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The Efficacy of the Supplementation of Selenium on the Semen Quality and Serum Concentrations of IL-6 and TNF-α in Infertile Men

Yaseen Khashman Hussein [1], Zainab Samir Yahya Hammo [2], Sawsan Salman Hosi [3]
[1] Department of Physiology, College of Medicine, University of Tikrit, Iraq dr.yaseen_ykh@tu.edu.iq
[2] Department of Physiology, College of Medicine, University of Tikrit, Iraq zainab.samir@tu.edu.iq
[3] Department of Biochemistry, College of Medicine, University of Tikrit, Iraq sawsan.salman@tu.edu.iq

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ABSTRACT

For male fertility, normal sperm quality is essential. Approximately 20% of men in relationships experience male infertility, defined as the inability to achieve conception with the same partner after one year of frequent, unprotected sexual activity. Elevated levels of pro-inflammatory cytokines have been associated with male infertility. Selenium, due to its antioxidant properties, may protect cells from the harmful effects of oxidation and infection. Furthermore, it has the potential to improve semen parameters, thereby enhancing sperm quality and male fertility. This research aims to investigate the impact of selenium on the improvement of sperm quality and the levels of Tumor Necrosis Factor Alpha (TNF-α), Interleukin 6 (IL-6), and C-Reactive Protein (CRP) in infertile men. A follow-up study was conducted on infertile male patients at a private urology clinic in Baghdad, Iraq. In this study, 25 infertile men were administered a daily dose of 200 mg of selenium for three months, from January 1 to March 31, 2024. Tests for TNF-α, IL-6, CRP, and semen analysis were performed before and after the treatment to assess the outcomes. The findings of this study revealed that the infertile group had significantly reduced semen parameters compared to the regular control group. Additionally, before treatment, the infertile group exhibited significantly higher levels of TNF-α, IL-6, and CRP than the control group. Furthermore, when comparing the treated infertile group to the untreated infertile group after therapy, there was a significant decrease in TNF-α, IL-6, and CRP levels, along with a notable increase in semen parameters. The results of this research suggest that selenium supplementation leads to a substantial reduction in TNF-α, IL-6, and CRP levels in infertile men and a marked improvement in semen parameters after treatment. These findings support the conclusion that selenium is an essential therapeutic agent for improving semen parameters and reducing TNF-α, IL-6, and CRP levels in infertile men.

1. Introduction

Approximately 10–15% of couples worldwide experience infertility, defined as the inability to conceive after one year of regular, unprotected sexual activity (Safarinejad, 2012). Furthermore, 15% of couples globally are affected by male infertility, which is similarly defined as the inability to conceive after one year of consistent, unprotected sexual activity (Babakhanzadeh et al., 2020; Ko et al., 2014).

According to Duntas and Benvenga (2015), selenium (Se) is a vital trace element for maintaining homeostasis in the human body. Selenium is an essential dietary micronutrient required for preserving male fertility (Shuai Yuan et al., 2024). Selenium deficiency has been associated with impaired sperm production, which contributes to 20–40% of male infertility cases (Sneha and Selvakumar, 2020; Gesthimani et al., 2019). Moreover, selenium plays a significant role in sperm

* Corresponding author.
E-mail address: zainabsamir1986@gmail.com

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production and is critical for maintaining normal sperm quality (MacFarquhar et al., 2010; Carla and Rossella, 2008; Ahmed, 2023).

The regulation of spermatogenesis and sperm quality appears to be significantly influenced by inflammatory cytokines and adipokines. Although cytokines play a role in cell-to-cell communication, their function in male infertility within the human reproductive system remains largely unexplored (Vassiliki et al., 2018; Shuai Yuan et al., 2024).

Elevations in pro-inflammatory cytokines, such as TNF-α and IL-6, along with inflammation and obesity, are linked to issues with male reproductive health (Uddesh and Abilash, 2023). These abnormalities likely contribute to male infertility as they impair sperm quality (Beckett et al., 2004; Arthur et al., 2003; Kate et al., 2017; Hiba Hasan et al., 2022).

Due to its anti-inflammatory and antioxidant properties, selenium (Se) may reduce inflammatory marker levels and enhance male fertility by improving sperm quality (Ko et al., 2014; Shalini and Bansal, 2005; Beckett et al., 2004; Ata et al., 2022).

According to Zhu et al. (2016) and Valentina et al. (2022), selenium may also reduce pro-inflammatory cytokines TNF-α and IL-6 in various conditions, as well as mitigate the inflammatory response, inflammatory cell infiltration, infertility, sperm production damage, and pathological harm.

