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Clinical Effect Of Plasma Exchange In Patients With Rheumatoid Artritis

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Abstract

Rheumatoid arthritis (RA) is a chronic systemic connective tissue disease with multiple organ impairment and unknown aetiology.

Rheumatoid arthritis leads to activation of immune processes and formation of abnormal antibodies. They participate in antigen-antibody complexes and accumulate in various tissues (mainly in synovial tissue). The removal of circulating complexes through plasmapheresis (PP) has good clinical effect (elimination of the nodules in RA).

The aim of the study is to monitor the clinical effect and to establish the clinical changes after plasma exchange (PE) in patients with RA.

PP achieves immunomodulation but it is necessary to continue the supporting cytostatic therapy to avoid the so called rebound effect.

Introduction

Rheumatoid arthritis and arthroses present with an extensive set of symptoms which accounts for the variety of methods and medication used for treatment. The aim of the therapy is to relieve the pain syndrome as well as to significantly reduce the inflammatory process. The effect of physical exercises cannot guarantee success while the inflammatory process and the pain are dominant (1, 2).

Anti-rheumatic medications as non-steroidal anti-inflammatory drugs (NSAID) and corticosteroids are applied mainly because of their ability to suppress the inflammation that damages the joints. Their effect on the main disease process is minimal (6).

It is common to prescribe modifying the disease anti-rheumatic drugs. The term ‘modifying’ comes from their ability to slow down and even hold the advance of rheumatoid arthritis rather than treat the symptoms. Their efficacy is observed in two-thirds of patients who take them regularly. In recent years modifying drugs are prescribed in the early stages of the development of rheumatoid arthritis. Due to their slower action they should be taken for months until their beneficial effect is established. Most often they are combined with NSAID or corticosteroids (9).

Rheumatoid arthritis (RA) is a chronic systemic connective tissue disease with multiple organ impairment and unknown aetiology.

Treatment with plasma exchange (PE) is applied successfully in more than 100 different diseases but the effect of the treatment is proven in about 40 of them. Most often the method is applied for diseases in neurology, nephrology, haematology and rheumatology.

In rheumatoid arthritis the immune tolerance is disrupted and abnormal antibodies are formed. They participate in antigen-antibody complexes and accumulate in various tissues (mainly in synovial tissue). The removal of circulating complexes through plasmapheresis (PP) has good clinical effect (elimination of the nodules in RA).

Another mechanism for effect of PE is on cellular immunity through returning to normal of T-suppressor and T-helper cells. That influences the beneficial therapeutic effect of the treatment for a long time.

According to K. Takahashi, apart from circulating immune complexes (CIC), the application of PE in RA eliminates rheumatoid factors, cryoglobulins and other unidentified plasma components. By eliminating those factors, the reticulo-endothelial system is de-blocked. A combined treatment of PE and pulse steroidal and/or non-steroidal therapy is recommended (9, 11, 12).

Jaffe (1963) is the first who administered treatment with PE in 4 patients with RA. Many authors acknowledge the increase in CIC as a main indicator for RA activity. The use of PE removes from the organism antigens, antibodies, auto-antibodies, CIC, fibrinogen and other substances (8, 13, 14).

It is recommended to include treatment with PE in cases with high level of RA activity and rapid progress as well as in those not affected by standard

medication treatment. Symptoms of rheumatoid vasculitis are also indication for PP (9, 10, 15).

Methods

The aim of the study is to monitor the clinical effect and to establish the clinical changes after plasma exchange (PE) in patients with RA.At the Clinic for Dialysis at St Marina University Hospital in Varna, plasma exchange was applied in 8 patients (6 women and 2 men) with mean age of 53.04 years and duration of the main illness 2-3 years. The plasma exchanges were performed with plasma filters 'Plasmaflux P'. A total of 22 plasma exchanges were carried out at an interval of 4.73 days with extraction of average 1,304 ml plasma per procedure. The exchange was done by infusion of native plasma and water-electrolytes solutions in approximately equal quantities.

During the sessions the patients showed stable haemodynamic indicators of blood pressure, heart rate and heart rhythm.

Review

At the beginning of the treatment the patients displayed severely suppressed phagocytic activity of the polymorphonuclear leucocytes. PP showed a de-blocking function in relation to the overloaded reticulo-endothelial system characterised with phagocytosis stimulation and reaching normal parameters (Fig. 1).

A decrease in insignificant values was established in the three classes of immunoglobulins. Similar results were achieved in the complement and its C3 fraction. The decrease in CIC values after PP was significant (Fig. 2).

The results received correlate with results reported by other researchers.

Authors inform about recovery of necrotic changes in the knee joint established by X-ray. Others report application of PP in acute exacerbations in rheumatoid arthritis. Administration of PP in the overall treatment allows for reduction of the intake of non-steroidal anti-inflammatory drugs, hence lower risk of gastric ulcer. A relatively good but short-term clinical and paraclinical effect achieved in patients presented in

1. Decrease of pain intensity;
2. Decrease of 'morning stiffness' duration;
3. Decrease in CRP values.

No change was registered in the titre of the agglutination test of Waaler-Rose.

