ERUPTIVE PSORIASIS AND TREATMENT WITH RIFAMPICIN

N. Tsankov, I. Grozdev*, J. Kazandjieva

Department of Dermatology and Venereology,
Medical Faculty, Sofia, Bulgaria

ABSTRACT

Introduction: Psoriasis is considered a T-cell mediated inflammatory disease. Numerous studies show that rifampicin causes immunosuppression and inhibits T-cell function in conventional doses.

Object: Our object is to confirm the therapeutic effect of rifampicin in eruptive psoriasis and to explain its mode of action.

Materials and methods: Twenty-six patients, divided into two groups, were given 600 mg single-dose rifampicin daily for at least 60 days. Only emollients were used as adjuvant therapy. The efficacy was assessed using the PASI score, calculated at baseline and on 60th day.

Results: Group A presented the following: mean PASI at baseline 7.42. At end of treatment it was 2.04; 44.40% of the patients from Group A have PASI 75 or more at end of treatment. Group B presented the following: mean PASI at baseline 11.27; at end of treatment it was 2.35; 35.25% of the patients from Group B have PASI 75 or more at end of treatment.

Conclusion: The results as well as more than 10-year Bulgarian experience with rifampicin in the treatment of psoriasis show that its therapeutic effect in psoriasis is due to its immunosuppressive properties.

Key Words: eruptive psoriasis; rifampicin; PASI.

INTRODUCTION

Rifampicin (Rp) is a semi-synthetic derivative of Rifamycin B, which is a representative of rifamycin – macrocyclic antibiotics produced by Streptomyces mediterranei (1,2).

Rp inhibits the growth of most Gram-positive bacteria, as well as many Gram-negative microorganisms, such as Escherichia coli, Pseudomonas, indole-positive and indole-negative Proteus, and Klebsiella. Rp is active against Staphylococcus aureus and coagulase-negative Staphylococci (3).

Rp blocks the DNA-dependent-RNA-polymerase of mycobacteria and other microorganisms. A stable drug-enzyme complex is formed and the initiation phase of the RNA-synthesis is suppressed.

The use of antibiotics in the treatment of psoriasis appeared in the literature soon after the introduction of penicillin in clinical practice (4). In 1982 Rosenberg et al (5), published the hypothesis that psoriasis is an inflammatory disease caused by alternative activation of the complement by yeasts, Gram-negative microorganisms or Streptococci. Later on excellent results were reported on treatment of Streptococcus-associated psoriasis with antibiotic combinations including Penicillin and Rifampicin, as well as with Erythromycin and Rifampicin (6). The authors administered Penicillin or Erythromycin 250 mg q.i.d for 10-14 days. In the last 5 days of this schedule they added Rifampicin in 600 mg daily dosage.

Vincent et al (7) conducted a randomised controlled study to confirm or to reject the effectiveness of antimicrobial agents in psoriasis. They examined 20 patients with Streptococcus-associated psoriasis. A group of 10 randomly selected patients was given Penicillin or Erythromycin for 14 days with placebo during the last 5 days. The rest 10 patients were given the same antimicrobial therapy and Rifampicin (600 mg daily) in the last 5 days. The authors concluded that there was no apparent benefit for patients with Streptococcus-associated psoriasis from a course of oral penicillin or erythromycin in combination with rifampicin. It has to be
stressed that the group of Rosenberg and the group of Vincent both administered Rifampicin for only 5 days. Tsankov et al (3,8) were the first who used Rifampicin in severe forms of psoriasis administered in a single daily dose of 600 mg for at least 30 days and encouraging results were reported. Later the authors created other methodology proceeding from the hypothesis that Rifampicin has an independent action in psoriasis and it is not related with the effect on the Streptococci (9). On the other hand Kazandjieva et al (10,11), described two cases of pulmonary tuberculosis associated with inveterate psoriasis. The two patients were treated with Rifampicin for the pulmonary tuberculosis for a year. The authors observed clinical remission of the co-existing psoriasis which lasted 6 months after the treatment with Rifampicin. Nevertheless the patients did not use any topical or systemic treatment or take any special cares for the skin disease.

Our previous studies with 87 psoriatic patients (12,13,14,15) showed that Rp had a very good effect in patients with psoriasis associated with streptococcal infection as well as in patients without data for such an infection.

MATERIALS AND METHODS

We present 30 patients (16 women and 14 men, aged between 12 - 72 years) with eruptive psoriasis. They were divided into two groups according to the following criteria:

- Clinical evidence of dental, ear, nose, throat or genitourinary infection;
- Bacterial culture from the pharynx or vaginal smear;
- Positive antistreptolysin titre (>200).

Two groups were defined:

- **Group A** (9 patients) - *with* evidence of concomitant streptococcal infection.
- **Group B** (17 patients) - *without* evidence of concomitant streptococcal infection.

Four of them (one from group A and three from group B) were excluded from the study because of lack of compliance. Patients from the two groups were treated with Rifampicin administered orally in a 600 mg daily dosage for at least 60 days. The patients were given only emollients for topical therapy.

The efficacy of the treatment was assessed using the PASI (Psoriasis Area Severity Index) score. PASI includes the total body surface area affected with psoriasis and the severity of the most typical clinical symptoms of psoriasis – redness, scaling, and thickness of the lesions (16). PASI was measured at the beginning of the treatment and on the 60th day.

<table>
<thead>
<tr>
<th>Patients (women/men)</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI baseline</td>
<td>7.42</td>
<td>11.27</td>
<td>7.96</td>
</tr>
<tr>
<td>PASI 60th day</td>
<td>2.04</td>
<td>2.35</td>
<td>2.43</td>
</tr>
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RESULTS

The results were assessed on the 60th day using the PASI score. They are shown on Table 1:

Mean PASI in Group A at the end of the treatment was 2.04 (Figure 1). A 75% reduction of PASI is considered as a very good result of the treatment with great improvement of the disease. 44.40% of the patients from Group A achieved PASI 75 on the 60th day (Figure 3).

