

Inhibition of cryoglobulin synthesis as an effective method of positive influence on spermogram indices

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RESEARCH

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ABSTRACT

Background

Clinical signs of cryoglobulinemia syndrome depend on localization of affected vessels, and vascular pathology is a frequent cause of sexual disorders. Thus, the article presents correlation between cryoglobulinemia and spermatogenesis impairment.

Aims

The aim of our investigation was to study reference between cryoglobulinemia and spermatogenesis impairment. The method of intradermal autoleukocyte immunization was used for inhibition of cryoglobulin synthesis.

Methods

The research involved patients with idiopathic oligoasthenoteratozoospermia and various severe forms of infertility, when cryoglobulinemia of the 2nd and 3rd types was detected. Leukocytes for immunization were isolated from plasma of a patient's heparinized venous blood by centrifuging at 400g for 8 minutes, after that the residue

was resuspended in 1–1.5ml of own blood serum and injected intradermally in 0.1ml dose into the back. Spermogram indices were compared before and in 10–15 days after immunization.

Results

In most patients (75.0 per cent) with idiopathic oligoasthenoteratozoospermia and cryoglobulinemia, spermogram indices completely returned to norm due to inhibition of cryoglobulin synthesis. In men with severe forms of infertility, elimination of cryoglobulins also had a positive impact on spermatogenesis (100 per cent), which resulted in normalization of spermogram indices and improved the conditions for assisted reproductive technologies.

Conclusion

The results of investigation indicate that a considerable reduction of cryoglobulinemia has a positive impact on spermatogenesis. Therefore, it is expedient to include the method for detection of cryoglobulins into methodical recommendations/instructions for examination of patients with impairment of male fertility. Immunization with own leukocytes is recommended for inhibition of cryoglobulin synthesis.

Key Words

Spermogram, cryoglobulinemia, intradermal autoleukocyte immunization

What this study adds:

1. What is known about this subject?

Influence of cryoglobulinemia on spermatogenesis has not been studied completely. The presented data are the first ones in this area.

2. What new information is offered in this study?

The method of reduction of cryoglobulinemia by means of autoleukocyte immunization is suggested for improvement of spermatogenesis.

3. What are the implications for research, policy, or practice?

Implementation of the suggested technique promotes improvement of treatment efficacy of male infertility.

Background

One of the basic causes of sexual disorders is vascular pathology. However, in literature on andrology problems, pathogenic association with mixed cryoglobulinemia – frequent cause of vascular damage, is not regarded.

In our previous investigations,¹⁻³ it was established that inhibition of cryoglobulin synthesis in most patients with idiopathic spermatogenesis impairment leads to improvement (85.71 per cent) and complete normalization of spermogram indices (75.0 per cent). In further investigation, patients with various severe forms of infertility were involved.

Method

Totally 68 patients with idiopathic oligoasthenoteratozoospermia (1st group) and 40 patients (2nd group) with other types of infertility: 8 patients with secretory infertility; 15 – with excretory-toxic infertility; 13 – with varicocele and 4 patients with secondary secretory infertility and autoimmune thyroiditis were involved in the research. All patients were examined according to methodical recommendations of WHO⁴ as well as for cryoglobulin level. The difference in optic density of peripheral blood serum was determined before and after cooling for detection of cryoglobulins by spectrophotometry method. The difference was expressed in conditional units (CU), norm ≤ 10 CU. Types of cryoglobulins were determined by the method of historesistant curves. These methods were described in detail earlier.¹⁻³

In patients with cryoglobulinemia, HCV was excluded. Qualitative detection of HCV RNA was performed with the test-system AmpliSens (Russia).

The method of intradermal autoleukocyte immunization was used for inhibition of cryoglobulin synthesis. Thus, leukocytes were isolated by precipitation of a patient's heparinized peripheral venous blood in thermostat at 37°C for 90–140 minutes. After precipitation, blood plasma was carefully aspirated, leukocytes were precipitated by centrifuging at 400g for 8 minutes. The residue was resuspended in 1–1.5ml of own blood serum and injected with a syringe intradermally in 0.1ml dose into 8-12 points of the skin in the back. This method was also described earlier.^{1-3,5,6}

Results

On examination of 68 patients with idiopathic oligoasthenoteratozoospermia, cryoglobulins of the 2nd (n=10) and the 3rd (n=14) types were detected (n=24; 35.29 per cent). The amount of spermatozoa was below 5mln/ml in 16 of them (66.67 per cent), and in other individuals (n=8; 33.33 per cent) – within 5–10mln/ml. In 10–15 days after autoleukocyte immunization, index of cryoglobulinemia returned to normal or decreased by ≥ 50 per cent and spermogram improved (87.5 per cent; $p < 0.001$) in 21 patients (out of 24); level of spermatozoa increased to ≥ 15 mln/ml, their progressive motility and percentage of normal forms became normal in 18 individuals (75.9 per cent).

Out of 40 patients of the second group, cryoglobulins were found in 23 (57.50 per cent), namely: in five patients with primary secretory infertility, in 4 – with secondary secretory infertility, in 11 – with excretory-toxic infertility, in 3 – with varicocele. After autoleukocyte immunization, amount of cryoglobulins considerably decreased in 20 patients 86.96 per cent (the index became normal in 12 of them, in 8 – decreased by 40 per cent and more); different ranges of spermogram improvement occurred, i.e., the level of spermatozoa reached ≥ 15 mln/ml in 11 patients out of 20 (55 per cent). Pregnancy in natural cycle occurred in wives of two patients with varicocele and in five individuals with excretory-toxic infertility (n=7; 35 per cent). In cases when spermatogenesis normalization did not occur (n=9; 45 per cent), the level of spermatozoa increased and improvement of their functional ability was observed anyway, thus, possibility for assisted reproductive technologies appeared or the chances for effective artificial fertilization improved.

Discussion

The complexity of the investigated issue involves the problem that the mechanism of a negative influence of cryoglobulinemia on spermatogenesis has not been studied completely; there are only some reports about correlation between cryoglobulinemia and male infertility.¹⁻³

Since cold-shock precipitating proteins result in vascular damage,⁷⁻¹⁰ a negative influence of cryoglobulins on spermatogenesis can be explained by vascular pathology, because it is regarded as a frequent cause of sexual disorders.¹¹ Depending on localization and intensity of vascular damage, various pathological processes can occur, in particular, renal insufficiency, mono- and polyneuropathy, impairment of cerebral circulation, which, according to scientific literature, can have a negative impact on spermatogenesis.

Thus, cryoglobulinemia can indirectly influence spermogram indices; however, it may have a direct negative influence on the condition of hematotesticular barrier, as well as morphological peculiarities and functional activity of spermatozoa.

Male infertility, caused by cryoglobulinemia, is often considered as being idiopathic, though, by our data, it can be referred to the group of immunological infertility.

However, it is difficult to explain a positive effect of autoleukocyte immunization on spermogram indices due to its wide range of curative influence. Thus, autoleukocyte immunization has a beneficial influence not only on cryoglobulinemia syndrome, but also other autoimmune processes,¹² a significant number of which can lead to spermatogenesis impairment.^{11,13}

The mechanism of effect of autoleukocyte immunization is described in scientific literature.¹²

Conclusion

Thus, patients with fertility disorders should be examined for cryoglobulinemia. Such approach should be included to methodical guide/ instructions for infertility treatment. The suggested method saves time and costs for treatment, increases chances for gamete quality, and, thus, a chance for pregnancy.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

The study was approved by the local Ethical Committee of Danylo Halytsky Lviv National Medical University. Before the research, all patients were informed and gave consent for the investigation.