International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 02, 2020
ISSN: 1475-7192

Comparison of the Effectiveness of Various Doses of Ointment from a Dry Extract of Radix Glycyrrhizae in Contact Allergic Dermatitis

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Abstract— *It was established when comparing the effectiveness of different doses of ointment obtained from dry extract of radix glycyrrhizae in different doses, 5% ointment provides a more effective treatment of contact allergic dermatitis than 1%, 3% of the dose of this ointment, psilo-balm and topical celestoderm B. Accordingly, the index of reduction in severity of skin manifestations (Ind) was higher in this group than in others. All studied doses: 1%, 3% and 5% ointments of radix glycyrrhizae extract significantly reduced the thickness of the skin fold compared with the control group. Of the three doses of ointment, 5% ointment removed the swelling of the skin fold to its original position by 11th day than other doses of the ointment.*

Keywords— *glycyrrhizae, psilo-balm, celestoderm B, glucocorticosteroids (GCS),*

I. INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease. The prevalence of atopic dermatitis is increasing every year [6,7,8]. The prevalence of atopic dermatitis among children is up to 40%, among adults 1-3% [2,3].

External therapy plays a major role in the treatment and prevention of atopic dermatitis in children and adults.

Topical glucocorticosteroids (GCS) are widely used in the treatment of atopic dermatitis. With prolonged use, their safety and effectiveness have not been clarified, and the possibility of side effects is quite high [4]. In this regard, herbal medicines have more perspectives than other medicines [1].

Radix glycyrrhizae is a valuable medicinal raw material. Medicines based on it have a wide range of biological activity. The mechanism of anti-inflammatory action of glycyrrhizae is associated with the stimulating

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DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

effect of glycyrrhizic acid on the adrenal cortex. This pharmacological property of the plant is considered that the most important [1,8].

Purpose of the study. Comparison of the effectiveness of various doses of ointment from a dry extract of radix glycyrrhizae in contact allergic dermatitis in experimental animals.

II. MATERIALS AND METHODS

From the dry extract of radix glycyrrhizae and vegetable oils and animal fats obtained from local raw materials, a new hydrophobic ointment with the main properties was obtained by the biotechnological method, and developed a technology for producing 1%, 3%, 5% concentration.

Allergic contact dermatitis (ACD) was caused by double application of 5% alcohol-acetone 2,4-dinitrochlorobenzene (DNCB) on guinea pigs weighing 300-400 gr according to the method of E.Ya.Ivleva and P.M.Zalkan (1965). The sensitization centre was created on the back area of 3x3 cm² from which the coat was previously removed. DNCB was applied to the skin in a dose of 0.1 ml of 5% alcohol-acetone solution (2: 1). Animals with ACD one day after the second application of the allergen were given a current dose of ointment from a dry extract of radix glycyrrhizae. DNCB is a strong allergen with a high penetrating ability to be applied to the skin and provoking the development of a pronounced inflammatory reaction of an allergic nature, which, according to clinical signs, is adequate to the manifestations of allergic dermatitis in humans.

For the experiment used 36 guinea pigs weighing 300-400 gr. Experimental animals were divided into 6 groups of 6 animals each. Each group received an appropriate ointment.

1 group - intact control;
2 group - 1% ointment from a dry extract of radix glycyrrhizae;
3 group - 3% ointment from a dry extract of radix glycyrrhizae;
4 group - 5% ointment from a dry extract of radix glycyrrhizae;
5 group - applied antihistamine medicine - psilo-balm (diphen-hydromine);
6 group - applied ointment containing topical GCS celestoderm B.

For animals of groups 2-4, used therapeutic ointments were made on the basis of vegetable oils of local raw materials and hydrophobic fats of animal origin.

The above ointments were applied to animals of all groups, according to the scheme 1 time per day for 11 days. Observations of changes in the skin were carried out on the 1st, 3rd, 5th, 7th, 9th and 11th days of treatment, after the last application of the allergen (DNCB). The degree of development of dermatitis was assessed by the general condition and course of the allergic process on the skin: visually, allergic inflammation and the size of the skin fold with a micrometer.

