Interleukin 6 and interleukin 8 concentrations in seminal plasma of male with seminogram abnormalities

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Abstract

Male infertility is a major diagnostic and therapeutic problem. Inflammatory process seems to be one of the most important factor influencing the parameters of seminogram. As currently used methods in above pathologies are still insufficient it has been postulated that novel parameters are necessary to make the diagnostics more accurate. Proinflammatory cytokines i.e. interleukins 6 (IL-6) and 8 (IL-8) seem to play an important role in inflammatory processes in male genital tract.

The aim of present study was to evaluate their significance in semen diagnostic in correlation to seminogram parameters as well as to well established inflammatory signs i.e. leukocytospermia.

We evaluated the correlation between the level of IL-6 and the rate of immobile spermatozoa in men with asthenoteratozoospermia that suggests its influence on impaired sperm motility. This observation was reinforced by the fact, that IL-6 level negatively correlated with slow progressive type of movement in this group of men.

The increased levels of IL-6 and IL-8 in seminal plasma of men with leukocytospermia and correlation between IL-6 level and number of leukocytes in semen in this group of men suggested relation of IL-8 and 6 with mobilization of inflammatory infiltrate in male reproductive system.

Key words: *male infertility, IL-6, IL-8, cytokines.*

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Introduction

Male infertility is a major diagnostic and therapeutic problem. Inflammatory process seems to be one of the most important factor influencing the parameters of seminogram.

As currently used diagnostic methods in inflammation are insufficient it has been postulated that novel parameters are necessary to make the diagnostics more accurate. Proinflammatory cytokines i.e. interleukins (IL-6) and (IL-8) seem to play an important role in inflammatory processes in male genital tract.

Interleukin 6 is believed to be one of the major mediators of the acute phase of the inflammatory reaction [20]. It is produced by Sertolli cells and may potentially act as a physiological paracrine factor [2, 16] in testis. The role of IL-6 in physiological reproductive processes was suggested by Naz and co-workers who observed its stimulating influence on capacitation and acrosomal reaction in an animal model [26]. The interdependence between the activity of gonadotropins, testosterone, and IL-6 and their relation to the development of the testis and spermatogenesis was also reported [32]. Additionally in experimental research, it was shown that IL-6 is also produced by LPS stimulated sperm cells [13].

Interleukine 8 is also called a neutrophil attractant and belongs to the group of chemokines.

It plays a crucial role in the inflammatory reaction (during the anti-infectious response it stimulates phagocytosis and bactericidal activity of neutrophiles), myelopoiesis, hematopoiesis, lymphopoiesis, graft rejection mechanisms, formation of inflammatory infiltration in autoimmune disorders, and in pathogenesis of allergic diseases [9]. Interleukin 8 has also an angiogenic activity and is involved in the formation of metastases [10, 37]. Similar to other cytokines, IL-8 is present in the human seminal plasma [7, 19, 37]. It was also observed that in normospermic men an average seminal plasma level

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of IL-8 far exceeds its blood level [37]. Koumantakis and coworkers noticed that in healthy men it is 31.5 times higher than the upper limit for blood concentration. So high a difference can suggest that IL-8 is originally produced within the reproductive system.

The aim of present study was to evaluate significance of IL-6 and IL-8 in semen diagnostic in correlation to seminogram parameters as well as to well established inflammatory signs i.e. leukocytospermia.

Material and methods

The study involved 107 men who in years 2004-2006 attended the Andrology Outpatient Clinic at the I Chair and Clinic of Obstetrics and Gynecology of Medical University of Warsaw. All patients underwent andrological examination. The semen obtained by masturbation after 3 to 10 days of sexual abstinence was collected to the sterile container. The semen was left for app. 30 minutes in the room temperature to liquefy, then a standard semen examination was performed. Laboratory assistants performed the semen examination manually in accordance with the 1999 WHO standards.

According to the results of semen examination, the patients were divided into three groups: asthenoteratozoospermia (44 patients), oligoasthenoteratozoospermia (20 patients), and azoospermia (12 patients). A separate group included the patients with normal semen parameters (15 patients).

The remaining portion of the semen sample was centrifuged at 1000 × g for 10 minutes and thus obtained seminal plasma was frozen in minus 18 centigrade to prepare it for evaluation of the levels of IL-1β and IL-18 with commercially available sets (R&D System, USA; MBL, Japan).

