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Açıklanamayan İnfertil Hastalarda Lökosperminin Sperm Parametreleri Üzerine Etkisi

The Effect of Leukospermia on Sperm Parameters in Couples With Unexplained Infertility

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ÖZET

Amaç: Seminal sıvıdaki lökositler ile semen kalitesi arasındaki ilişki literatürde hala bir tartışma konusudur. Bu çalışmada amaç, açıklanamayan infertil hasta grubunda lökosperminin semen parametreleri üzerine etkilerini araştırmaktır.

Materyal Metod: Haziran 2011 ile Aralık 2011 tarihleri arasında Ankara'da üçüncü basamak bir eğitim araştırma hastanesinin tüp bebek kliniğinde yapılan semen analizleri retrospektif olarak incelendi. Açıklanamayan infertilite nedeni ile başvuran çiftlerden erkeğe ait sonuçlar bu veriler arasından seçildi. Toplamda intrauterine inseminasyon ve in-vitro fertilizasyon siklusları için hazırlanmış olan 1637 semen analizi çalışmaya dahil edildi. Azospermik ve oligospermik erkekler çalışma dışı bırakıldı. Lökospermi saptanan 348 semen analizi ile (Grup I) saptanmayan 1289 semen analizi sonucu (Grup II) karşılaştırıldı.

Sonuç: Lökospermi (>10^6/mL) 348 hastada tespit edildi. Prevelansı toplamda %21.2 olarak değerlendirildi. İki grup arasında yaş, semen motilite ve morfolojisi açısından herhangi bir fark saptanmadı. (p>0.05) Semen hacmi, pH, konsantrasyon ve total sperm sayısı açısından ise iki grup arasındaki farkı istatistiksel olarak anlamlı olduğu izlendi. (p<0.05)

Tartışma: Bu çalışma sonuçları, açıklanamayan infertilite nedeni ile başvuran çiftlerin erkek partnerlerinde lökospermin sık olarak izlendiğini göstermiştir. Motilite ve morfoloji lökospermiden etkilenmiyor gibi görünse de, semen hacmi, sperm konsantrasyonu ve total sperm sayısı üzerine etkisi nedeniyle açıklanamayan infertile hasta grubunda lökospermi detaylı bir araştırmayı hak etmektedir.

Anahtar Kelimeler: Lökospermi, açıklanamayan infertilite, in-vitro fertilizasyon, intrauterin inseminasyon.

ABSTRACT

Objective: The association between seminal leukocytes and semen quality is still a matter of debate in the literature. The purpose of this study was to evaluate the effect of leukospermia on semen parameters in unexplained infertile men.

Materials and Methods: Semen analysis performed between June 2011 and December 2011 at infertility and in-vitro fertilization (IVF) clinic of a tertiary research and education hospital in Ankara were studied retrospectively. Results of the male partners of the couples with unexplained infertility were selected. A total of 1637 semen analysis of intrauterine insemination and in-vitro fertilization cycles were included in the study. Results of oligospermic and azospermic males were excluded. Semen parameters of 348 men with leukospermia (Group I) and 1289 without leukospermia (Group II) were compared.

Results: Leukospermia (>10^6/mL) was found in 348 patients. The prevelance was found to be 21.2% in total. There were no differences between two groups according the age, semen motility and morphology (p>0.05). With regard to semen volume, pH, concentration and total sperm count the difference between two groups were found to be statistically significant (p<0.05).

Conclusion: The results of this study showed that leukospermia occurs frequently in in male partners of couples with unexplained infertility. Although motility and morphology do not seem to be influenced by leukospermia, it deserves a detailed investigation in couples with unexplained infertility due to its effect on semen volume, sperm concentration and total sperm count.

Keywords: Leukospermia, unexplained infertility, in-vitro fertilization, intrauterine insemination.

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Introduction

Male infertility represents an important etiological factor for infertile couples to consider, and semen analysis is the backbone of male infertility evaluation that guides diagnosis. Among the parameters evaluated in the seminal analyses, the white blood cell count is considered, as are sperm concentration, motility and morphology. According to the World Health Organization (WHO), a leukocyte count ≥1 x 10^6/mL in a semen sample is indicative of leukocytospermia and is present in 10-20% general male population and more frequent in infertile men (1).

It is presumed to be a clinical sign of genitourinary tract infection or inflammation (2), multiple other causes as exposures to environmental toxins, vaginal products used during intercourse, tobacco products, alcohol, marijuana, and certain medications may lead to elevated leukocyte count in seminal fluid (3,4). A history of genitourinary surgery (vasovasostomy and uretheroplasty), presence of varicoceles, and autoimmunity are also potential noninfectious causes of leukospermia (5).

There are conflicting reports in the literature about the influence of leukocospermia on male fertility (6-8). However studies demonstrated that leukospermia has a negative impact on semen quality through the formation of reactive oxygen species (ROS) (9-11). ROS can cause lipid peroxidation of the sperm plasma membrane (12) and have been linked to increases in DNA fragmentation index (13,14). Additionally, if there is a breach in the blood-testis/genital tract barrier from a significant infectious or inflammatory process, anti-sperm antibodies (ASA) may be formed, which may impair sperm motility and fertilization ability (13). It is also implicated that the presence of leukocytes in seminal fluid ejaculate would be the best indicator of an atypical sperm penetration assay in normal semen analysis (15).