On the first day of observation, limited reddish spots were detected in animals of group 1 (control group), in some with diffuse hyperemia, the state was estimated at an average of 0.6 ± 0.1 points. On the 3rd day, acute hyperemia, edema, hemorrhagic crusts and large ulcers were detected on the skin, an average of 4.6 ± 0.2 points. The condition on 5th day was similar to the third day of observation, averaging 4.3 ± 0.3 points. On the 7th, 9th and

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

11th day, the indicated changes persisted and amounted to 4.4 ± 0.4 and 4.0 ± 0.4, respectively. The total score of this group was 21.9 (Table 1).

In group 2, on day 1, some animals showed limited reddish spots and slight diffuse hyperemia, an average of 0.6 ± 0.1 points. By the 3rd day, the process was acute, with redness, swelling, hemorrhagic crusts and ulcers, and was estimated at 4.7 ± 0.2 points. A similar situation was observed on the 5th and 7th days. Only on the 9th day, there was a clear hyperemia and edema, an average of 3.0 ± 0.2 * points, and a significant decrease was revealed in comparison with the control group. By day 11, limited red spots and mild diffuse hyperemia were observed, an average of 1.8 ± 0.3 * points. The total score was 19.0. The cutaneous severity reduction index (Ind) was 13.2%.

In animals of the 3rd group of our experiment, on the first day, redness and slight hyperemia were detected, an average of 1.1 ± 0.2 points.

Table 1 Assessment of the severity of skin processes in the treatment of experimental contact allergic dermatitis.

Groups (M±m; n=6)	**The severity of skin processes in points, the days of the study**						**Total points**	**Ind %**
	1	3	5	7	9	11		
1-group (group control)	0,6±0,1	4,6±0,2	4,3±0,3	4,4±0,4	4±0,4	4,0±0,4	21,9	
2-group 1% ointment of dry radix glycyrrhizaeextract	0,6±0,1	4,7±0,2	4,6±0,2	4,3±0,2	3,0±0,2 *	1,8±0,3*	19,0	13,2
3-group 3% ointment of dry radix glycyrrhizaeextract	1,1±0,2	4,8±0,1	4,1±0,3	3,3±0,3 *	2,3±0,2 *	1,7±0,3*	17,3	21,0
4-group 5% ointment dry extract of radix glycyrrhizae	0,8±0,1	4,6±0,2	3,6±0,4	2,7±0,2 *	0,8±0,3 *	0,36±0,2 *	12,9	41,0
5- group psilo-balm	0,7±0,1	4,8±0,2	5±0	4,4±0,2	3,2±0,2 *	2,3±0,2*	20,4	6,84
6-group Celestoderm B	0,7±0,1	4,7±0,2	4,5±0,2	3,2±0,2 *	2,4±0,2 *	1,5±0,3*	17	22,4

* P≤0.05 ratio to the control group

On the 3rd day, the process was acute, with redness, swelling, hemorrhagic crusts and ulcers, an average of 4.8 ± 0.1 points. On the 5th day, the process was slightly weakened, with obvious hyperemia, swelling, severe redness and hemorrhagic crust and a small ulcer, estimated at 4.1 ± 0.3 points. By the 7th day of observation, the skin condition improved, mild diffuse hyperemia, obvious hyperemia were detected, accompanied by edema and severe redness, which averaged 3.3 ± 0.3*points. During the remaining days of observation, the indicators of this group relative to the control significantly decreased. By 9th day, limited red spots, slightly diffuse hyperemia, and obvious hyperemia with edema averaged 2.3 ± 0.2*points. By 11th day, the skin of two animals was completely restored - there was no reaction, limited red spots in one experimental, moderate diffuse hyperemia in two, and

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

obvious hyperemia was established in one case, with an average score of 1.7 ± 0.3*. The overall average score was 17.3, and the index for reducing the severity of skin manifestations (Ind) was 21.0%.