In statistical analysis Mann-Whitney test and Spearman correlation were used.

Results

In patients with normospermia, the average sperm density was 49.60 ±1.80 mln/ml. The rate of spermatozoa characterized by type A motility was 27.50 ±0.7% and by type B motility 28.83 ±0.53%. The rate of immobile spermatozoa was 35.83 ±0.97%. The rate of abnormal spermatozoa was 68.00 ±0.43%.

In patients with asthenoteratozoospermia, the average sperm density was 56 ±3.36 mln/ml. The rate of spermatozoa characterized by type A motility was 14.37 ±0.66% and by type B motility 21.25 ±0.56%. The rate of immobile spermatozoa was 53.13 ±0.84%. The rate of abnormal spermatozoa was 74.50 ±0.38%.

In patients with oligoasthenoteratozoospermia, the average sperm density was 5.68 ±0.9 mln/ml. The rate of spermatozoa characterized by type A motility was 9.17 ±1.31% and by type B motility 15.00 ±0.71%. The rate of immobile spermatozoa was 63.33 ±2.08%. The rate of abnormal spermatozoa was 79.00 ±0.80%.

The level of IL-6 was not significantly different in patients with normospermia, asthenoteratozoospermia, and oligoasthenoteratozoospermia. However, it was distinctly different from the IL-6 level in patients with azoospermia (the values of $p < 0.05$ were found when patients with normospermia, asthenoteratozoospermia, and oligoasthenoteratozoospermia were compared to those with azoospermia) (Fig. 1.).

Interleukin 8 level in the seminal plasma of men with asthenoteratozoospermia showed significantly higher values than in men with normal semen parameters ($p < 0.01$). The IL-8 level was also demonstrated to be higher in men with oligoasthenoteratozoospermia than in men with normospermia, however this difference was on the border of statistical significance ($0.1 > p > 0.05$).

In the group of azoospermic men, IL-8 level was found to be significantly lower than in men with astheno-

