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Dermatological Health

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Analysis of the Effect of Zygomatic Fat Pad Lifting Combined with Ultra-High SMAS Technique on the Improvement of Nasolabial Folds (Lower Eyelid Margin Incision)

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Abstract: This paper aims to explore the effect of zygomatic fat pad lifting combined with ultra-high superficial muscular aponeurotic system (SMAS) technique on the improvement of nasolabial folds. From December 2021 to June 2022, 40 patients with facial sagging were selected in our hospital to perform zygomatic fat pad lifting combined with ultra-high SMAS technology for large facelift surgery. Combined with lower eyelid incision and zygomatic fat pad degloving, the middle and lower face lift surgery, the improvement of the nasolabial fold, and the reduction of the apple cheeks were evaluated to assess the surgical effect. Statistics were collected on the improvement of nasolabial folds and apple cheeks aesthetic units before and after operation in 40 follow-up patients, and the satisfaction degree of nasolabial fold elevation and apple cheeks reduction was investigated and analyzed. The facial nasolabial folds and apple cheeks aesthetic units of 40 patients were followed-up after operation and compared with those before operation, and the difference was statistically significant ($P < 0.05$). After surgical treatment, 95% of patients were satisfied with the improvement of nasolabial folds, and 97.5% were satisfied with the reduction of apple cheeks. Zygomatic fat pad lifting combined with ultra-high SMAS technique has a significant effect on the reduction of apple cheeks zygomatic fat pad and nasolabial fold elevation, and it has clinical application value.

Keywords: Malar fat pad; Ultra-high SMAS technique; Nasolabial fold; Apple cheeks

Online publication: September 26, 2023

1. Introduction

In all kinds of large-scale facelifts nowadays, the peeling of the largest range of skin flaps generally reaches the limit of peeling at the vertical line of the outer corner of the eye. This kind of face lift is still very limited to the improvements of apple cheeks or nasolabial folds and Indian lines [1]. The main reasons are:

(1) The zygomatic fat pads of the apple cheeks is basically in an unstripped state.

(2) The important anatomical basis of the nasolabial fold is the buccal maxillary ligament.

(3) Most of the anatomical basis of the Indian striae is involved with the zygomatic ligament.

(4) The zygomatic fat pad cannot achieve complete reduction and healing.

(5) The orbicularis oculi ligament, the buccomaxillary ligament, the zygomatic ligament, and the ligament around the inferior orbital fissure are all involved in the zygomatic fat pad, which affects the oblique outward and upward elevation of the zygomatic fat pad.

(6) The formation factors of the nasolabial fold are not only the fixation of the buccal maxillary ligament, but also the aging hyperplasia of subcutaneous fat in the nasolabial fold area, and the pyriform foramen, osteoporosis, bone resorption, aggravation of periosteum absorption depression, and the influence of muscle movement near the fossa axis.

The presence of these factors makes nasolabial fold resolution very difficult. The ordinary SMAS double-layer technique can be stripped to the origin of the zygomaticus major at the vertical line of the outer canthus [2]. There are still a lot of ligaments in the inner part of the apple cheeks, and the local subcutaneous SMAS is very thin, which is difficult to peel off. Based on this, this study selected 40 patients with facial sagging in our hospital as the research objects, and used the zygomatic fat pad lifting combined with the ultra-high SMAS technique for large facelift treatment. The effect is significant, and the report is as follows.

2. Materials and methods

2.1. General information

A total of 40 patients with facial sagging admitted to our hospital from December 2021 to June 2022 were selected as the research subjects, all of whom were female, aged 40 to 67 years old, with an average age of 51.4±7.2 years old. The study hospital was approved by the ethics committee. All patients are operated on by the same team of skilled surgeons.

2.2. Methods

The surgical procedure is as follows. Mid-lower face lift combined with lower eyelid incision and degloving of zygomatic fat pad was performed. After designing and drawing the line, the drape was sterilized with iodophor, and after general anesthesia, the sterile drape and skin were sutured for fixation. Tumescent fluid was injected into the surgical area. Swelling solution 500ml, with proportion of 8 sticks of 2% lidocaine, 5ml sodium bicarbonate, 500ml normal saline, 0.5ml adrenalin. The swelling fluid was uniformly injected into the subcutaneous fat layer of the face and neck, and the mixed solution of ropivacaine and lidocaine was used for nerve block anesthesia on the sensory nerve.

