the researchers to assess the stress and anxiety for the experimental group before and immediately after each session (on the 2nd day of menstruation pre-posttest (1), the 9th day of menstruation pre-posttest (2), and the 11th day of menstruation pre-posttest (3).
- Tool (IV) was used by the researcher to assess the ovulation predictors based on the transvaginal ultrasound result, which the obstetrician made a routine for these cases on the 9th and 11th days of menstruation.

• The difference between pre- and posttests among both groups was calculated to determine the effectiveness of the intervention.

Statistical analysis:

- The collected data were categorized, coded, digitized, and computed using the Statistical Package for Social Sciences (SPSS) version 23 software, and then they were examined.
- The categorical variables of both groups were described and summarized using statistical techniques like cross tabulation.
- Analytical and descriptive statistics, including percentages, mean, and SD, were used, while the Chi-square and Fisher Exact tests were employed to identify differences in the results at a significance level of less than 0.05 (5%).

Ethical Considerations:

- After describing the aim of the study, getting the subject's signed informed consent.
- The study participants' privacy was guaranteed.
- The gathered information is kept private and confidential.
- Each participant was informed that she might withdraw from the study at any time and that participation is entirely voluntary.

Results

Table (I) illustrates how infertile women distributed based their on sociodemographic characteristics .The study group's mean age was 28.70 ± 3.50 years, while the control group was 83 ± 4.42 years. Education level also showed that slightly less than two-fifths of the study and control groups (42.5 and 42.5 percent, respectively) had completed secondary school. Furthermore, occupation revealed that just over half (52.5%) of the study group were housewives, while 62.5 percent of the control groups were the same. However, compared to 15% and 55% of the control group, respectively, less than half of the study group (40 and 46.6%) were farmers and merchants.

Regarding current residence and type of family, it demonstrated that was significantly people the more experimental and control groups lived in urban areas (70% and 67.5%, respectively), while 47.5% and 52.5% of them had extended families. In conclusion, threequarters (75%) of the study group had sufficient family income, while around twothirds (67%) of the control group did not. Nevertheless, there were no statistically significant discrepancies between demographic data of the two groups, indicating that they were homogeneous.

Table (II) presents the distribution of infertile women according to menstrual history. The mean age at menarche was 12.28 ± 1.18 years for the study group and 28 ± 1.43 years for the control group. Regarding the amount of menstrual flow, it manifested that slightly more than half (62.5%) of the study group, compared to 55.5% of the control groups, had a moderate amount of menstrual flow. However, the mean menstrual intervals of the study and control groups were 27.10 \pm 2.52 and 27.90 ± 2.56 , respectively. All the study and control groups had regular menstrual cycles with intervals between 22 and 35 days. The mean duration of menstrual bleeding was 5.08 ± 1.14 days for the study group compared to 4.70 ± 1.16 days for the control group. Additionally, slightly more than half (52.5%) of the study group participants reported no dysmenorrhea, compared to about twothirds (65%) of the control group. No statistically significant differences were observed between both groups concerning the previously mentioned items (p = 1.000, 0.363, 0.163., 0.263, 0.256, and 0.149).

The mean duration of infertility in the study and control groups was. 53 ± 3.02 and 4.83 ± 2.71 , respectively. The percentage of female causes of infertility is equal to 60%

among the study and control groups. No statistically significant differences were observed between both groups in relation to their type of infertility, mean duration of infertility, or cause of infertility (p = 1.000, 0.310, and 0.984, respectively).

Table 3 compares the studied subjects' stress levels before and after intervention. As regards stress levels at day 2 of induction before intervention, the majority (87.5%) of the study group compared to slightly more than three-quarters (77.5%) of the control group had moderate stress levels, with no statistically significant difference observed among both groups

(p = 0.267). This picture was changed after the intervention, where one-half (50%)) of the study group compared to only 7.5% of the control group had a mild level of stress with a statistically significant difference between the two groups (P = 0.010*).