Materials and Methods

Semen analysis performed between June 2011 and December 2011 at infertility and in-vitro fertilization (IVF) clinic of a tertiary research and education hospital in Ankara were studied retrospectively. Results of semen analysis of male partners of couples with unexplained infertility were selected for the study.Patients were excluded from the study when oligospermia and azospermia was detected. A total of 1637 samples, 348 with leukospermia and 1289 without leukospermia were found to be eligible for the study. After patients had been instructed to void urine and cleanse their hands and genitalia with soap and warm water, semen samples were collected in the hospital by masturbation into a sterile container following a 3–4 days of sexual abstinence. The sample was processed within 90 minutes of collection. After liquefaction of ejaculates, computer-assisted semen analysis including sperm volume, pH, count, progressive motility and morphology was performed following the 2010 World Health Organization (WHO) guidelines (16). Leukospermia was defined in this study as use the standard WHO definition for leukocytospermia (1 x 106 leukocytes/mL).

Statistical analysis was performed using IBM SPSS Statistics 19.0 (SPSS). Results are reported as means ± SD, unless other wise specified. The 2-test and Pearson's correlation analysis was used to determine the relationship between leukospermia and other parameters of semen analysis. P<0.05 was considered statistically significant.

Results

A total of 1637 semen analysis of intrauterine insemination and in-vitro fertilization cycles were included in the study. Semen parameters of 348 men with leukospermia (Group I) and 1289 without leukospermia (Group II) were compared.

The rate of leukospermia in this unexplained infertility group was 21.2%. The comparison of semen parameters among two groups is summarized in Table 1. There is no statistically significant difference in sperm motility and morphology between two groups (p>0.05). There is a statistically significant deterioration in semen volume, concentration and total sperm count in group with leukospermia (p<0.05). pH is significantly higher in patients with leukospermia (p>0.05).

Discussion

The results of this study showed that leukospermia occurs frequently in male partners of couples with unexplained infertility. Although motility and morphology do not seem to be influenced by leukospermia, deterioration in semen volume, concentration and eventually total sperm count is evident.

Leukospermia is considered to be one of the causes of male infertility (17). Although in vivo effects of leukocytes are less clear, in vitro studies have shown that a high level of leukocytes can induce oxidative stress and alter sperm parameters (18). Sperm damage occurs via generation of reactive oxygen species (ROS) of which levels were positively correlated

Table 1. Semen analysis of patients with and without leukospermia.

	With Leukospermia (n=348)	Without Leukospermia (n=1289)	p values
Age (years)	31.9 ± 6.3	31.8 ± 5.9	0.898
Volume (mL)	2.9 ± 1.4	3.1 ± 1.4	**0.015***
pH	8.2 ± 4.5	8.0 ± 1.9	**0.006***
Concentration (million/mL)	37.4 ± 28.8	46.5 ± 35.5	**0.001***
Motility (%)			
a+b+c	38.0 ± 13.9	38.2 ± 13.5	0.945
a	14.4 ± 8.5	14.2 ± 8.3	0.805
b	23.2 ± 113.3	17.6 ± 23.2	0.632
Morphology (%)	8.3 ± 4.3	8.2 ± 4.2	0.825
Total sperm count (million)	96.3 ± 79.2	136.0 ± 113.7	**0.001***

*Statistically significant

with leukocyte count (19) and major source of ROS production (11). Intrinsically, the pathophysiological pathway of ROS-induced deleterious spermatozoa effects can be explained through a mechanism named lipid peroxidation (18) which is initiated by the attack of sperm membrane by ROS. Once ROS invade the sperm, they destroyed the genetic material of the cell including mitochondrial DNA, thus causing DNA damage and disrupting ATP production of the spermatozoa (18). Although the correlation between leukospermia and decreased sperm motility was previously shown by many reports in the literature (20,21), Ziyyat et al. reported an increase in sperm motility in semen samples with moderate leukocytospermia, but observed a paradoxical decrease in sperm motility in semen samples exceeding a threshold of 1 x 10^6 leukocytes/mL(22) which is also confirmed by Lackner et al (23). They concluded that the relationship between leukocytes and semen parameters is a complex one which may involve different factors and the effects of leukocytes on semen parameters may be concentration dependent. Not only the ROS, but also total antioxidant capacity of the seminal plasma clearly effects the damage to the sperm. Our results also could not demonstrate ant significant difference between two groups regarding the sperm motility.

On the other hand, the effects of leukocytes on sperm morphology remains controversial. Some authors have reported deteriorating sperm morphology with increased leukocyte concentration (15, 24-26) while others reported that a high number of leukocytes showed no significant association with abnormal sperm morphology (27,28). Conversely, a positive effect of leukocytes on sperm morphology has been reported by several researchers (6,29). In their recent study, Cavagna et al. Reported that no significant difference was found between sample with or witout leukospermia regarding the average numbers of sperm with normal form (18) which is consistent with the previously published study by Barraud-Lange et al (30). In line with the latter reports, percentage of morphologically normal sperms in both groups did not show a significant difference.

The relation between leukospermia and sperm concentration is more clear. Moskovtsev et al. indicated that leuko- cytospermia has a significant negative effect on the standard semen parameters of concentration (31).

Barraud-Lange et al. analysed 1955 semen samples and found a significant correlation between the amount of leukocytes and the deterioration of sperm countand total sperm number (32). Domes et al. also analyzed 7852 semen samples retrospectively and demonstrated a significant deterioration in sperm concentration (13). On the other hand, Aziz et al. failed to show any negative correlation between the leukocytic concentration in semen and sperm concentration (21). Our results also demonstrated a clear deterioration in sperm volume and concentration, both of which make a contribution to the decreased total sperm count.

As a conclusion, leukospermia occurs frequently in male partners of couples with unexplained infertility. Although motility and morphology do not seem to be influenced by leukospermia, it deserves a detailed investigation in couples with unexplained infertility due to its destructive effect on semen volume, sperm concentration and total sperm count.

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