Mean PASI in Group B at the end of the treatment was 2.35 (Figure 2). 35.25% of the patients from Group B achieved PASI 75 on the 60th day (Figure 3).

DISCUSSION

Numerous studies in recent years consider psoriasis as an autoimmune disease of Th1 type.

Infections in psoriasis are a well-established triggering factor of psoriasis. Provoking infections could be traced in 44% of a mixed series of psoriatic patients (17). In the 1990s many authors considered the focal infections as a triggering factor of psoriasis (18,19,20,21). In recent times Blok et al (22) published a hypothesis that it is likely that a subgroup of psoriasics exists who is prone to exacerbation following infections as a genetic trait rather than a variable expression in the entire population of psoriatics.
Owen et al (23), suggested that although both antibiotics and tonsillectomy have frequently been advocated for patients with guttate psoriasis, there is to date no good evidence that either intervention is beneficial.

Rifampicin, administered in conventional doses, suppresses the T-cell function and the skin hypersensitivity towards tuberculin. In animal models Rifampicin causes immunosuppression. On the other hand the drug does not inhibit the production of antibodies to influenza vaccine and there are no data that the Rifampicin-induced immunosuppression has a harmful effect in patients who take the drug (24).

The review of the literature from the 1970s revealed that a number of authors considered Rifampicin as a drug which
suppresses both humoral and cellular immunity at the level of T-cells in vitro and in vivo. This warranted us to suggest that Rifampicin acts as an immunosuppressant. This fact had been discussed in numerous experimental studies (25,26,27,28).

It is speculated that the sensitivity to Rifampicin is more increased in the case of cells, which have pinocytic properties, namely macrophages, certain lymphocytes, and other immunocompetent cells. If this is the case, Rifampicin could exert its action at the level of phagocytic cells so that these cellular events would be associated with suppression of both antibody synthesis and delayed hypersensitivity (25).

Paunescu et al (25), investigated the effect of Rifampicin on the ability of rabbits and guinea-pigs to respond with circulating antibodies and delayed hypersensitivity to an antigen persisting for prolonged periods. The experimental findings showed that the continuous administration of Rp exerted an immunosuppressive effect, which was correlated with the dose. Thus, the dose of 20 mg/kg caused a delay, or even a suppression, of both immunological responses tested, whereas the dose of 40 mg/kg exerted a complete and constant immunosuppressive effect. The immunosuppressive action of Rp is reversible. In vitro in cultures of lymph nodes immunized with bovine serum albumin, the presence of Rp in the culture medium inhibits the production of the antibodies. Paunescu et al suggested an in vitro and in vivo immunosuppressive action of Rp, involving antibody production and certain cell-mediated forms of immunity, at least the delayed type of hypersensitivity. This effect is reversible in vivo and can be obtained when two or four times the therapeutic human doses are used.

Nilsson et al (26) found that stimulated human lymphocytes were significantly inhibited by Rp. Such an experimental system is a model of cell-mediated immune responses. The results suggested that Rp could suppress the DNA synthesis as well as the protein synthesis in the cells, which mediate the immune response to tuberculosis infection in man.

Gupta et al (28) conducted the following trial. They investigated 29 patients with pulmonary tuberculosis divided into two groups. Patients in group A (11 patients) received chemotherapy but no Rp was used. Patients in group B (18 patients) received Rp, 600 mg daily, for 2-35 weeks. The control group included 20 healthy persons. Total and differential leucocyte counts were done on peripheral blood. The main results of this study were as follows:

1. The T-cell levels in patients taking Rp were significantly lower than those in patients who did not take Rp.
2. Eight of the 18 patients in group B had significant suppression of the T-cells.
3. Of the eight patients who had T-lymphocyte suppression, only one patient had received Rp for less than 6 weeks, while only 4 out of 10 patients without T-cell suppression had received the drug for more than 6 weeks.
4. In the normal subject who had received Rp for 28 days the initial level of T-cells decreased significantly by 40% of the initial value at the end of 2 weeks.

Gupta et al found considerable T-lymphocyte suppression 2-3 weeks after the initiation of the Rp therapy. The cellular suppression, evident after 28-day treatment with Rifampicin, is transient when the drug is discontinued.

Nowadays new data for the immunosuppressive properties of Rp have appeared in the literature. Mlambo et al (29) reported that at high doses Rp moderately suppressed TNF-α and these findings suggested that Rp had differential immunomodulatory effects on the innate immune mechanisms. Rp can also modify cytokine production and Ziglam et al (30) published that the secretion of IL-1β and TNF-α were significantly inhibited (p<0.002) whereas secretion of IL-6 and IL-10 were significantly increased (p<0.003) by Rp treated mononuclear cells.

CONCLUSION

Our results express that there was no significant difference between group A and group B and the effect of Rp could not be related only to its antimicrobial properties. The clinical results warrant us to recognise the statements of Paunescu, Nilsson, Gupta, Mlambo and Ziglam and to consider that Rp could be given to patients with eruptive psoriasis. The therapeutic effect most probably is due to its immunosuppressive properties.

In the forthcoming era of the biological agents the use of Rp in psoriasis should seem naïve. But till the elucidation of their properties and their side effects we are convinced that Rp could be used in cases with eruptive psoriasis.
REFERENCES

29. Mlambo G, Sigola LB. Rifampicin and dexamethasone have similar effects on macrophage phagicytosis of zymosan, but differ in their effects on nitrite and TNF-