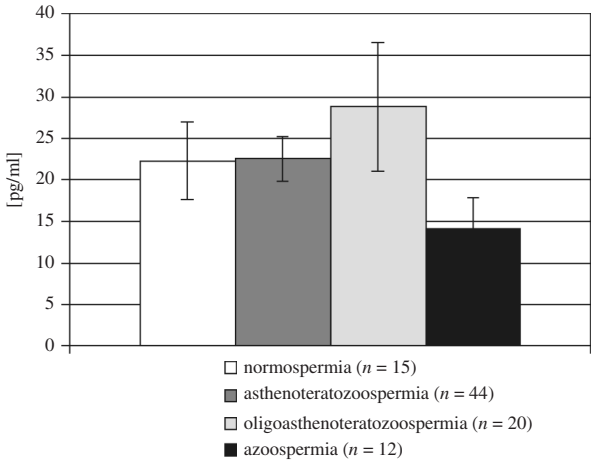

Fig. 1. Interleukin 6 concentrations in seminal plasma of examined groups

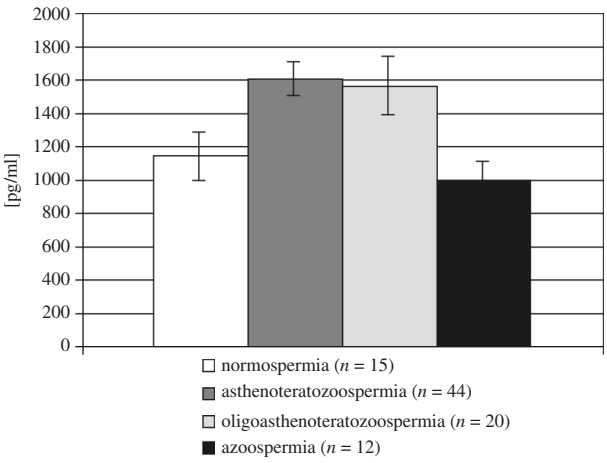

Fig. 2. Interleukin 8 concentrations in seminal plasma of examined groups

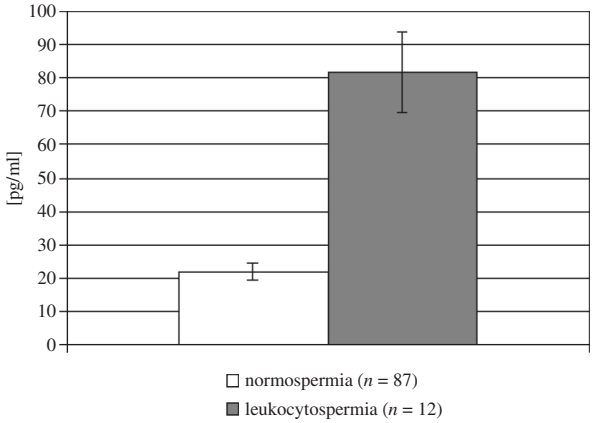

Fig. 3. Interleukin 6 concentrations in men with leukocytospermia

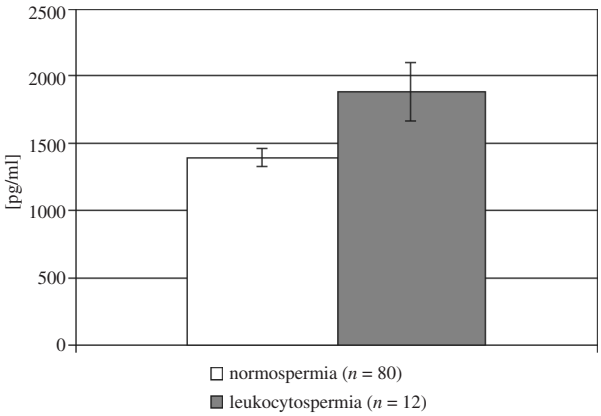

Fig. 4. Interleukin 8 concentrations in men with leukocytospermia

teratozoospermia ($p < 0.02$) and oligoasthenoteratozoospermia ($p < 0.03$) (Fig. 2).

The concentration of IL-6 in seminal plasma of men in whom leukocytes were observed in semen examination was demonstrated to be significantly higher than in control group ($p < 0.001$) (Fig. 3). Similarly, IL-8 level was observed to be higher in men with leukocytospermia than in men without increased leukocyte count in their semen ($p < 0.04$) (Fig. 4).

No correlation was found between the rate of spermatozoa with type B motility and IL-8 level. The statistically significant negative correlation between IL-6 level and the rate of spermatozoa showing type B motility was demonstrated. No correlation was found between the rate of immobile spermatozoa and the level of IL-6 (the result on the border of statistical significance) and IL-8. There was no correlation between the rate of abnormal spermatozoa and IL-8 level, however there proved to be a statistically significant correlation between the rate of abnormal spermatozoa and the level of IL-6 in the seminal plasma (Tab. 1).

The correlation was shown between IL-6 level and the number of leukocytes in the group of men with normal leukocyte count in semen examination. There was also a statistically significant correlation between the number of leukocytes in the semen and the level of IL-6 in the seminal plasma of men with leukocytospermia (Tab. 2).

Table 1. Correlation between IL-6 concentrations and sperm motility and pathology in men with asthenoteratozoospermia

Correlation	*R*	*p*	*n*
% type B motility spermatozooa vs. IL-6	–0.32	0.049	44
% immobile spermatozooa vs. IL-6	0.32	0.05	44
% of abnormal spermatozoa vs. IL-6	0.45	0.01	44

Table 2. Correlation between IL-6 concentrations and leukocytes count in men with leukocytospermia

Correlation	*n*	*R*	*p*
Leukocytes count vs. IL-6	12	0.83	0.001
Leukocytes count vs. IL-8	12	0.35	0.26

Discussion

Our results did not show any differences in the levels of IL-6 in seminal plasma in relation to the results of semen examination. Similar results were obtained by Huleihel's group that also did not found any differences [14].

The analysis of our results revealed significantly higher IL-6 levels in men with leukocytospermia as compared to the group with normal leukocyte count. This result was independent of semen parameters (number, motility, and morphology of spermatozoa).This findings confirm the observations of Swatowski [38] and other authors [28].

The role of IL-6 in the pathogenesis of impaired fertility associated with the infectious factor was confirmed by Elhija and coworkers who reported the increased level of this cytokine in the homogenates of mice testes in the response to systemic inflammatory reaction stimulated with LPS [6].