Furthermore, since selenium functions as a potent antioxidant, it may protect against inflammation, cancer, sperm quality degradation, and sperm production damage (Rossella et al., 2021; Vessey et al., 2014; Arthur et al., 2009). This study aims to assess the impact of selenium on pro-inflammatory cytokine levels and sperm quality improvement in infertile men.

2. Methodology

Samples for this research were collected from private clinics between January 1 and May 1, 2024. A longitudinal study was conducted on infertile adult males who visited a private urology clinic based in Baghdad. Before the semen analysis, a set of questions was developed to verify the information provided by the infertile men. These questions covered name, age, smoking habits, duration of marriage, chronic illnesses, and genetic history. Selenium tablets (200 mg) were administered to patients once a day for three months as treatment for infertility. The infertile patient group for this study consisted of 25 male residents of Baghdad, Iraq, who had visited the clinic seeking treatment for their infertility issues.

After at least two days of no sexual activity, the seminal samples were collected by masturbation into a sterile container early in the morning, prior to the first meal (Figure 1). The seminal volume, sperm cell density, total sperm count, motility, percentage of live spermatozoa, and normal morphology of all semen samples were evaluated according to WHO recommendations to assess sperm quality. After comparing the semen parameters, the results were shared with the patients and used in this study for evaluation (WHO, 2010).

The analysis of pro-inflammatory cytokines was performed according to standard protocols. Seminal plasma was analyzed to measure the levels of TNF-α and IL-6, with the results expressed in picograms per milliliter (pg/ml) (Packer and Sies, 2008).

The mean and standard deviation of each data set were calculated. The Student's t-test was used to compare the means of the variables. P-values were considered significant if they were less than 0.05 or 0.01.

The mean and standard deviation of each set of data were shown. The Student T test was used to compare the variable means. P values were considered significant if they were less than 0.05 or 0.01.

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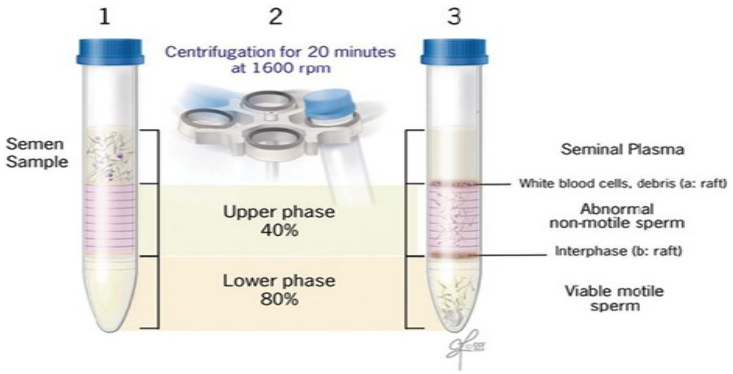

Figure 1: Laboratory Handling of Retrieved Sperm

3. Results and discussion

The mean and standard deviation (S.D.) of the semen parameters for the infertile men's group and the normal control group are shown in Table 1 and Figure 2. When comparing the infertile group to the normal group, there was a noticeable decline in sperm-related parameters, including count, motility, viability, normal sperm morphology, ejaculate volume (in milliliters), and non-motile sperm. It was evident that there were differences in semen parameters between the infertile group and the healthy control group.

Table (1): The mean and standard deviation of semen parameters analysis of control group and infertile males' group

Parameters	Patients	Control	P value
Count	21±4.132	93±3.573	0.01
Active	26±5.352	92±7.814	0.01
Normal sperm	33.72±3.12	88±9.816	0.01
Abnormal sperms	77.45±8.36	12±514	0.01
Total motility	19±5.247	84±7.136	0.01
immotile	85±1.592	18±2.443	0.01
Viability	28.41±11.41	87.75±4.312	0.01
Volume	1.2	3.4	0.01

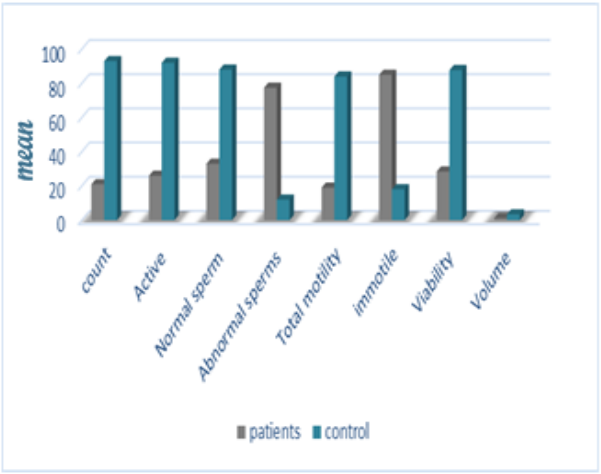

Figure 2: compare between patients and control groups

The data in Table 2 and Figure 3 show the results obtained before and after treating infertile males with selenium. These data indicate a significant increase in semen parameters in the infertile males after selenium supplementation, compared to the infertile male group before treatment.