The skin and subcutaneous fat layer were cut through the standard incision of the face lift. The temporal part was peeled first, and the layer of peeling was the superficial fascia layer. The principle is that the hair follicles are faintly visible and do not damage the hair follicles. The temporal part was dissected forward to 2.5cm lateral to the temporal ridge. Then the area in front of the ear was peeled off, and the subcutaneous fat was split to ensure that there is a uniform fat and capillary network under the skin. The skin in front of the ear was peeled off to 2.5cm outside the vertical line of the outer corner of the eye. Then the ear was peeled off to the back of the ear, and to 7cm below the ear and to 6cm behind the ear. After the first layer stripping is done, design the SMAS stripping area. From the level of the eye fissure, preauricular dissection to the emergence of the orbicularis muscle, the dissection layer was the superficial layer of the SMAS fascia and did not enter the middle temporal fascia. After the orbicularis muscle was dissected, it was dissected downwards, and the zygomatic ligament, the parotid cortex ligament, and the suspensory ligament of the platysma muscle were interrupted. After reaching the skin peeling boundary, the complex peeling under the SMAS was carried out and continued to move forward, exposing the zygomaticus major muscle and the masseter muscle encapsulated by

the buccal fat pad. The zygomaticus major was continued to be carefully dissected under the zygomatic fat pad, and all ligaments that restricted the movement of the zygomatic fat pad were severed, for further exposure of the zygomatic minor muscle. At the same time, the ligament around the zygomatic minor muscle was severed. The fibrous ligament around the buccal fat pad was severed, the masseter cutaneous ligament was fully severed, and the SMAS was dissected down to the vicinity of the pupil. Using the lower eyelid incision to enter, the attachment of the orbicularis muscle to the orbital rim is first dissected. Then tissue scissors were used to gently peel off the medial side, separate the orbicularis muscle and the levator alar nasi muscle, slide along this gap into the nasolabial fold area, and large blood vessel forceps were used to stretch and release the buccomaxillary ligament. The complete release of the ligament at the nasolabial fold was observed, the lower middle part of the lower eyelid was peeled off, center on the infraorbital foramen, and tissue scissors were used to peel off the attachment of the buccomaxillary ligament to protect the vascular and nerve bundles. After the release of the central ligament, it was observed that the malar fat pad was completely without gap. The outside was continued to be peeled off. First, the surface of the periosteum was peeled outward, and then the surface of the periosteum of the zygoma was peeled to about 3cm outside the outer corner of the eye. At the lower part of the dissection, on the surface of the zygomaticus major and minor muscles, the zygomatic ligament was carefully dissected to allow the zygomatic fat pad to be further dissected, and it was observed that the gap had been dissected and penetrated with the lateral SMAS. At this time, the SMAS was lifted and it was observed that the entire middle and lower face is tightened and lifted without resistance, and the peeling is completed. The wound was washed, with the bleeding stopped, the parotid gland was folded and sutured, the excess buccal fat pad was released and sutured The SMAS was sutured in the deep temporal fascia through multi-point suspension, the SMAS was interrupted from the mandibular line, with the excess SMAS removed, and the SMAS incision line was sutured. The firmness of the face was observed, the apple cheeks were reset, the wound was rinsed and sutured again. Three upper drainage tubes were attached, and the same was done for the opposite side. Then, it was covered with sterile dressing and elastic bandage for compression.

2.3. Evaluation indicators

The same doctor took natural photos of the face before the operation and one year after the outpatient follow-up. According to the data, the improvement of the nasolabial fold and the reduction of the apple cheeks were evaluated to assess the effect of the operation. Statistics were collected on the improvement of nasolabial folds and apple cheeks aesthetic units before and after operation in 40 follow-up patients, and the satisfaction degree of nasolabial fold elevation and apple cheeks reduction was investigated and analyzed.

2.4. Statistical processing

The relevant data before and after the operation were entered into an Excel table, and the results were counted by SPSS26.0, and the count data were analyzed by *t* test. $P < 0.05$ indicated that the difference was statistically significant.

3. Results

3.1. Esthetic unit score before and after surgery for the improvement of nasolabial folds and apple cheeks reduction

Based on **Table 1**, the facial nasolabial folds and apple cheeks aesthetic units of 40 patients in the postoperative follow-up were improved compared with those before the operation, and the difference was statistically significant ($P < 0.05$).

