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Research Article

Pulse Immunomodulatory Mesotherapy of Psoriasis

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Abstract

Pulse immunomodulatory mesotherapy (PIMT) for mild and moderate forms of psoriasis is described. A suspension of a prolonged-acting glucocorticoid in a mini-dose - betamethasone 7 mg (or triamcinolone 40 mg) - is diluted with a saline solution of sodium chloride, 10-15 mg of methotrexate is added as an injection solution, and this mixture of drugs is injected intradermally into the lesions 1 time per month. The effectiveness of PIMT in psoriasis, which is an immune-dependent chronic disease, has been shown. PIMT is a convenient alternative to local corticosteroids - for the treatment of adults, adolescents and partly children. With a mild course of psoriasis, PIMT has a sufficient and pathogenetic effect. Advantages of PIMT: treatment is carried out no more than 1 time per month, simultaneously; the effect is manifested from the first days, stable; relapses become less frequent and weaker; the total dose of glucocorticoid with PIMT is no more (even less) than required with external corticosteroid therapy; the safety of PIMT is ensured by an acceptable fixed dose of the drug and its reliable natural decrease. Quality of life is improving (service and management are higher): the "ointment dependence" has been eliminated, the procedures are rare, not burdensome; temporary disability is reduced, hospitalization is not required. There is an economic benefit.

Keywords: Psoriasis; Pulse Immunomodulatory Mesotherapy; Mini-Dose of Glucocorticoid; Quality of Life

Psoriasis often occurs in mild to moderate severity. In this case patients are forced to use ointments for a long time and regularly, including corticosteroids, which is not always convenient. Meanwhile, the treatment of mild and moderate forms of psoriasis can be carried out in the form of single and rare (1 time per month or less) procedures. However, their action should be selective and directed [1]. Mesotherapy corresponds to these conditions: the right drug is injected little, rarely and in the right place – intradermally (!), into foci (M.Pistor). It is important to take into account the peculiarities of the pathogenesis of the disease [2,3].

Psoriasis is considered an immune-dependent disease. The effectiveness of local corticosteroids in this case is explained not just by the symptomatic, anti-inflammatory effect, but by the pathogenetic, immunomodulatory action. It has been established that topical corticosteroids in low ("subthreshold") doses that do not cause a systemic effect reduce the activity of NF-AT (nuclear T-cell activation factor), AP (activator protein), and NF-kB (nuclear transcription factor) in the skin. As a result, the expression of several dependent genes and the formation of proinflammatory cytokines/interleukins associated with them are inhibited [2]. The use of topical corticosteroids is grounded and justified. At the same time, using ointments and creams for chronic recurrent disease is not always convenient, even burdensome. In addition, it is difficult or impossible for the doctor to control how the patient himself reduces the dose/concentration of external corticosteroids and the area of their application. And it is necessary to dose corticosteroids,

although their concentration in ointments and creams does not exceed 0.1%, in order to avoid accumulation and the appearance of a systemic side effect.

The aim of the work is to summarize the experience of using pulse immunomodulating mesotherapy (PIMT) as an alternative to corticosteroid ointments and creams in the treatment of psoriasis; to evaluate the effectiveness of PIMT without additional "traditional" treatment, as well as the safety of this method and its possible prospects.

Material and Methods

155 patients with mild and moderate forms of psoriasis (83 men and 72 women) aged 15-60 years, median age Me = 30 ± 7 years were under observation. To assess the severity of the disease, the PASI index (Psoriasis Area and Severity Index) was used [4]. Mild degree of lesion: <10 PASI points, on average 4-7(±2) points, was observed in 46 people. The average degree of lesion: <50 PASI points, on average 20-30 (±10) points, - in 109 people. PIMT was not performed in severe forms of psoriasis: psoriatic arthritis, erythroderma, with PASI >50 points, as well as in the presence of severe general diseases (cardiovascular system, kidneys, liver, severe diabetes mellitus, etc.). This method was not recommended for pregnant and lactating women.

When assessing the general condition of patients, clinical blood and urine tests, ultrasound of internal organs, conclusions of specialist doctors on concomitant pathology, in particular, on the presence of foci of chronic infection (dental caries, sinusitis, tonsillitis, cholecystitis, etc.) were taken into account. The rehabilitation of the identified foci of infection was carried out beforehand or (in mild cases) simultaneously with treatment psoriasis. For statistical data processing, we used the determination of the confidence limits of the frequency of cases as a percentage (at p = 0.05) using special tables for small samples [5]. In this case, p = 0.05 means that the probability of error of the confidence bounds may be ± 5%.