Concerning stress levels at day 9 of induction (45% & 42.5%, respectively of the study and control groups had severe stress levels before intervention, with no statistically significant difference observed among both groups (p = 0.130). A statistically significant difference was prominent between the study and control groups (P = 0.001*) on day 9 of the induction after the intervention, as none (0.0%) of the study group compared to slightly less than one-half (45%) of the control group had a severe stress level after the intervention.

Finally, it was found that (50% & 55%) of the study and control groups had a severe stress level at day 11 of induction before the intervention, with no statistically significant difference observed among both groups (p = 1000). Surprisingly enough, slightly less than four-fifths (87.5%) of the study group compared to only 5% of the control group had a mild stress level at day 11 of induction postintervention, with a statistically significant difference among the two groups (P = 0.010*).

Table 4 exhibits the comparison between the studied subjects according to Spielberger state-trait anxietv inventory. On the second day of induction, both the study and control groups, approximately 67.5% and 70%, respectively, had moderate anxiety levels before the intervention. However, the two groups had no statistically significant difference (p = 0.809). This picture was changed after the intervention, where three-quarters (75%) of the study group, compared to only 5% of the control group, had a mild stress level with a statistically significant difference between the two groups (P = 0.014*).

Concerning day 9 of induction, it was found that (77.5% & 80%), respectively, of the study and control groups had a severe anxiety level before the intervention, with no statistically significant difference observed among both groups (p = 0.064). Virtually none (0.0%) of the study group compared to four-fifths of the control had a severe level of anxiety at day 9 of induction after intervention, with a statistically significant difference between the two groups (P = 0.001*).

Concerning anxiety levels at day 11 of induction, this table presented that (82.5% & 80%) respectively of the study and control groups had a severe anxiety level before intervention with no statistically significant difference observed among both groups (p = 0.633). Furthermore, 85% of the study group, compared to only 2.5% of the control group, had a mild anxiety level at day 11 of induction after intervention, with a statistically significant difference between the two groups (P = 0.001*).

Table 5 shows that the mean E2 level of the study group at day 2 of induction was (39.53 ± 5.87) compared to (36.40 ± 7.36) of the control group, while the mean E2 level at day 9 of induction was 196.75 ± 18.01 and 176.25 ± 33.21 of both groups, respectively. As regards the E2 level at day 11 of induction, the mean score (285.40 ± 28.95) of the study group was higher among the study group than the control group

 (245.05 ± 47.77) . A statistically significant difference was observed among the study and control groups regarding E2 level at days 2, 9, and 11 from induction, where (p = 0.039* and p= 0.001*& p <0.001*) in favor of the study group.

Table 6 exhibits that the mean diameter of follicles of the study group at day 9 of induction was (13.03 ± 1.05) compared to (10.98 ± 2.21) of the control group, while the mean diameter of follicles at day 11 of induction was 15.75 ± 0.90 and 13.58 ± 2.45 of both groups, respectively. A statistically significant difference was observed among the study and control groups regarding the diameter of follicles at days 9 and 11 from induction, where (p <0.001*and p <0.001*), respectively, in favor of the study group.

Discussion

Infertility represents a significant life crisis that impacts individuals globally, with About 186 million people and 48 million couples are impacted. Women experiencing infertility frequently undergo heightened levels of anxiety and depression, which may detrimentally affect their overall health, encompassing mental, emotional, sexual, dimensions. and spiritual Relaxation include techniques various methods. therapies, or activities designed to facilitate relaxation, enhance tranquility, or alleviate tension, anxiety, anger, or discomfort. These methods may help lower blood pressure, pulse rate, breathing rate, and tense muscles among other physiological benefits. Generally, these practices are integrated into a holistic stress management framework (Elhussein et al., 2019).

Progressive muscle relaxation (PMR), a technique aimed to alleviating anxiety, was first introduced in the 1930s by the American physician Edmund Jacobson (Chaudhary & Garg, 2024). PMR is recognized as a form of mind-body therapy that has demonstrated significant efficacy in alleviating stress and anxiety in women facing infertility, which may subsequently

affect ovulation and overall reproductive health. By fostering individuals' awareness of muscle tension and facilitating its release, mind-body therapies enable patients to assume greater agency over their stress and anxiety. Progressive Muscle Relaxation (PMR) exemplifies the therapeutic efficacy of deliberate relaxation in enhancing overall well-being and advancing the healing trajectory. Consistent engagement in PMR sessions assists individuals, particularly those experiencing infertility, in cultivating heightened self-awareness while alleviating stress and anxiety (Gaitzsch et al., 2020).