Table 1. The improvement of nasolabial fold and the reduction of apple cheeks in patients before and after aesthetic unit score (±s).

Time	*n*	Grading by aesthetics unit	
		Facial nasolabial folds	Apple cheeks
Before surgery	40	2.602±0.517	3.823±0.409
After surgery	40	2.295±0.438	2.576±0.314
t		7.037	10.256
P		0.003	0.000

3.2. Survey of patients' satisfaction with nasolabial fold improvement and apple cheeks reduction

After the application of zygomatic fat pad lifting combined with ultra-high SMAS technology, the patients were satisfied with the improvement of nasolabial folds. Among them, 32 cases were very satisfied, 4 cases were relatively satisfied, 2 cases were satisfied, and the satisfaction rate was 95%. For the satisfaction of apple cheeks reduction, 30 cases were very satisfied, 6 cases were relatively satisfied, 3 cases were satisfied, and the satisfaction rate was 97.5%.

3.3. Comparative analysis of preoperative and postoperative cases

The comparison between preoperative and postoperative effects of zygomatic fat pad lifting combined with ultra-high superficial muscular aponeurotic system (SMAS) technique on the improvement of the nasolabial fold and the reduction of the apple cheeks is shown in **Figure 1**.

Figure 1. Comparison of preoperative and postoperative effects of patient 1

4. Discussion

With age, the loss of fat accelerates, the subcutaneous tissue becomes thinner, and the apple cheeks become smaller and plump. In this study, the zygomatic fat pad lifting combined with the ultra-high SMAS technology for large face lift program added the eye bag incision. Peeling was performed under direct vision. The approach is the anterior zygomatic space, as shown in **Figure 2** [3].

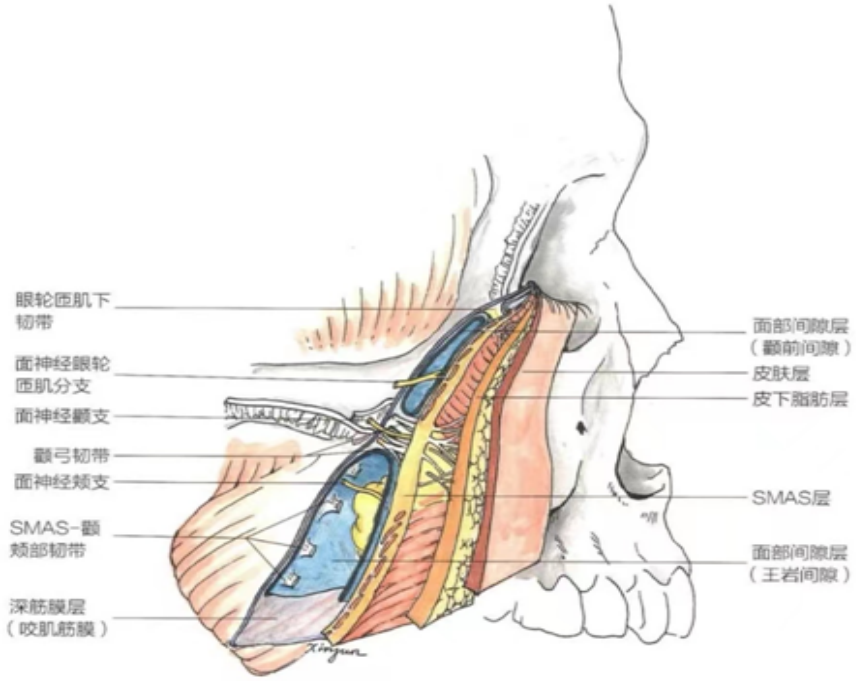

Figure 2. The supporting ligaments of the face play the role of identifying, guiding, stabilizing, and protecting the branches of the facial nerve

Translation: (on the left, from top to bottom) suborbicularis ligament, orbicularis oculi branch of facial nerve, zygomatic branch of facial nerve, zygomatic ligament, SMAS-malar buccal ligament, deep fascia (masserus fascia); (on the right, from top to bottom) facial space layer (prezygomatic space), skin layer, subcutaneous fat layer, SMAS layer, facial space layer (Wang Yan space).