The technique of pulse immunomodulating therapy (PIMT). A glucocorticoid of prolonged action in the form of a suspension for injection, 1 ml, - betamethasone 7 mg (Diprospan) or triamcinolone 40 mg (Kenalog), - is diluted with a saline solution of sodium chloride up to 5-10 ml (in a syringe), methotrexate 10-15 mg is added (in the form of an injection solution), and the resulting mixture is injected with an insulin syringe, with a needle with a diameter of 0.30-0.36 mm, intradermally into the main lesions. Thus, the drug is deposited in the skin at the sites of localization of the process. Age-appropriate doses are used for children. This procedure is repeated after 1 month if necessary. In case of skin lesions on the face, it is advisable to administer the drug regionally, behind the auricles. Regional and peri-focal administration is recommended for localization of the lesion in prominent places, since sometimes (apparently individually) an atrophic trace may remain. Sufficient dilution of the drug with saline solution and fractional administration at several points significantly reduce the risk of this complication. Children sometimes tolerate the injection more calmly at the border with the sore spot.

Results

In patients with psoriasis, 3-4 days after a single procedure of PIMT, the rash began to pale and flatten, progression stopped, and the feeling of discomfort decreased. With a mild degree of lesion (<10 PASI points; 46 patients), lenticular and partly numular papules gradually resolved, and after 3 weeks in 32 of 46 patients (in 53-81% of cases, at P = 0.05), the rashes disappeared or their number decreased to single ones. In the remaining 14 out of 46 patients (19-47% of cases, with P = 0.05), the manifestations of psoriasis after a single PIMT became noticeably less pronounced, and their number decreased significantly. After 1-2 more PIMT procedures, the skin cleared of rash in 37 out of 46 people (in 66-90% of cases, with P = 0.05). Remissions have lengthened, often up to 1 year or more. Only individual patients - 9 out of 46 (11-34% of cases, with P = 0.05) - required a monthly 3-fold PIMT to stabilize the normal condition of the skin. The papules that sometimes remained "on duty" were easily eliminated with ointments and UVL during a period of stable remission.

With psoriasis of moderate severity (<50 PASI points, on average 20-30 points; 109 patients) after a single PIMT, a decrease in redness, infiltration, peeling of lenticular papules, as well as some plaques, was observed after 3-5 days. Part of the lenticular papules gradually disappeared. Papules and plaques have become paler and less infiltrated. In general, 2-3 weeks after a single PIMT, the skin lesion decreased (according to PASI scores) by half or more in 22 patients out of 109 (15-32% of cases, with P = 0.05).

The lesion decreased by ¼-½ of the initial value in 32 (23-42% of cases), and by less than ¼ in 55 (45-65% of cases, at P = 0.05). After repeated PIMT (after 3-4 weeks), the result improved significantly. And after 2-3 PIMT, 90 out of 109 patients (in 82-95% of cases, at P-0.05) achieved almost complete skin release from rashes (with the exception of sometimes single "duty" papules) and, in addition, there were quite long remissions. PIMT was performed a little longer in 19 people (13-29%, P = 0.05).

Best of all, and often from the first time, psoriasis foci on the hands, on the feet, on the scalp, on the face, i.e. on the most "problematic" areas for the patient and for the doctor, succumbed to treatment! The effect was noted after the first PIMT and was fixed after 1-2 subsequent procedures. Also by pustular psoriasis on hands and feet. PIMT is most effective if it is carried out at the beginning of the progressive stage. In the stationary stage, it is possible to carefully supplement the treatment with ultraviolet irradiation of lesions.

Discussion

Pulse immunomodulatory mesotherapy (PIMT) should not be identified with systemic hormone therapy, in which the total dose of glucocorticoid is many times higher, by an order of magnitude and more than with PIMT. In addition, a mini-dose of glucocorticoid with PIMT is deposited for a whole month (7 mg/month. or 40 mg/month). This is facilitated by: prolonged action of the drug, as well as its intradermal administration. Unlike external corticosteroids, uncontrolled application of which can create a risk of exceeding the permissible dose, - with IPMT, the amount of the drug is deliberately limited to injection, 1 time per month. Contrary to fears, the total dose of glucocorticoid in IPMT is not higher (and even lower!) than in the treatment with corticosteroid ointments/creams. Let's make a simple comparative calculation. To treat a chronic skin process, at least 1 tube (15 g) of external corticosteroid will be required for 2 weeks. At a drug concentration of 0.1% (= 1/1000), this will be 15 mg: (15 g x 1/1000 = 0.015 g). For example, only half will be absorbed, i.e. 7 mg. So, the dose of glucocorticosteroid with external therapy is 7 mg in 2 weeks, and with PIMT - 7 mg (betamethasone) in 4 weeks, i.e. the dose for a week with PI MT is 2 times less! With PIMT with triamcinolone (40 mg/month), the shock dose of the drug decreases spontaneously within 4 weeks to 0. The average dose is no higher than 10 mg/ week, which is comparable to the average dose of external corticosteroids. The PIMT method is essentially based on the modern concept of SELECTIVE, "point" exposure [1], and the technique is borrowed from mesotherapy (M. Pistor): the desired drug is injected little, rarely, in the right place, intradermally. Target – skin lesions; the "therapeutic trigger" is a glucocorticoid in the minimum effective dose (like a "fuse"!). A chain reaction is triggered: glucocorticoid – specific receptor – glucocorticoid–receptor complex – nuclear DNA – transcription of the corresponding genes - cytokines/interleukins… The local action of glucocorticoids (in immune-dependent dermatoses) can be considered pathogenetic, since mini-doses of glucocorticoids inhibit the activity of the T-cell activation nuclear factor (NF-AT) and transcription factor (NF-kV) in the skin. Thus, they inhibit the transcription of dependent genes responsible for the formation of pro-inflammatory cytokines, interleukins [2].