Table 2: Results of semen parameters analysis of infertile men after treatment with selenium

Parameters	Patient	Treated	P value
Count	21±4.132	75±4.132	
Active	26±5.352	82±5.352	0.01
Normal sperm	33.72±3.12	72±3.12	0.01

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Abnormal sperms	77.45±8.36	22.45±8.36	0.01
Total motility	19±5.247	74±5.247	0.01
immotile	85±1.592	28±1.592	0.01
Viability	28.41±11.41	79.41±11.41	0.01
Volume	1.2	2.3	0.05

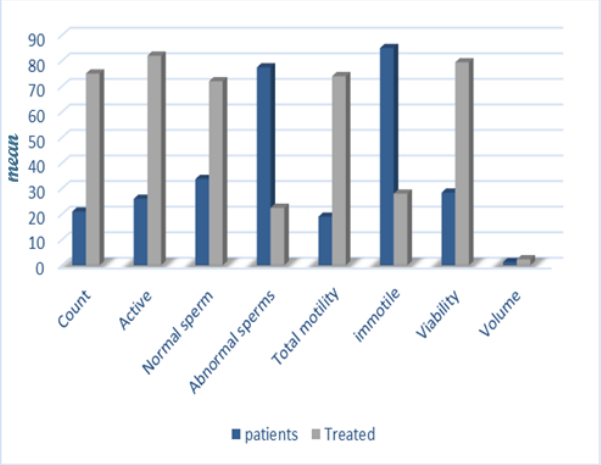

Figure 3: Semen parameters analysis of infertile men after treatment with selenium

When comparing the infertile group to the control group (Table 3), there was a notable increase in the TNF-α concentration. Additionally, infertile males had significantly higher levels of IL-6 and CRP than the healthy control group (Figure 4).

Table 3: Displays the TNF-α, IL-6, and CRP values for the control and infertile groups.

Parameters	Infertile Patients	Control	P Value
TNF-α	18.1±4.2	4.9±2.7	0.01
IL-6	19.4±7.3	5.7±1.4	0.01
CRP	20±61	3.8±2.9	0.01

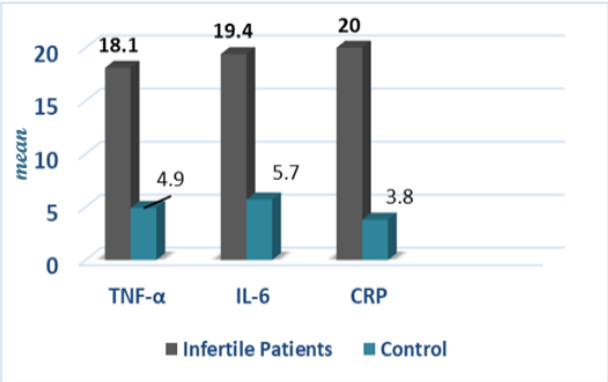

Figure 4: TNF-α, IL-6, and CRP values in the infertile group and the treated infertile male group

The findings showed a significant decrease in TNF-α levels in the treated infertile men compared to the untreated infertile men (Table 4). Furthermore, the use of selenium as a therapeutic agent demonstrated a notable reduction in IL-6 and CRP levels in infertile men receiving selenium treatment, compared to the infertile male group (Figure 5).

Table 4: Displays the TNF-α, IL-6, and CRP values in the infertile group and the treated infertile male group.