The current study's results indicate that experimental and control groups displayed comparable socio-demographic and clinical attributes alongside reproductive histories (Tables I-III). This finding suggests that many women seeking treatment at El-Shatby Maternity University Hospital are from a relatively uniform socioeconomic background. The homogeneity of the participants' profiles mitigated extraneous variables that could have impeded the impact of the intended intervention on the ovulatory indicators. Furthermore, it facilitated the understanding and ensured the validity and generalizability of the prospective findings of the current investigation.

In accordance with the findings of the current study, which assessed the influence of the progressive muscle relaxation technique on stress levels in infertile women, a considerable percentage of participants within both the experimental and control groups reported moderate stress levels prior to the intervention, with no statistically significant discrepancies evident between the two groups (p = 0.267). Nevertheless, subsequent to the intervention, the stress levels within the study group diminished to a moderate state in contrast to the control group, signifying a highly significant difference favoring the study group (p < 0.0001). In accordance with the findings of the current study, which assessed the influence of the progressive

muscle relaxation technique on stress levels infertile women. a considerable percentage of participants within both the experimental and control groups reported moderate stress levels prior to the intervention, with no statistically significant discrepancies evident between the two groups (p = 0.267). Nevertheless. subsequent to the intervention, the stress levels within the study group diminished to a moderate state in contrast to the control group, signifying a highly significant difference favoring the study group (p < 0.0001).

This outcome can be attributed to two main factors. First, the progressive muscle relaxation approach helps reduce parasympathetic nervous system activity by eliciting a relaxation response, which counteracts the stress response. Second, the technique involves participants gradually tightening and relaxing various muscle groups throughout their bodies, promoting a sense of comfort and relaxation. This process may help reduce stress, divert attention from stressors, and alleviate muscle tension.

The current findings align with previous studies in several ways. **Firstly**, a study conducted in Egypt by Ibrahim et al. (2020). They found that women who participated in progressive muscle relaxation programs reported significantly lower stress scores than those who did not engage in such interventions (p < 0.05). This underscores the effectiveness of relaxation methods as alternative therapeutic options for managing stress related to infertility.

Secondly, a systematic review and metaanalysis by Ha and Ban (2021). Showed that mind-body programs successfully reduced stress levels and enhanced the quality of life of infertile women, which in turn had a beneficial impact on pregnancy rates. In order to improve infertile women's emotional health and pregnancy outcomes, the authors suggested that mind-body programs be taken into consideration for a wider audience. Thirdly, a randomized controlled trial by Aulakh et al. (2024) showed that, following the intervention program, there was a statistically significant difference (p < 0.001) in the stress levels among the study and control groups. Fourthly, Mousavi et al. (2020). Their findings showed a substantial difference between the experimental and control groups, with the intervention significantly reducing stress levels.

In evaluating the efficacy of the progressive muscle relaxation technique on anxiety levels among infertile women, the findings of the current study revealed that the majority of participants in both the and control groups study exhibited moderate anxiety levels prior to the intervention, with no statistically significant differences identified between them (p = 0.809). Conversely, following intervention, the anxiety levels within the study group were reduced to a mild state relative to the control group, indicating a highly statistically significant difference favoring the study group (p < 0.0001). Such outcomes may be attributed to the premise that progressive muscle relaxation, as an integral aspect of mind-body therapy, can enhance the perception of control, improve the capacity to manage intrusive cognitions, and foster overall relaxation, thereby contributing to the reduction of anxiety levels.

The current findings align with those of four other studies. Firstly, a study by Sahraian et al. (2024) investigated the "Effectiveness of Mindful Self-Compassion Therapy on Psychopathology Symptoms, Psychological Distress, and Expectancy in Infertile Women Treated with In Vitro Fertilization: A Two-Arm Double-Blind Parallel Randomized Controlled Trial." Their results revealed that psychological relaxation techniques, including progressive muscle relaxation, contributed to decreased anxiety levels undergoing assisted among women reproductive technologies (ART), such as IVF. The findings suggested that these

techniques not only alleviate anxiety but may also enhance the chances of successful pregnancy outcomes.