Accessing from standard pouch incision myocutaneous flap, tissue scissors are used to first peel off the adhesion between the medial orbicularis oculi muscle and the periosteum, and carefully peel off 3–5mm to decapitate the orbicularis oculi muscle. The suborbicularis oculi fat (SOOF) is peel off and its upper layer is peeled off with tissue scissors on the middle and outer sides, only to the inferior orbital fissure. The outer side is stripped under the SOOF near the periosteum to 3cm outside the outer corner of the eye. This dissection protects the portion of the zygomatic nerve branch that enters the orbicularis muscle under the SMAS. After the lower lateral side is stripped to the surface of the zygomaticus major, it is continued to the lower medial side. The main layer is under the malar fat pad. The blunt tissue shearing and dissection is continued along the zygomaticus major muscle to the inner and lower sides. The dense ligament tissue is cut off with scissors. Careful blunt dissection with scissors near the infraorbital foramen finds and protects the nerves and blood vessels in the infraorbital foramen. The surrounding tissues and ligaments are cut off on the inside, along the lower part of the orbicularis muscle, and along the gap between the orbicularis muscle and the levator lip nasius muscle, it is easy to enter the nasolabial groove. No active bleeding was observed after apple cheeks peeling was completed. Then the standard ultra-high SMAS technique was performed, it is peeled from the outer corner of the eye 1cm below the mandibular angle to the inside, and the 3cm of the outer corner of the eye under the SMAS is kept without peeling. The periosteum has already been peeled here. In this way, the outer SMAS dissection can be penetrated and released to the nasolabial fold. Nasolabial folds and marionette lines can be lifted very lightly [4]. **Figure 3** shows the structures of the whole face, the brow area, and the brow space eyebrow fat pad.

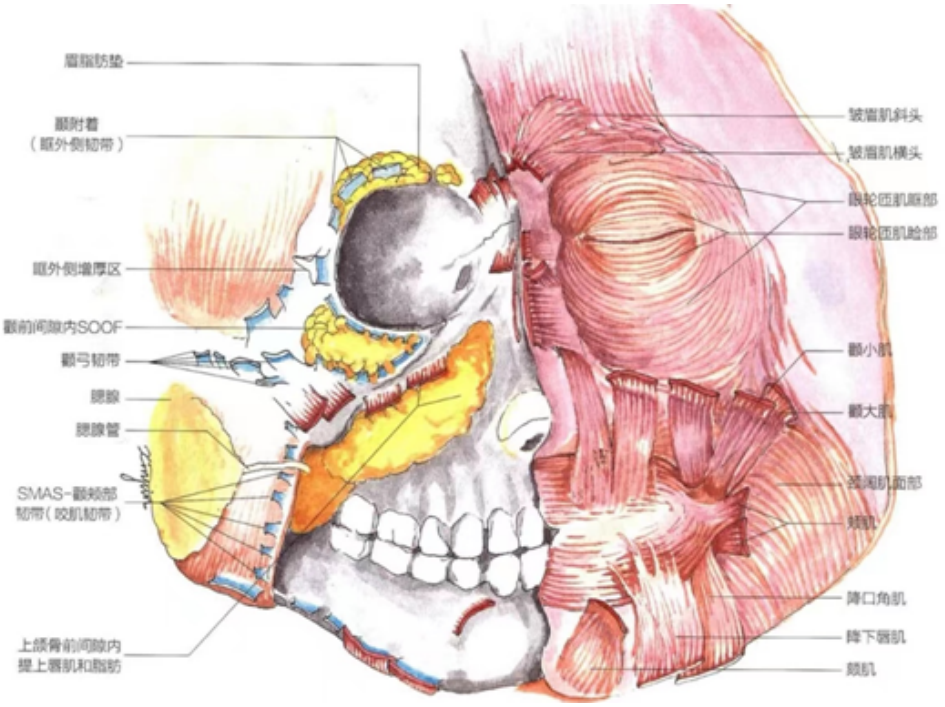

Figure 3. The structures of the whole face, the brow area, and the brow space eyebrow fat pad

Translation: (on the left, from top to bottom) zygomatic attachment (lateral orbital ligament), lateral orbital thickening, SOOF in prezygomatic space, zygomatic ligament, parotid gland, parotid duct, SMAS-zygomaticobuccal ligament (masseroid ligament), levator labii muscle and fat in the anterior space of the maxilla; (on the right, from top to bottom) corrugator diagonal, corrugator horizontal, orbicularis oculi orbital, orbicularis oculi eyelid, zygomaticus minor, zygomaticus major, platysma face, buccal muscle, depressor anguli oris muscle, lower lip muscle, buccal muscle.