Positive possibilities of IPMT in the treatment of psoriasis: 1) procedures no more than once a month and once-only ; 2) the effect is stable from the first days; 3) remissions lengthen, relapses weaken; 4) the course dose of glucocorticoid with IPMT is no more (often less) than with external corticosteroid therapy; 5) safety is ensured by a fixed, permissible dose of glucocorticoid and a reliable, gradual reduction to 0; 6) the quality of life improves: there is no "ointment dependence", hospitalization is not required, temporary disability is significantly reduced; the cost of an injectable drug is lower than most corticosteroid ointments and creams. Thus, the expediency of the IPMT method can be considered not only from a medical point of view, but also in terms of socio-psychological assistance and even in the financial and economic aspect.

With IPMT, no significant side effects were noted. The risk of an atrophic trace at the injection site (in some patients) can be significantly reduced due to sufficient dilution of the drug with a saline solution of sodium chloride and fractional administration at several points. It is also recommended to choose closed injection sites in certain cases, near the foci, or to do them regionally (for example, behind the auricles, if the lesion is on the face).

Contraindications for glucocorticosteroids in PIMT are the same as for external corticosteroid therapy.

Methotrexate is an effective drug for psoriasis [6], used, in particular, parenterally. It is believed that it inhibits the increased

proliferation of keratinocytes and the production of certain inflammatory mediators. With PIMT, methotrexate is used no more than once a month, only, which significantly reduces the likelihood of side effects.

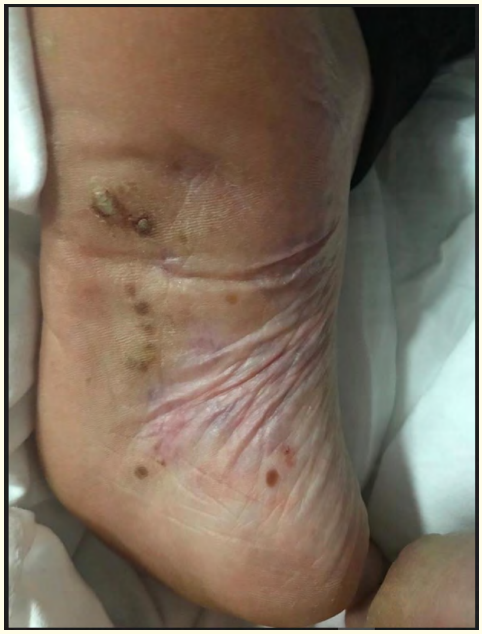

Figure 1: Pustular psoriasis on the sale.

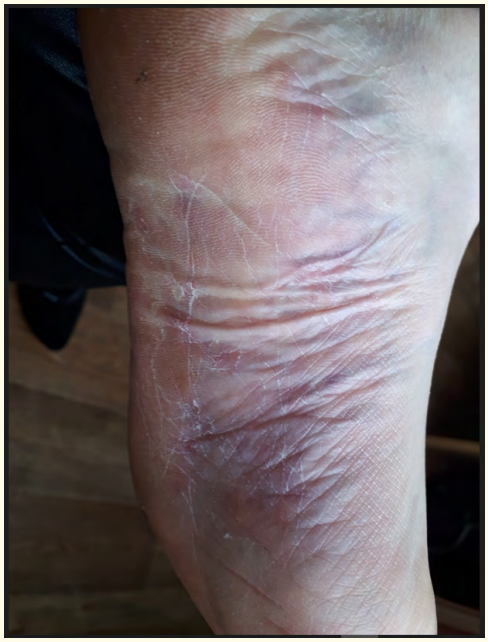

Figure 2: After 1 procedure of PIMT, - stable normal state.

Conclusions

- Pulse immunomodulatory mesotherapy (PIMT) it is based on the deposition of drugs in the lesions (intradermally), 1 time a month, in a minimally sufficient dose; in particular, a depot of a glucocorticoid of prolonged action is created. Thus, the inhibition of inflammation is initiated, up to 3-4 weeks. Often this is enough to normalize the condition of the skin..
- PIMT is a convenient alternative to external corticosteroids for mild and moderate forms of psoriasis and can be considered a clinically convenient and pathogenetic method of treatment.
- The safety of PIMT is ensured by the use of only a fixed and permissible dose of the drug, in particular glucocorticoid, once, with a long interval between repeated procedures (1 time per month or less).
- IPMT can significantly improve the quality of life of patients suffering from chronic relapsing disease, since a fairly long-lasting positive effect is achieved - almost immediately, after a single and quick, unencumbered procedure...

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