Secondly, the previously mentioned study by Ha and Ban (2021) found that the mind-body program effectively reduced anxiety levels among infertile women, improving their quality of life and ultimately increasing pregnancy rates. Thirdly, Kiyak and Kocoglu-Tanyer (2021) posited that women undergoing in vitro fertilization (IVF) treatment who availed themselves of progressive muscle relaxation laughter therapy exhibited enhancements in their psychological wellbeing, as evidenced by the intervention group's lower scores in depression and trait anxiety in comparison to the control group on the day of oocyte retrieval. Fourthly, the aforementioned study conducted by Aulakh et al. (2024) identified a significant decrease in anxiety levels, with a highly statistically significant difference between the study and control groups (p < 0.001) following the intervention program.

In evaluating the impact of the progressive muscle relaxation technique on ovulatory predictors among infertile women, the findings of the current study indicated a statistically significant difference between the study and control groups concerning E2 levels at days 2, 9, and 11 post-inductions, with p-values of 0.039, 0.001, and p < 0.001 favoring the study group, respectively, in assessing the influence of the progressive muscle relaxation technique on ovulation rates among infertile women.

These results may be attributed to the reduction of stress hormones is crucial; stress and anxiety can significantly impact fertility and ovulation, as anxiety is linked to increased levels of stress hormones, particularly cortisol. Elevated cortisol can disrupt the normal functioning of the hypothalamic-pituitary-gonadal (HPG) axis, which regulates reproductive hormones. This dysregulation may lead to irregular menstrual cycles, anovulation, and impaired implantation of embryos. Therefore, PMR

has been shown to significantly lower these hormone levels, potentially restoring the hormonal balance necessary for ovulation.

The current findings align with three other studies. The previously mentioned study by Aulakh et al. (2024) revealed that the pregnancy outcome rate improved after the intervention. They recommended that the application of relaxation techniques for infertile women should be comprehensive rather than solely focused on medical treatment to achieve better pregnancy outcomes. Similarly, Chaudhary and Garg (2024) confirmed the effectiveness of progressive muscle relaxation techniques in reducing anxiety levels among infertile women after intervention. Additionally, a study by Gong and Li (2018) investigated "Effects of Psychological Intervention on Pregnancy Outcomes in Infertility Patients Treated by In Vitro Fertilization and Embryo Transplantation." The results indicated that psychological interventions, including relaxation techniques. significantly affected pregnancy rates, with interventions mind-body showing standardized mean difference (SMD) of 1.37 (95% CI = 1.01–1.85; p = 0.040; $I^2 =$ 0%).

Conclusion

Based on the findings of the present study, it can be concluded that the progressive muscle relaxation technique significantly reduced both stress and anxiety levels among infertile women who participated in the intervention. Additionally, this technique had a notable positive effect on improving the ovulation rate in this population.

Recommendations

Based on the obtained results from the present study, our recommendations are:

- Incorporate Progressive Muscle Relaxation into Standard Care: The progressive muscle relaxation technique should be offered as a standard component of care for women

- undergoing infertility treatment. This integration can help address the psychological aspects of infertility and improve overall treatment outcomes.
- Training for Healthcare Providers: Inservice training programs should be implemented for healthcare providers who care for infertile women. These programs should focus on increasing awareness of the positive effects of progressive muscle relaxation in managing psychological symptoms associated with infertility.
- Promote Progressive Muscle Relaxation as an Effective Modality: The progressive muscle relaxation technique can be recommended as an effective strategy for managing stress and anxiety, while also respecting the individual desires and preferences of infertile women. This personalized approach can enhance compliance and overall satisfaction with treatment.

Authors' contributions:

Wafaa Ahmed Ebrahim, Assistant professor Supervising research and dissertation stages. Contributed to conceptualization study designs and final review of the dissertation.