After the stripping is completed, the buccal fat pad is suspended outward and upward for suture. The parotid folds were narrowed with sutures. Then the SMAS is suspended at multiple points to the deep temporal fascia and sutured. The nasolabial fold can be completely flattened and disappeared, and the firmness reaches the limit. The bleeding is stopped and sutured, and the skin was removed according to the standard surgical procedure. Lastly, a part of the dermis is taken with the epidermis removed. The bilateral nasal bases are filled through the incision in the nostrils. On the one hand, it supplements the capacity and allows the nasolabial fold to receive better support, thereby reducing rebound. The excess fascia crescent is removed and filled into the lateral buccal depression [5]. On the other hand, through this set of procedures, the face can be reduced to a smaller face, and it can be transformed into a V-apple cheeks with an aesthetic arc, the nasolabial folds can also be resolved to the maximum extent, and the degree of rebound is greatly reduced. **Figure 4** shows the zygomatic fat pad.

In this study, the combination of zygomatic fat pad lifting and ultra-high SMAS technology is used to treat the SMAS fascia layer deep in the tissue, and at the same time, the skin and other tissues attached to it are jointly lifted to improve the signs of aging on the face. This approach not only effectively restores the plump state of the apple cheeks, but also improves the fatigue caused by the midface depression, reduces nasolabial folds, and lifts and tightens loose skin. In this study, the patient satisfaction of this method was very high. The facial nasolabial folds and apple cheeks aesthetic units of 40 patients were followed-up after surgery, and the difference was statistically significant. After surgical treatment, 95% of patients were satisfied with the

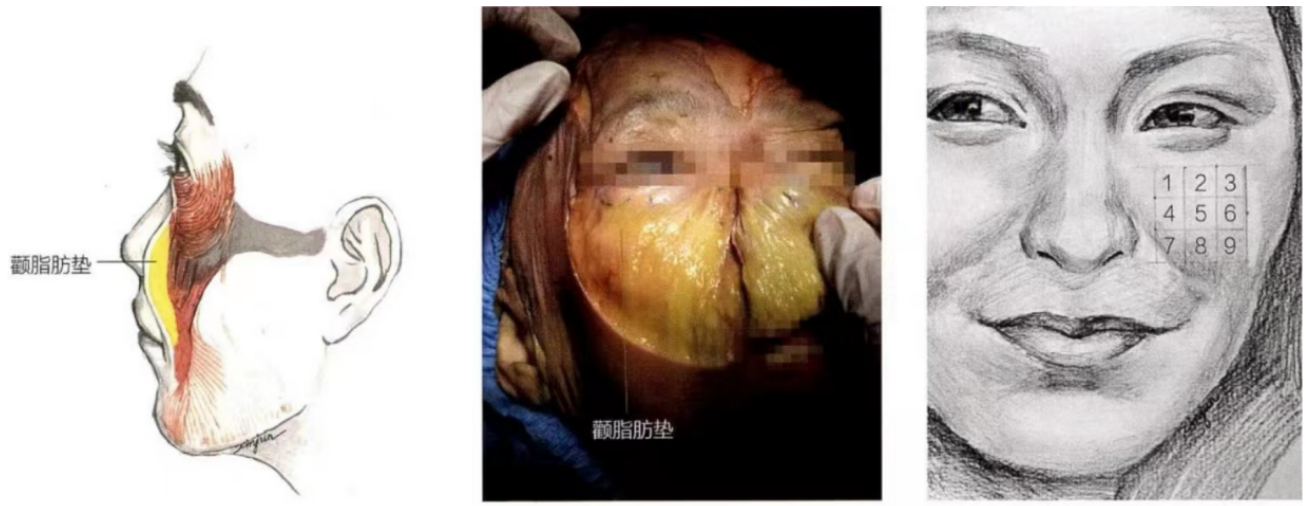

Figure 4. (From left to right) Diagram of zygomatic fat pad (Translation: zygomatic fat pad), anatomy of zygomatic fat pad (Translation: zygomatic fat pad), subcutaneous fat in midface (zygomatic fat pad)

improvement of nasolabial folds, and 97.5% were satisfied with the reduction of apple cheeks. Therefore, the application of zygomatic fat pad lifting combined with ultra-high SMAS technology, especially the reduction of apple cheeks zygomatic fat pad and the lifting of nasolabial fold, has significant effects and is worth clinical application value.