Present results also show that there is a strong correlation between the level of IL-6 in seminal plasma and the number of leukocytes in semen examination. Those results are in agreement with the reports of other authors who either correlated the level of IL-6 with the activity of granulocyte elastase [18] or with the total number of leukocytes in semen [30].

Our findings are also in agreement with the report of Matalliotakis, who did not found any relation between IL-6 level and results of semen examination, but noticed increased levels of IL-6 in men with accessory gland infection [24].

In turn, Furuya reported the correlation between decreased number of spermatozoa and the IL-6 level in the group of infertile men with oligozoospermia [8]. The main difficulty in comparing those results to our observations lies in the absence of men with isolated oligozoospermia in our material. This is because in our patients, the decrease in the number of spermatozoa was usually accompanied by abnormalities in their morphology.

As it was already mentioned, our study did not show any differences in the levels of IL-6 in relation to results of semen examination. However, a negative correlation was observed between the level of this cytokine and slow progressive sperm movement (type B) and, at the same time, a positive correlation was found between the rate of immobile spermatozoa and the level of IL-6 in seminal plasma of men with asthenoteratozoospermia. In addition, in this group of patients there exists a correlation between IL-6 level and the rate of abnormal spermatozoa.

Gruschwitz and coworkers found a negative correlation between fast progressive movement and the IL-6 level. Those authors, however, did not observed any relation of this cytokine to the rate of abnormal spermatozoa. Similar to other reports, they found increased levels of IL-6 in the group of patients with infection [11].

Additional observations on the influence of IL-6 on the sperm motility come from the research by Yoshida who reported the negative influence of IL-6 and sIL-6R on sperm motility in *in vitro* setting [39]. That report confirms clinical observations made in our study.

There are also studies pointing not only to the relation of abnormal semen examination to the level of IL-6 but also to the negative influence of this cytokine on penetration test results, i.e. directly on the semen fertilizing capacity [27], which further emphasizes its role in impairing fertility.

There is some doubt as regards the lack of differences in IL-6 level in the groups of men with different semen examination results, both in this study and in other reports dealing with this kind of analysis [40], while there is a correlation with semen parameters in the group of men with impaired motility and increased rate of abnormal spermatozoa. Possibly, it may be related to the increased concentration of soluble IL-6 receptor, i.e. changes in its biologic availability.

Even though, Huleihel and coworkers showed that the level of soluble IL-6R does not differ in infertile and fertile men [12], contrary findings were presented by Matalliotakis who reported higher sIL-6R level in men with accessory gland infection than in control subjects [23].

From the cited reports, it seems that activity of IL-6 in the infection of male accessory glands is affected by its absolute concentration and also other factors, such as the presence of antagonists or the bio-availability of its receptor.

It should be stressed that the evaluation of IL-6 level in seminal plasma strongly correlates with the presence of leukocytes, which highlights the role of IL-6 in the pathogenesis of inflammation of male accessory glands.

The role of IL-6 in the diagnostics of inflammation of accessory glands was denied only in one report by Dousset [4], however, it seems that those results could have been affected by the heterogeneity of the evaluated group of men as regards the result of semen examination and clinical diagnosis.

At the same time, according to present results, one can conclude that this cytokine is involved in spermatogenesis affecting its proper course. The correlation with the rate of immobile spermatozoa and negative correlation with progressive movement confirms its role in impairing the quality of semen. It seems, that the induction of oxidative stress by IL-6 activated leukocytes in inflammatory infiltrate is a main mechanism behind those abnormalities [17].

This theory seems to be confirmed by observations of Camejo, who found a strict relationship between the level of IL-6 and the level of peroxidation of cellular membranes of spermatozoa of infertile men [1].

In addition to the increase in IL-6 level, the quality of semen deteriorates due to the decrease in the concentration of cytokines with immunosupresive activity, (for example: IL-10), which intensifies conception problems [1].

The relation between the levels of IL-6, IL-8, and CAF (monocyte chemotactic and activating factor) in seminal plasma of infertile men [36] which points to the presence of the net of mutual relationships between cytokines leading to the formation of inflammatory infiltrate, leukocyte activation, and deterioration of semen parameters in the consequence of the infection of male accessory glands.

The clinical confirmation of the significance of observation of increased levels of IL-6 is also to be found in the study by Nallella, who reports on an increased IL-6 level in men with the varices of the spermatic cord [25].