Yasser Saad El-Kassrar, Professor

Supervising research and dissertation stages. Contributed to conceptualization study designs and final review of the dissertation

Faeza Hashem Abdel Fattah Elessawy, nursing specialist: played a significant role in data collection, analysis and interpretation.

Neama Saad Mahmoud Shokhba,

Lecturer: Directing research and dissertation stages. Contributed to conceptualization study designs and final review of the dissertation.

Mahmoud Mohamed Khedr Lecturer: Directing research and dissertation stages. Contributed to conceptualization study designs and final review of the dissertation

Table (1): Distribution of the studied groups according to their socio-demographic characteristics

	Study group (n = 40)		Contro (n =		Test of sig.	р
Age						
Min. – Max.	23.0 - 35.0		20.0 - 35.0		t=0.981	0.329
Mean \pm SD.	28.70 =	± 3.50	27.83	± 4.42	1-0.981	0.329
Level of education	No.	%	No.	%		
- Illiterate, R & R	6	15.0	4	40.0		
- Primary	6	15.0	11	27.5		
- Secondary	17	42.5	17	42.5	$\chi^2=3.031$	$^{ m MC}{ m p}{=} 0.580$
- University	10	25.0	8	20.0		0.00
- More	1	2.5	0	0.0		
Occupation	No.	%	No.	%		
- Housewife	19	47.5	25	62.5	2_1 010	0.178
- Working	21	52.5	15	37.5	$\chi^2=1.818$	
Type of work	No.	%	No.	%		
- Profession	7	33.3	5	33.3		^{мс} р= 0.567
- Employee	5	23.8	2	13.3		
- Worker	4	19.0	6	40.0	$\chi^2=4.136$	
- Merchant	2	9.5	1	6.7		
- Farmer	3	14.3	1	6.7		
Current residence	No.	%	No.	%		
- Rural	12	30.0	13	32.5	w ² -0.059	0.000
- Urban	28	70.0	27	67.5	$\chi^2 = 0.058$	0.809
Type of family	No.	%	No.	%		
- Nuclear	21	52.5	19	47.5	2-0.200	0.655
- Extended	19	47.5	21	52.5	$\chi^2 = 0.200$	0.055
Family income	No.	%	No.	%		
- Enough	30	75	27	67.5	··2-5 9.46	0.054
- Not enough	10	25.0	13	32.5	$\chi^2 = 5.846$	0.034
Age at marriage						
- Min. – Max.	19.0 –	29.0	18.0 - 31.0		. 0.000	1.000
- Mean \pm SD.	23.10 =	± 2.53	23.10	± 3.52	t=0.000	1.000

SD=Standard deviation, t=independent t-test, χ^2 =Chi square test p=p-value for comparing the Study group and Control group

MC=Monte Carlo

Progressive Muscle Relaxation Technique, Anxiety, Stress, Ovulatory predictors, Ovulatory induction.

Table (2): Distribution of the studied groups according to their menstrual history

	Study group (n = 40)		Contro (n =		Test of sig.	р
Age of menarche						
- Min. – Max.	10.0 -	- 15.0	9.0 –	15.0	t=0.000	1.000
- Mean \pm SD.	12.28	± 1.18	12.28	± 1.43	ι-0.000	1.000
Amount of menstruation	No.	%	No.	%		
- Scanty	6	15.0	3	7.5		MC
- Moderate	25	62.5	22	55.0	$\chi^2 = 2.632$	$^{MC}p=0.336$
- Excessive	9	22.5	15	37.5		0.550
Menstrual interval						
- Min. – Max.	22.0 -	32.0	24.0 -	- 35.0	<u>-1 400</u>	0.162
- Mean \pm SD.	27.10	± 2.52	27.90	± 2.56	t=1.409	0.163
Frequency	No.	%	No.	%		
- Regular	22	55.0	23	57.5	2 1 251	0.263
- Irregular	18	45.0	17	42.5	$\chi^2=1.251$	
Presence of dysmenorrhea	No.	%	No.	%		
- Yes	19	47.5	14	35.0	2 1 200	0.256
- No	21	52.5	26	65.0	$\chi^2=1.289$	
Menstrual duration						
- Min. – Max.	3.0 - 7.0		2.0 - 7.0		t=1.458	0.149
- Mean \pm SD.	5.08 ±	1.14	4.70 ±	1.16		
Duration of infertility						
- Min. – Max.	1.0 –	13.0	1.0 -	12.0	U=695.5	0.310
- Mean \pm SD.	5.53 ±	3.02	4.83 ±	± 2.71	0=693.3	0.310
Cause of infertility	No.	%	No.	%		
- Male factor	5	12.5	6	15.0		0.984
- Female factor	24	60.0	25	62.0	2 0 150	
- Both	7	17.5	6	15.0	$\chi^2 = 0.158$	
- Unknown causes	4	10.0	3	7.5		