Disclosure statement

The authors declare no conflicts of interest.

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Clinical Efficacy and Safety Analysis of 308nm Excimer Ultraviolet Light Combined with Carbon Dioxide Fractional Laser in the Treatment of Refractory Vitiligo

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Abstract: This paper aims to explore the clinical effect and safety of combined application of 308nm excimer ultraviolet light and carbon dioxide fractional laser in the treatment of refractory vitiligo. The study was carried out from January 2020 to December 2022. 60 patients with refractory vitiligo were selected and divided into the study group (n = 30) and the control group (n = 30) through the lottery method of medical record envelopes. The patients in the control group were treated with 308nm excimer ultraviolet light, and the patients in the study group were treated with 308nm excimer ultraviolet light combined with carbon dioxide fractional laser treatment. The clinical effective rate, leukoplakia area, IgG level, and incidence of adverse reactions were compared between the two groups. The clinical effective rate of the study group was higher than that of the control group ($P < 0.05$). After treatment, the leukoplakia area of the study group was lower than that of the control group ($P < 0.05$), and the IgG level of the study group was lower than that of the control group ($P < 0.05$). The incidence of adverse reactions in the study group was lower than that in the control group ($P < 0.05$). The combined application of 308nm excimer ultraviolet light and carbon dioxide fractional laser therapy for patients with refractory vitiligo has a significant effect, can reduce the area of leukoplakia and IgG levels, and has high treatment safety, which can be widely applied in clinical practice.

Keywords: 308nm excimer ultraviolet light; Carbon dioxide fractional laser; Vitiligo

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1. Introduction

Melanin is the pigment in the skin, which can determine the skin color. If the skin melanocytes are destroyed, it can lead to the lack of melanin, white spots on the skin tissue, and vitiligo. Vitiligo can occur in multiple parts of the body. White patches of different sizes can be seen in the skin tissue of patients. Some patients are accompanied by inflammatory lesions such as tinea corporis and eczema. Vitiligo can affect the patients' appearance and normal social interaction, so early treatment is needed [1,2]. The routine clinical treatment of vitiligo is 308nm excimer ultraviolet light. Its main mechanism of action is to kill T lymphocytes, induce the

synthesis of melanin, and reduce the area of leukoplakia [3]. Patients with refractory vitiligo have a long course of disease, and long-term use of 308nm excimer ultraviolet light cannot obtain satisfactory curative effect. Some studies believe that combined application of carbon dioxide fractional laser can achieve ideal therapeutic effect [4]. In this study, 60 samples of patients with refractory vitiligo were selected to explore the clinical value of combined application of 308nm excimer ultraviolet light and carbon dioxide fractional laser treatment.

2. Materials and methods

2.1. General information

The sample selection and research process of this study were approved by the Medical Ethics Committee. The study was carried out from January 2020 to December 2022. 60 samples of patients with refractory vitiligo were selected and divided through the lottery method of medical record envelopes into study group (n = 30) and control group (n = 30). In the study group, there were 17 males and 13 females, with an age range of 33–58 years, with an average of 45.58±3.06 years old. The skin lesions included face and neck in 11 cases, extremities in 9 cases, and trunk in 10 cases. In the control group, there were 18 males and 12 females, with an age range of 35–57 years old, with an average of 45.63±2.98 years old. The skin lesions included 12 cases on the face and neck, 9 cases on the extremities, and 9 cases on the trunk. The general data of the two groups were comparable (P > 0.05).

Inclusion criteria were patients that meet the diagnostic criteria for refractory vitiligo in the Consensus on Vitiligo Diagnosis and Treatment, patients without other skin tissue lesions, and those that signed the research consent document.

Exclusion criteria included patients that recently received vitiligo treatment, contraindications for ultraviolet radiation therapy, patients complicated with major organ diseases such as liver and kidney.