In observations of animals of the 4th group, on day 1, no reaction was detected on the skin of one animal, the remaining five animals showed limited red spots, which was estimated at 0.8 ± 0.1 points. On the 3rd day, there was a sharp change with a sharp reddening, swelling, hemorrhagic crusts and ulcers, an average of 4.6 ± 0.2 points. Starting from the 5th day, the skin of the animals improved, hyperemia, edema, and severe redness were observed, which were estimated at 3.6 ± 0.4*points. Reliable dynamics of changes in this group compared with the control was identified from this day of observation. By 7th day, the skin of the animals had slight diffuse hyperemia, distinct hyperemia, edema, an average of 2.7 ± 0.2*points. By the 9th day, the skin of one animal was completely restored - no reaction, the remaining five had limited red spots, estimated at 0.8 ± 0.3*points. On 11th day, the skin of four animals was completely restored, one had a limited red spot, and another had diffuse hyperemia, an average of 0.36 ± 0.2*points. The overall score was 12.9, and the cutaneous severity index (Ind) was 41.0%. It should be noted that during the experiment there was no case of death of experimental animals.

On the 1st day of our observation, experimental animals of the 5th group showed limited red spots and hyperemia with an average score of 0.7 ± 0.1, and on the 3rd day - acute redness, swelling, and in some animals hemorrhagic crusts and small wounds, an average of 4.8 ± 0.2 points. On the 5th day of the experiment, all animals showed hyperemia, edema, severe redness, hemorrhagic crusts and large ulcers, with an average score of 5.0 ± 0. By the 7th day, allergic inflammation on the skin of animals improved, there was great hyperemia, edema, severe redness, hemorrhagic crusts and small wounds, on average 4.4 ± 0.2 points. By the 9th day, the healing processes of the skin had a positive trend, there were sharp redness, swelling, hemorrhagic crusts and an average of 3.2 ± 0.2*points. From this moment, the indicators in this group have significantly changed in comparison with the animals of the control group. On the 9th day, the healing process of the skin in animals improved, that is, there were mild hyperemia and edema, an average of 2.5 ± 0.1*points. On the 11th day of observation, diffuse hyperemia was characterized on the skin of 2 animals, 2 had pronounced hyperemia and edema, 2 had sharp redness and slight edema, which was estimated at an average of 2.3 ± 0.2*points. The total score was 20.4. an index of reduction in the severity of cutaneous manifestations (Ind) was 6.84%.

In the 6 groups of animals in our observation, on the 1st day of the experiment, the same changes were noted as in the other groups: limited red spots and hyperemia and were estimated at 0.7 ± 0.1 points. By the 3rd day, acute redness, swelling, and in some hemorrhagic crusts and minor ulcers, which averaged 4.7 ± 0.2 points, were revealed. On the 5th day of our experiment, in some animals hyperemia and edema were observed, in some - redness and swelling, hemorrhagic crusts and small wounds, an average of 4.5 ± 0.2 points. By the 7th day, allergic inflammation on the skin of animals improved, with slight hyperemia, edema, in some with severe redness, hemorrhagic crust, an average of 3.2 ± 0.2*points. From this day until the end of the experiment, the indicators in this group significantly changed compared with the indicators in the control group. On the 9th day, the healing process of the skin of animals improved, that is, there was obvious hyperemia, severe redness, swelling, an average of 2.4 ± 0.2*points. On the 11th day of observation, 1 animal had no reaction, 2-diffuse hyperemia on the skin, 1-

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

diffuse hyperemia and 2-obvious hyperemia, with an average score of 1.5 ± 0.3*points. The total score was 17.0. The cutaneous severity index (Ind) was 22.4%.

During the experiment, another indicator of allergic dermatitis was measured - skin folds of animals (Table)

It was found that in animals of the 1st group (control group), before the experiment, the size of the skin fold was on average 0.27 ± 0.02 cm. In animals of this group, this indicator remained unchanged on the 1st day (0.43 ± 0.01 cm) and increased from the 3rd to the 7th (3rd day, 2.36 ± 0.1 cm, 5th day - 2.9 ± 0.16 cm, 7th day 3.0 ± 0,2 cm) days. Only from the 9th day did it begin to decline (10th day 2.3 ± 0.1; 13 days, 1.6 ± 0.1).