 $\begin{array}{lll} SD{=}Standard\ deviation, & t{=}independent\ t{-}test, & U{=}Mann\ Whitney\ test \\ \chi^2{=}Chi\ square\ test & FE{=}Fisher\ Exact & MC{=}Monte\ Carlo \\ \end{array}$

p=p-value for comparing the Study group and Control group

Table (3): Comparison between the studied subjects according to their stress level before and after intervention

	Before intervention		A	After intervention				Significant between Before and After		
Stress level	Study (n =		Contro (n =			group 40)	Contro (n =		Study group	Control group
	No.	%	No.	%	No.	%	No.	%	group	group
Day 2 of induction										
- Mild stress level	0	0.0	3	7.5	20	50.0	3	7.5		
- Moderate stress level	35	87.5	31	77.5	18	45.0	31	77.5	MH =	MH =
- Severe stress level	5	12.5	6	15.0	2	5.0	6	15.0	<0.001*	0.705
Sig. bet. Groups.	χ^{2}	= 2.978,	$^{MC}p = 0.2$	67	χ^{2}	=8.230*,	$^{MC}p=0.01$	0^*		
Min. – Max.	85.0-	116.0	72.0-	114.0	70.0-	104.0	75.0-	116.0	t ₀ =10.245*	t ₀ =0.520
Mean \pm SD.	96.60	0.8±0	92.6±	=11.3	82.7	±6.8	93.1	±9.6	p ₀ <0.001*	p ₀ =0.606
Sig. bet. grps.		t=1.826	,p=0.072		t	=5.543*,	p<0.001*	,		
Day 9 of induction										
- Mild stress level	7	17.50	6	15.0	21	52.5	3	7.5		
- Moderate stress level	15	37.50	17	42.5	19	47.5	19	47.5	MH =	MH =
- Severe stress level	18	45.00	17	42.5	0	0.0	18	45.0	<0.001*	0.527
Sig. bet. Groups.	χ^2	2 = 4.216	$^{MC}p=0.13$	50	χ^2	=21.249*	,p<0.001*			
Min. – Max.	85.0-	116.0	75.0-	114.0	67.0	-88.0	71.0-	112.0	t ₀ =11.651*	t ₀ =0.180
Mean \pm SD.	96.60	0.8±0	93.2	±9.4	76.1	±5.0	92.9±	10.9	$p_0 < 0.001^*$	$p_0 = 0.858$
Sig. bet. grps.		t=1.709	,p=0.092		t=	=10.137*	,p<0.001	*		
Day 11 of induction										
- Mild stress level	1	2.5	1	2.5	36	87.5	2	5.0		
- Moderate stress level	19	47.5	17	42.5	4	12.5	16	40.0	MH =	MH =
- Severe stress level	20	50.0	22	55.0	0	0.0	22	55.0	<0.001*	0.125
Sig. bet. Groups.	λ	$\chi^2 = 0.346$,p= 1.000)	χ^2	2=73.895*	,p<0.00	1*		
Min. – Max.	78.0-	113.0	83.0-	120.0		-83.0	79.0-		t ₀ =16.876*	t ₀ =0.437
Mean \pm SD.	94.5	±7.3	92.3±	=10.1	70.0	±5.6	91.6	±6.2	$p_0 < 0.001^*$	$p_0=0.665$
Sig. bet. grps.		t=1.870,	p = 0.065		t=	=12.202*	,p<0.001	*		
F (p ₁)			0.523(<0.001*)				
Sig. bet. Periods.										
p ₂	1.0	000	0.5	56	<0.0	01*	1.0	00		
р3	0.3	18	1.0	00	<0.0	001*	0.9	80		
p 4	0.3	18	1.0	00	<0.0	01*	1.0	00		