Chemokines are cytokines of a well-known significance for the reproductive processes. They act as mediators in many processes associated with angiogenesis during formation of placenta and are involved in mechanisms affecting the dilation of uterine cervix in labor. The increased levels of chemokines are also observed in pathologic conditions of reproductive organs (for instance in ovarian tumors) [9].

At present, it is believed that IL-8 also plays a crucial role in pathology of male reproductive system, especially in male infertility. This fact is confirmed by observations of Koumantakis, who reported that seminal plasma level of this cytokine can be 30 times as high as blood level [19].

Our research revealed that IL-8 level in seminal plasma of men with asthenoteratozoospermia and oligoasthenoteratozoospermia is significantly higher than in men with normospermia.

Similar research was conducted by numerous authors. The previously cited author did not found statistically significant differences in IL-8 levels in groups of men with different etiopathogenesis of infertility. From the clinical standpoint however, this observation seems a little bit

imprecise, when one takes into account the fact, that it is often hard to unequivocally establish the cause of male infertility. In a great deal of cases, the etiology of infertility is multifactorial and it is hard to expect that such a classification would precisely account for a real etiologic factor of infertility.

The study by Matalliotakis and coworkers showed that IL-8 level was significantly higher in men with oligoasthenoteratozoospermia with infertility problem when compared to fertile and azoospermic men [22]. Those results are in agreement with the results of our study.

In addition, we found significantly higher levels of IL-8 in men with leukocytospermia. No correlation was found between the number of leukocytes in semen and IL-8 level in men with abnormal number of leukocytes in semen.

It is probable that IL-8 is an indicator of inflammation of male accessory glands which results in the abnormal result of semen examination. Our results agree with observations of other authors and highlight the role of IL-8 in the pathogenesis of inflammation in male reproductive system [21, 37].

It should be stressed that the presence of IL-8 was also noticed in the seminal plasma of men without leukocytospermia. This finding was previously reported by Depuydt and coworkers [3]. Those authors, however, suggest the correlation between the number of spermatozoa in semen and IL-8 level. In our material, such a correlation was not present in any of evaluated groups of patients. Thus, it seems that on the basis of our results, one cannot suggest the regulatory effect of IL-8 on spermatogenesis.

Pannekoek and coworkers published an analysis of IL-8 levels in the seminal plasma of men with bacteriologically confirmed Ureaplasma urealyticum and Mycoplasma hominis infection. Those authors did not find increased levels of IL-8 in evaluated patients, which, in their opinion, suggests that isolation of those microorganisms alone proves only colonization, not necessarily infection of male genitor-urinary tract [29].

The Eggert-Kruse group also reported the correlation between IL-8 and IL-6 level and positive bacteriologic cultures of semen, at the same time noticing the relation between the levels of those cytokines and leukocytospermia [5].

With reference to our results, it is probable that the absence of increased IL-8 level in those men can be explained by the fact that positive bacteriologic cultures were obtained in an early stage of infection, whereas the real increase in the concentration of mediators of inflammatory reaction was a later phenomenon. The authors did not explore the relation between IL-8 level and leukocytospermia, so it is hard to discriminate whether those men were only carriers or have an active inflammation.

In our study, no corelation was found between IL-8 level and semen parameters. Furuya and coworkers arrived at similar results. Our observations are also confirmed by one of the major studies dedicated to this problem conducted in Marburg University [18].

It seems that IL-8 does not independently influence spermatogenesis. Probably, its influence is exerted through mobilization of leukocyte infiltrate and stimulation of secretion of other proinflammatory cytokines. One of mechanisms that could explain the effects of IL-8 on spermatogenesis is overproduction of free oxygen radicals [33]. It is believed that the mobilization of leukocyte infiltrate and stimulation of metabolic activity of phagocytes by this cytokine leads to the overproduction of reactive forms of oxygen, that directly disturb spermatogenesis [34, 35]. Recent also reports underline the role of IL-8 as a highly sensitive marker of prostitis [15, 31].

Conclusions

The correlation that was found between the level of IL-6 and the rate of immobile spermatozoa in men with asthenoteratozoospermia suggests its influence on impaired sperm motility. Moreover, this observation is reinforced by the fact, that IL-6 level negatively correlates with slow progressive type of movement in this group of men.