In animals of the 2nd group, the average rate of skin fold before the experiment was 0.23 ± 0.02 cm and began to increase from 1 day to 5 days (1 day 0.51 ± 0.03 cm, 3 days 1.43 ± 0,13*cm, 5th day 2.8 ± 0.1 cm). From the 7th day, a significant decrease in indicators was established in comparison with the control (7th day 2.0 ± 0.15*cm, 9th day 1.46 ± 0.1*cm, 11th day 0.91 ± 0.08*cm),

In animals of group 3, indicators of skin change were similar to those of group 2, the average value of which before the experiment was 0.22 ± 0.02 cm, and increased from 1 to 5 days (1 day 0.42 ± 0.01 cm, 3th day 1.47 ± 0.1 cm, day 5 2.8 ± 0.1 cm) and significantly decreased from 7th day (7th day 1.81 ± 0.06*cm, 9th day 1.28 ± 0.07*cm, 11th day 0.77 ± 0.08*cm).

Table 2 The influence of the studied medicines on the thickness of the skin fold in guinea pigs in experimental contact allergic dermatitis.

Groups	**The thickness of the skin fold, cm / days study, days of observation**						
	Exodus	**1**	**3**	**5**	**7**	**9**	**11**
1 group (control group)	0,27±0,02	0,43±0,01	2,36±0,1	2,9±0,16	3,0±0,2	2,3±0,1	1,6±0,1
2 group (1% ointment from a dry extract of radix glycyrrhizae)	0,23±0,02	0,51±0,03	1,43±0,13*	2,8±0,1	2,0±0,15*	1,46±0,1*	0,91±0,08*
3 group (3% ointment from a dry extract of radix glycyrrhizae)	0,22±0,02	0,42±0,01	1,47±0,1*	2,8±0,1	1,81±0,06*	1,28±0,07*	0,77±0,08*
Group 4 (5% ointment from dry radix glycyrrhizaeextract)	0,23±0,02	0,45±0,02	1,43±0,1*	2,63±0,1	1,73±0,1*	1,23±0,06*	0,46±0,05**
5 group (psilo-balm)	0,23±0,21	0,46±0,03	1,78±0,04*	3,0±0,2	2,08±0,13*	1,43±0,11*	1,1±0,08*
6 group (celestoderm B)	0,21±0,01	0,51±0,03	1,81±0,04*	3,25±0,2	1,86±0,14*	1,3±0,05*	0,93±0,04*

≤P 0,05 relation to the initial data

Our observations of animals of the 4th group determined 0.23 ± 0.02 cm before the start of the experiment and the increase from 1 to 5 days (1 day 0.45 ± 0.02 cm, 3 days 1.43 ± 0.1*cm, 5th day 2.63 ± 0.1 cm), and from the

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

7th day there was a significant decrease compared with the control group (7th day 1.73 ± 0.1*cm, 9th day 1.23 ± 0.06*cm, day 11 0.46 ± 0.05*cm), which was closer to healthy values before the experiment.

The average values before the experiment in animals of groups 5 and 6 were: if in group 5 0.23 ± 0.02 cm; in the 6th group 0.21 ± 0.01 cm, then in both groups from 1 to 5 days of the experiment the size of the skin folds increased (5th group: 1 day 0.46 ± 0.03 cm, 3 days 1.78 ± 0.04 cm, day 5 3.0 ± 0.2 cm; group 6: 1 day 0 51 ± 0.03 cm, day 3 1.81 ± 0.04 cm, day 5 3.25 ± 0.2 cm), from the 7th day there was a significant decrease in values relative to the control group (5th group: 2.08 ± 0.13 * cm on the 7th, 1.43 ± 0.11*cm on the 9th, 1 , 1 ± 0.08*cm on the 11th day, 6th group: 1.86 ± 0 on the 7th day 14*cm, on the 9th day 1.3 ± 0.05*cm, on the 11th day , 93 ± 0.04*cm).