SD=Standard deviation,

t=independent t-test, t₀=Paired t-test

F= ANONA with repeated measures

p=p-value for comparing the Study group and Control group

Mild stress: <77
Average stress: 77 – 107

χ²=Chi square test MC=Monte Carlo

 p_0 =p-value for comparing Before and After receiving ovulatory induction in each group on each day

p₁: p-value for Adjustment for multiple comparisons: Bonferroni for comparison between three days

p₂: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 9

p₃: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 11 p₄: p-value for Adjustment for multiple comparisons: Bonferroni Day 9 and Day 11

^{*} Statistically significant p-value at ≤0.05

Table (4): Comparison between the studied subjects according to their Spielberger **State-Trait Anxiety Inventory level**

	Before intervention		After intervention				Significant between Before and After			
Overall S-Anxiety	Study (n =		Control (n =		Study (n =		Contro (n =		Study group	Control group
	No.	%	No.	%	No.	%	No.	%	group	group
Day 2 of induction										
 Mild anxiety 	0	0.0	0	0.0	30	75.0	2	5.0		
- Moderate anxiety	27	67.5	28	70.0	10	25.0	32	80.0	MH =	MH =
- Severe anxiety	13	32.5	12	30.0	0	0.00	6	15.0	<0.001*	0.070
Sig. bet. Groups.)	$\chi^2 = 0.058$,p=0.809)	$\chi^2 =$	8.606*,	$^{MC}p=0.01$	4*		
Min. – Max.	40.0-	69.0	40.0-	73.0	36.0-	67.0	36.0-	-73.0	$t_0=3.128^*$	t ₀ =0.508
Mean \pm SD.	52.7	±9.0	51.2±	:11.1	47.1	±8.8	52.2	±9.0	$p_0=0.003^*$	p ₀ =0.614
Sig. bet. grps.		t=0.665	p=0.508		t	$=2.549^*$	p=0.013	*		
Day 9 of induction										
Mild anxiety	2	5.0	2	5.0	25	62.5	1	2.5		
Moderate anxiety	7	17.5	6	15.0	15	37.5	7	17.5	MH =	MH =
Severe anxiety	31	77.5	32	80.0	0	0.0	32	80.0	<0.001*	0.053
Sig. bet. Groups.	χ^2	=4.991 , ¹	MC p= 0.06	54	χ^2	=26.296*	,p<0.001*			
Min. – Max.	38.0-	66.0	40.0-	67.0	33.0-	58.0	40.0-	74.0	t ₀ =3.571*	t ₀ =0.381
Mean \pm SD.	49.6	±9.7	52.3	±5.1	43.4	±7.3	51.6∃	=10.2	$p_0=0.001^*$	p ₀ =0.705
Sig. bet. grps.		t=1.541	p=0.129		t	=4.116*,	p<0.001	k		
Day 11 of induction										
Mild anxiety	1	2.5	1	2.5	34	85.0	1	2.5		
Moderate anxiety	6	15.0	7	17.5	6	15.0	7	17.5	MH =	MH =
Severe anxiety	33	82.5	32	80.0	0	0.0	32	80.0	<0.001*	0.782
Sig. bet. Groups.)	$\chi^2 = 0.914$,p=0.633	,	χ^2	=33.959*	,p<0.00	1*		
Min. – Max.	35.0-	-66.0	36.0-	71.0	31.0-	58.0	40.0-	76.0	t ₀ =5.922*	t ₀ =0.376
Mean \pm SD.	51.0∃	=11.5	51.7	±9.5	40.9	±5.9	51.2	±9.2	p ₀ <0.001*	$p_0=0.709$
Sig. bet. grps.		t=0.297	p=0.767		t=5.945*,p<0.001*					
F (p ₁)	1.974(0.168)	0.163(0.850)	12.990*(-	<0.001*)	0.155(0.856)		
Sig. bet. Periods.										
p ₂	0.0	58	1.0	00	0.03	31*	1.0	00		
p ₃	1.0	00	1.0	00	< 0.0	01*	1.0	00		
p ₄	1.0	00	1.0	00	0.01	10*	1.0	000		