The increased levels of IL-6 and IL-8 in seminal plasma of men with leukocytospermia and correlation between IL-6 level and number of leukocytes in semen in this group of men suggests its relation with mobilization of inflammatory infiltrate in male reproductive system.

References

1. Lipsky PE (2006): Interleukin-6 and rheumatic disease. Arthr Res Ther 8: S4-8.
2. Cudicini C, Lejeune H, Gomez E, et al. (1997): Human Leyding cells and Sertoli cells are producers of interleukins-1 and -6. J Clin Endocrinol Metab 82: 1426-1433.
3. Kishimoto T, Akira S, Taga T (1992): Interleukin-6 ad its receptor: a paradigm for cytokines. Science 258: 593-597.
4. Naz R, Kaplan P (1994): Increased levels of interleukin-6 in seminal plasma of infertile men. J Androl 15: 220-227.
5. Potashnik H, Elhija MA, Lunenfeld E, et al. (2005): Interleukin-6 expression during normal maturation of the mouse testis. Europ Cyt Net 16: 161-165.
6. Huleihel M, Lunenfeld E, Horowitz S, et al. (2000): Involvement of serum and lipopolysaccharide in the production of interleukin-1 – and interleukin-6 – like molecules by human sperm cells. Am J Reprod Immunol 43: 41-46.
7. Garcia-Velasco JA, Arici A (1999): Chemokines and human reproduction. Fertil Steril 71: 983-993.
8. Gawrychowski K, Skopińska Różewska E, Barcz E, et al. (1998): Angiogenic activity and interleukin 8 content of human ovarian cancer ascites. Eur J Gynaecol Oncol 19: 262-264.
9. Shimoya K, Matsuzaki N, Tsutsui T, et al. (1993): Detection of interleukin – 8 (IL–8) in seminal plasma and elevated IL-8 in seminal plasma of infertile patients with leukospermia. Fertil Steril 59: 885-888.
10. Friebe K, Bohring C, Skrzypek J, Krause W (2003): Levels of interleukin-6 and interleukin-8 in seminal fluid of men attending an andrological clinic. Androl 35: 126-129.