Parameters	Patients	Treated	P Value
TNF-α	18.1±4.2	6.5±1.8	0.01
IL-6	19.4±7.3	7.1±2.6	0.01
CRP	20±61	6.9±8.3	0.01

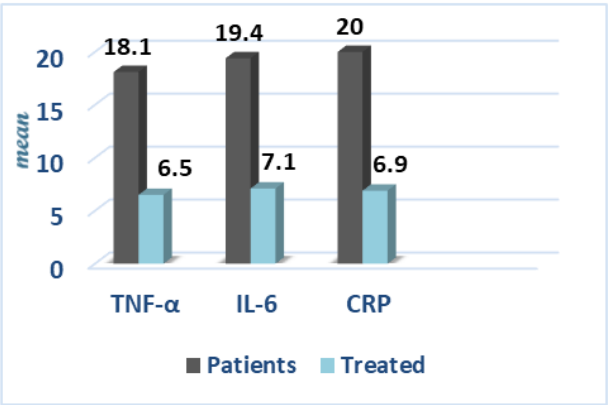

Figure 5: TNF-α, IL-6, and CRP values in the infertile group and the treated infertile male group

According to the study's findings, the semen parameters of infertile men significantly increased after treatment with selenium supplementation compared to their pre-

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treatment levels. The current study supports previous research (Agarwal et al., 2014), which indicated that selenium is crucial for spermatogenesis and improves semen parameters. Due to its antioxidant properties, selenium acts as an anti-inflammatory agent, protecting sperm from harmful conditions such as oxidative stress and infection. Because of selenium's antioxidant effect, there was a significant improvement in semen parameters after treatment, enhancing semen quality (Rossella et al., 2021). The findings of this investigation confirm those of previous studies, which found that selenium may function as an antioxidant, aid in sperm development, protect sperm, and enhance semen quality (Ata et al., 2022; Rayman, 2004).

Male infertility has been associated with inadequate sperm production, which is linked to selenium deficiency (Beckett et al., 2004; Behne et al., 1982). These findings corroborate the results of this research, which indicated that selenium intake is crucial for sperm production and for improving semen quality, both of which contribute to male infertility (Shuai Yuan et al., 2024; Arthur et al., 2003).

Selenium deficiency has been associated with inadequate sperm production, which is why selenium supplementation is important for sperm quality and production in male infertility (Shuai Yuan et al., 2024). Beckett et al. (2004) conducted another study that corroborated similar findings. According to this research, selenium has biological effects beyond male fertility (Ahmed, 2023), including preventing cancer, cardiovascular disease, viral mutations, influencing endocrine and immune system functions, enhancing the inflammatory response, and preventing inflammation. These effects align with the research of Beck et al. (2004).

In fact, it appears that selenium is essential for male fertility and the maintenance of normal spermatogenesis (Ahmed, 2023). When selenium is reintroduced, the testis absorbs it first, before other tissues (Carla and Rossella, 2008; Behne et al., 1982). In the event of a selenium deficiency, regulatory systems work to maintain an adequate level of this element within the male gonad. These findings, which align with the examiner's observations, underscore the importance of selenium in improving male fertility and semen quality (Sneha and Selvakumar, 2020).

In the current research, there was a significant decrease in the levels of TNF-α, IL-6, and CRP following treatment with selenium for three months in the treated infertile men, when compared to the infertile group before treatment. The findings of this study demonstrated that selenium reduces TNF-α, IL-6, and CRP levels, likely due to selenium's anti-inflammatory properties. These results align with previous research (Ata et al., 2022; Duntas, 2009).

These studies verified how selenium may decrease pro-inflammatory cytokine levels. The current research demonstrates a noteworthy reduction in TNF-α, IL-6, and CRP levels, supporting selenium's anti-inflammatory properties. A prior study corroborates this outcome (Valentina et al., 2022; Zamamiri-Davis, 2002). Increased concentrations of pro-inflammatory cytokines like IL-6 and TNF-α are believed to contribute to sperm dysfunction. Due to their impact on sperm quality, these aberrant sperm functions may lead to male infertility (Huleihel and Lunenfeld, 2004).

According to this research, selenium may also decrease levels of TNF-α, IL-6, and CRP, which protects sperm from the harmful effects of inflammation and improves sperm quality and male fertility. Furthermore, as this research has shown, selenium plays a crucial role in both sperm production and quality enhancement, both of which reduce male infertility. Therefore, infertile men may protect against inflammatory damage, increase sperm production, and improve the quality of their semen by consuming selenium, in line with the study reported by Fotios Dimitriadis et al. (2023).

The findings of this research show that selenium supplementation may decrease TNF-α, IL-6, and CRP levels in infertile men. This effect may be attributed to the mineral's antioxidant properties, which could also be beneficial in sperm production and enhance the overall quality of semen (Rossella et al., 2021).

4. Conclusion

This research concludes that selenium is considered an effective tool for enhancing semen quality and reducing levels of TNF-α, IL-6, and CRP, all of which may impact male fertility.

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Author Contributions

All authors contributed to data analysis, drafting and revising the article, provided final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Conflict of interest

The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be perceived as a potential conflict of interest.

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