SD=Standard deviation,

p=p-value for comparing the Study group and Control group

Mild anxiety from 20-39

Moderate anxiety from 40-59

Severe anxiety from 60-80

t=independent t-test, t₀=Paired t-test

F= ANONA with repeated measures

χ²=Chi square test MC=Monte Carlo

 p_0 =p-value for comparing Before and After receiving ovulatory induction in each group on each day p_1 : p-value for Adjustment for multiple comparisons: Bonferroni for comparison between three days

p₂: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 9 p₃: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 11

p₄: p-value for Adjustment for multiple comparisons: Bonferroni Day 9 and Day 11

^{*} Statistically significant p-value at ≤0.05

Progressive Muscle Relaxation Technique, Anxiety, Stress, Ovulatory predictors, Ovulatory induction.

Table (5): Comparison between the studied subjects according to their E2 level

E2 level	Study group (n = 40)	Control group (n = 40)	t	р
Day 2 of induction				
Min. – Max.	30.0 - 49.0	24.0 – 49.0	2.100*	0.039*
Mean \pm SD.	39.53 ± 5.87	36.40 ± 7.36	2.100	0.039
Day 9 of induction				
Min. – Max.	155.0 - 231.0	111.0 – 227.0	3.432*	0.001*
Mean \pm SD.	196.75 ± 18.01	176.25 ± 33.21	3.432	
Day 11 of induction				
Min. – Max.	195.0 - 355.0	154.0 - 331.0	4.569*	<0.001*
Mean \pm SD.	285.40 ± 28.95	245.05 ± 47.77	4.309	<0.001
F (p ₁)	1815.496* (<0.001*)	705.805* (<0.001*)		
Sig. bet. Periods.				
p ₂	<0.001*	<0.001*		
p ₃	<0.001*	<0.001*		
p 4	<0.001*	<0.001*		

SD=Standard deviation, t= independent t-test, F= ANONA with repeated measures p=p-value for comparing the Study group and Control group

p₁: p-value for Adjustment for multiple comparisons: Bonferroni for comparison between three days

p₂: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 9

p₃: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 11

p₄: p-value for Adjustment for multiple comparisons: Bonferroni Day 9 and Day 11

^{*} Statistically significant p-value at ≤0.05

Table (6): Comparison between the studied subjects according to their diameter of follicles

Diameter of follicles	Study group (n = 40)	Control group (n = 40)	t	р
Day 2 of induction				
Min. – Max.	0.0 - 0.0	0.0 - 0.0		
Mean \pm SD.	0.0 ± 0.0	0.0 ± 0.0	_	_
Day 9 of induction				
Min. – Max.	12.0 - 15.0	7.0 - 15.0	5 20.4*	<0.001*
Mean \pm SD.	13.03 ± 1.05	10.98 ± 2.21	5.294*	
Day 11 of induction				
Min. – Max.	14.0 - 18.0	9.0 - 17.0	5.274*	<0.001*
Mean \pm SD.	15.75 ± 0.90	13.58 ± 2.45	3.274	<0.001
F (p ₁)	6473.562*	1041.978*		
	(<0.001*)	(<0.001*)		
Sig. bet. Periods.				
\mathbf{p}_2	<0.001*	<0.001*		
p ₃	<0.001*	<0.001*		
p ₄	<0.001*	<0.001*		

SD=Standard deviation, t=independent t-test, F= ANONA with repeated measures p=p-value for comparing the Study group and Control group

p₁: p-value for Adjustment for multiple comparisons: Bonferroni for comparison between three days

p₂: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 9

p₃: p-value for Adjustment for multiple comparisons: Bonferroni Day 2 and Day 11

p4: p-value for Adjustment for multiple comparisons: Bonferroni Day 9 and Day 11

^{*} Statistically significant p-value at ≤0.05

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