The serum factor that agglutinates the sensitised sheep erythrocytes was found out as early as 1922, but it was in 1940 when Waaler emphasised its connection with rheumatoid arthritis. Rose et al. re-discovered the test in 1958 and in its final variant it carries the names of both authors: test of Waaler-Rose.

Treatment with methotrexate 7.5 mg/week and non-steroidal anti-inflammatory drugs continued. In 3 patients, due to early pulmonary fibrosis, the cytostatic therapy was replaced with corticosteroids (prednisolone – 30 mg/day).

No significant changes were established in the immunoglobulins and C3 fraction of the complement before and after administering PE.

It is proven that a large number of rheumatoid factors show activity of anti-nuclear antibodies, and that activity is best manifested in IgG. The cause for their activity is sought in the various possible mechanisms which probably provoke the synthesis of rheumatoid factors. They can be synthesized by B-lymphocytes not only under the influence of antigens of the type of allotype modified immunoglobulins but also by nuclear antigens and immune complexes (7).

The clinical importance for the established rheumatoid factors is significant in adult patients with rheumatoid arthritis. Although immunoglobulin M-RF is found regularly in patients with RA and presents a significant diagnostic criterion, its pathogenic role in joint changes is highly unlikely. It is considered that IgM-IgG immune complexes participate in the pathogenesis of vasculitis complications in rheumatoid arthritis (8).

Conclusion

In conclusion we can summarise that PE has a beneficial effect when included in the general treatment of patients with rheumatoid arthritis. The achieved immunomodulation contributes for an easier control of the severe autoimmune process.

Despite the small number of patients treated with PP,

the results give good reason to consider that PP in the general treatment of RA leads to insignificant and short-term clinical remission.

PP achieves immunomodulation but it is necessary to continue the supporting cytostatic therapy to avoid the so called rebound effect.

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Illustrations

Illustration 1

Circulating immune compelxes Changes after TPE

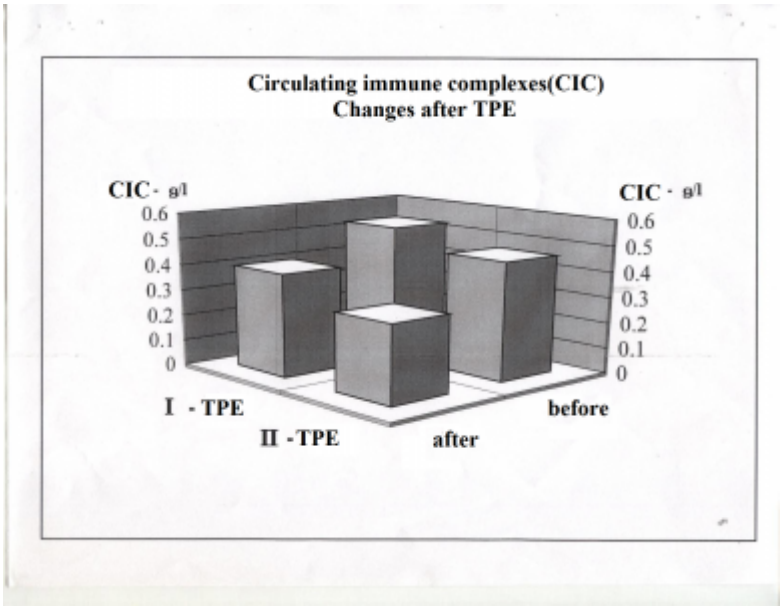
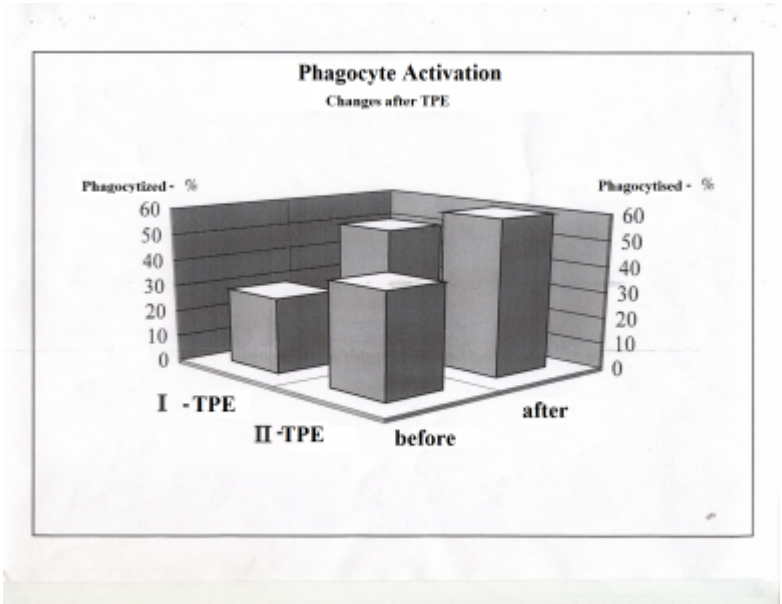


Illustration 2

Phagocyte activation Changes after TPE



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