III. RESULTS

Summarizing the results of our experiment, in animals of the 1st group (control group) moderate symptoms of ACD were observed on the 1st day and acutely progressed on the 3rd day. Despite the fact, that on the 5th day the reaction partially decreased, it did not significantly change until the end of the experiment. Changes in the skin that were observed in animals of group 2 were moderate. ACD on day 1, followed by a sharp increase in the next 3, 5, and 7 days and a significant decrease on day 9 with an (Ind) index of 13.2%. The same mild symptoms of ACD were observed in animals of the 3rd group on the 1st day, increased on the 3rd, a slight decrease on the 5th and a significant decrease on the 7th day, and the index (Ind) was 21.0%. In animals of the 4th group, mild symptoms of ACD were also revealed on the 1st day, which progressed to the 3rd and a significant decrease from the 7th day. The index for reducing the severity of skin manifestations (Ind) was 41.0%. In animals of group 5, mild allergic dermatitis was established on the first day of the experiment, but on the 3rd and 5th day the skin inflammation was acute, which was observed with a slight decrease on the 7th, with a significant decrease on the 9th day. The cutaneous severity index (Ind) was 6.84%. Observing the animals of group 6, we found that the symptoms of ACD were mild on the 1st day, as in the previous groups, and that on the 3rd and 5th days the inflammation process sharply progressed, and, starting from the 7th of the day, the data of this group significantly decreased compared with the control group. The cutaneous severity index (Ind) was 22.4%.

The results of the obtained data on the size of skin folds in the studied animals, it was found that from the 1st to 5th days of treatment an increase in skin folds was observed in all groups, and from the 7th day there was a significant decrease in skin folds in all groups, compared with control group. In particular, the skin folds of 2- and 4-groups of animals were close to an experimental healthy state in comparison with other groups.

Thus, we found that the use of 5% ointment in the treatment of dermatitis obtained from a dry extract of radix glycyrrhizae is more effective than other forms of ointment and psilo-balm and topical celestoderm B. And the index for reducing the severity of skin manifestations (Ind) was higher in this group than in others.

REFERENCES

1. Abjalelov B.B., Kujamberdieva S.Zh., Asemov A.B., Mutafa A.T. Getting glycyrrhizic acid from licorice root. // International Journal of Experimental Education. 2016.-№5 (1). -C.100-104.
2. Malonicheva T.G., Denisova S.N., Vakhrameeva S.N., Atopic dermatitis in children - modern features of the course and diagnosis. // Ross. Bulletin of Perinatology and Pediatrics. 2012.-№2. 109-103.

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020

3. Sabelnikova N.N., Pisareva N.A., Kochkarov V.I., Zhilyakova E.T., Novikov A.A. The results of a comparative study of the pharmacological activity of the submicrostructured substance of loratadine. The scientific result. // Network scientific and practical journal. 2015.-№3.-S.61-63.
4. Suyarov A.A., Japorov O.K., Batyrbekov A.A., Khatamov H.M. Antiallergic drug “Allergodaf”. Tashkent. 2017.116s.
5. Tamrazova O.B. Risk factors for the development of atopic dermatitis in infants. //Medical advice. 2018.-№17. -C.182-186.
6. Tikhomirov A.A., Korotky N.G. External therapy in children with atopic dermatitis: treatment, care, prevention. // Questions of modern pediatrics. 2011. -T.10. -№6. -C.66-71.
7. Kim D.H., Li K., Seo S.J., Jo S.J., Yim H.W., Kim C.M. et al. Quality of Life and Disease Severity Are Correlated in Patients with Atopic Dermatitis. // J. Korean Med. Sci. 2012.-№27 (11). -P.1327–32.
8. Nutten S. Atopic Dermatitis. Global Epidemiology and Risk Factors. // Ann Nutr. Metab. 2015.-Vol. 66. -№1. -R.8-16.
9. Fayziyev Shokhrud Farmonovich Medical law and features of legal relations arising in the provision of medical services. International journal of pharmaceutical research Volume 11, Issue 3, July - Sept, 2019 P. 1197-1200 doi:10.31838/ijpr/2019.11.03.088
10. Fayziev Shokhrud (2019) Legal Aspects of Transplantology in the Republic of Uzbekistan. Systematic Reviews in Pharmacy, ISSN: 0976-2779, Vol: 10, Issue: 2, Page: 44-47 doi:10.5530/srp.2019.2.08

DOI: 10.37200/IJPR/V24I2/PR200344
Received: 16 Dec 2019 | Revised: 02 Jan 2020 | Accepted: 15 Jan 2020