11. Koumantakis E, Matalliotakis I, Kyriakou D, et al. (1998): Increased levels of interleukin-8 in human seminal plasma. Androl 30: 339-343.
12. Huleihel M, Lunenfeld E, Levy A, et al. (1996): Distinct expression levels of cytokines and soluble cytokine receptors in seminal plasma of fertile and infertile men. Fertil Steril 68: 135-139.
13. Swatowski D, Jakiel G (2002): The influence of asymptomaic leucocytospermia in interleukin-2 and IL-6 levels in male semen plasma. Ginekol Pol 73: 841-844.
14. Ohta S, Wada H, Gabazza EC, et al. (2002): Evaluation of tissue factor antigen level in human seminal plasma. Urol Res 30: 317-320.
15. Elhija MA, Potashnik H, Lenenfeld E, et al. (2005): Testicular interleukin-6 response to systemic inflammation. Europ Cyt Net 16: 167-172.
16. Kopa Z, Wenzel J, Papp GK, Haidl G (2005): Role of granulocyte elastase and interleukin-6 in the diagnosis of male genital tract inflammation. Androl 37: 188-194.
17. Paradisi R, Mancini R, Bellavia E. T-helper type cytokine and soluble inteleukin-2 receptor levels in seminal plasma of infertile men (1997): Am J Reprod Immunol 38: 94-99.
18. Matalliotakis I, Kyriakou D, Fragouli Y, et al. (1998): Interleukin-6 in seminal plasma of fertile and infertile men. Arch Androl 41: 43-50.
19. Furuya Y, Akash T, Fuse H (2003): Soluble Fas and interleukin-6 and interleukin-8 levels in seminal plasma of infertile men. Arch Androl 49: 449-452.
20. Gruschwitz M, Brezinschek R, Brezinschek H (1996): Cytokine levels in the seminal plasma of infertile males. J Androl 17: 158-163.
21. Yoshida S, Harada T, Iwabe T, et al. (2004): A combination of interleukin-6 and its soluble receptor impairs sperm motility: implications in infertility associated with endometriosis. Hum Reprod 19: 1821-1825.
22. Naz R, Kaplan P (1994): Interleukin-6 enhances the fertilizing of human sperm by increasing capacitation and acrosome reaction. J Androl 15: 228-233.
23. Zalata A, Hafez T, Van Hoecke, Comhaire F (1995): Evaluation of beta-endorphin and interleukin-6 in seminal plasma of patients with certain andrological diseases. Hum Reprod 10: 3161-3165.
24. Huleihel M, Levy A, Lunenfeld E, et al. (1999): Expression of IL-12, IL-10, PGE2, sIL-2R and sIL-6R in seminal plasma of fertile and infertile men. Androl 31: 283-288.
25. Matalliotakis I, Arici A, Goumenou A, et al. (2002): Distinct expression pattern of cytokines in semen of men with gental infection and oligo-terato-asthenozoospermia. Am J Reprod Immunol 48: 170-175.
26. Dousset B, Hussenet F, Daudin M, et al. (1997): Seminal cytokine concentrations (IL-1beta, IL-2, IL-6, sR IL-2, sR IL-6), semen parameters and blood hormonal status in male infertility. Hum Reprod 12: 1476-1479.
27. Kocak I, Yenisey C, Dundar M (2002): Relationship between seminal plasma interleukin-6 and tumor necrosis factor alfa levels with semen parameters in fertile and infertile men. Urol Res 30: 263-267.
28. Camejo M, Segnini A, Proverbio F (2001): Interleukin-6 (IL-6) in seminal plasma of infertile men, and lipid peroxidation of their sperm. Arch Androl 47: 97-101.
29. Shimoya K, Matsuzaki N, Ida N, et al. (1995): Detection of monocyte chemotactic and activating factor (MCAF) and interleukin (IL)-6 in human seminal plasma and effect of leukospermia on these cytokine levels. Am J Reprod Immunol 34: 311-316.
30. Nallella KP, Allamanenni SS, Pasqualotto FU, et al. (2004): Relationship of interleukin-6 with semen characteristics and oxidative stress in patients with vericocele. Urol 64: 1010-1013.
31. Matalliotakis I, Goumenou A, Fragouli Y, et al. (2000): Soluble IL–6 receptor levels in the seminal plasma of infertile patients with accessory gland infection. Arch Androl 44: 237-242.
32. Maegawa M, Kamada M, Irahara M, et al. (2002): A repertoire of cytokines in human seminal plasma. J Reprod Immunol 54: 33-42.
33. Depuydt CE, Bosmans E, Zalata AA, et al. (1996): The relation between reactive oxygen species and cytokines in andrological patients with or without male accessory gland infection. J Androl 17: 699-707.
34. Pannekoek Y, Trum JW, Bleker OP, et al. (2000): Cytokine concentrations in seminal plasma from subfertile men are not indicative of the presence of Ureaplasma urealyticum or Mycoplasma hominis in the lower genital tract. J Med Microb. 49: 697-700.
35. Eggert-Kruse W, Boit R, Rohr G, et al. (2001): Relationship of seminal plasma interleukin IL-8 and IL-6 with semen quality. Hum Reprod 16: 517-528.
36. Rajasekaran M, Hellstrom W, Naz R, Sikka S (1995): Oxidative stress and interleukins in seminal plasma during leukocytospermia. Fertil Steril 64: 166-171.
37. Sanocka D, Jedrzejczak P, Szumala-Kąkol A, et al. (2003): Male genital tract inflammation; the role of selected interleukins in regulation of pro-oxidant and antioxidant enzymatic substances in seminal plasma. J Androl 24: 448-455.
38. Sanocka D, Kurpisz M (2004): Reactive oxygen species and sperm cells. Reprod Biol Endocrinol 2: 12-15.
39. Khadra A, Fletcher P, Luzzi G et al (2006): Interleukin-8 levels in seminal plasma in chronic prostatitis/chronic pelvic pain syndrome and nonspecific urethritis. Br J Urol Int 97: 1043-1046.
40. Penna G, Mondaini N, Amuchastegui S, et al. (2007): Seminal plasma cytokines and chemokines in prostate inflammation: interleukin 8 as a predictive biomarker in chronic prostatitis/chronic pelvic pain syndrome and benign prostatic hyperplasia. Eur Urol 51: 524-533.