2.2. Methods

The patients in the control group were treated with 308nm excimer ultraviolet light, by using the hospital's 308nm ultraviolet light skin therapy instrument. The doctor observed the patient's skin lesions, pointed the device at the skin lesion area, and determined the initial irradiation energy (300mJ/cm^2 for the limbs, 200mJ/cm^2 for the trunk, and 100mJ/cm^2 for the face). During the treatment period, the irradiation energy intensity was adjusted appropriately, once a week, for a total of 3 months.

The patients in the study group received 308nm excimer ultraviolet light combined with carbon dioxide fractional laser therapy, and the carbon dioxide fractional laser therapy was given priority. The treatment power was set to 15W, the wavelength was 10.6μm, the pulse width was 0.5ms, and the initial treatment energy was 30mJ/cm^2. During the treatment period, the spot size and energy intensity were adjusted according to the skin condition, and treatment was done once a month for a total of 3 months. After carbon dioxide fractional laser treatment, 308nm excimer ultraviolet light was performed, and the treatment plan was the same as that of the control group.

2.3. Evaluation criteria

The clinical effectiveness of the two groups was evaluated after 3 months of treatment. If the skin color is normal after treatment and the leukoplakia disappears, it is considered cured. If the lesion area is reduced by more than 60% after treatment, and the leukoplakia is significantly reduced, it is considered effective. If it does not meet the standards of "cured" and "effective," it is ineffective. The leukoplakia areas of the two groups were counted before treatment, after 1 month of treatment, and after 3 months of treatment. Venous blood samples

were collected from patients in the two groups before treatment, after 1 month of treatment, and after 3 months of treatment, and IgG levels were detected by enzyme-linked immunosorbent assay. Statistics on the incidence of adverse reactions in the two groups of patients was determined.

2.4. Statistical methods

SPSS23.0 software was used to analyze the research data, measurement data (±s) was *t* test, count data % was χ^2 test, $P < 0.05$ indicated that there was a statistical level difference.

3. Results

3.1. Comparing the clinical effectiveness

As shown in **Table 1**, the clinical effective rate of patients in the study group was higher than that in the control group ($P < 0.05$).

Table 1. Comparison of clinical effective rates between the two groups (n/%)

Group	Cured	Effective	Ineffective	Total effective rate
Study group (n = 30)	21	7	2	28 (93.3)
Control group (n = 30)	15	7	8	22 (73.3)
χ^2 value	-	-	-	4.320
P value	-	-	-	0.037

3.2. Comparing the areas of leukoplakia

As shown in **Table 2**, after treatment, the leukoplakia area of the study group was lower than that of the control group ($P < 0.05$).

Table 2. Comparison of leukoplakia area between the two groups (±s, cm^2)

Group	Before treatment	1 month after treatment	3 months after treatment
Study group (n = 30)	17.49±2.75	11.42±2.04	7.12±1.03
Control group (n = 30)	17.55±2.68	14.69±3.85	10.38±1.96
t value	0.086	4.111	8.064
P value	0.932	0.000	0.000

3.3. Comparison of IgG levels

As shown in **Table 3**, after treatment, the IgG level of patients in the study group was lower than that in the control group ($P < 0.05$).

Table 3. Comparison of IgG levels between the two groups (±s, mg/L)

Group	Before treatment	1 month after treatment	3 months after treatment
Study group (n = 30)	4.75±1.02	3.05±0.62	2.17±0.65
Control group (n = 30)	4.79±0.96	3.99±1.05	3.19±0.94
t value	0.156	4.222	4.888
P value	0.876	0.000	0.000

3.4. Comparison of the incidence of adverse reactions

As shown in **Table 4**, the incidence of adverse reactions in the study group was lower than that in the control group ($P < 0.05$).

Table 4. Comparison of the incidence of adverse reactions between the two groups (n/%)

Group	Scab	Swelling	Itchiness	Blisters	Incidence of adverse reactions
Study group (n = 30)	1	1	0	0	2 (6.7)
Control group (n = 30)	3	3	1	2	9 (30.0)
χ^2 value	-	-	-	-	5.454
P value	-	-	-	-	0.019

4. Discussion

The main pathological feature of vitiligo is the destruction of melanocytes in the skin tissue, and the lack of melanin in the patient's skin tissue leads to the formation of leukoplakia in the skin tissue. The causes of the disease are heredity, immune system disease, neurochemical substances, etc. White patches of different sizes can be seen in the skin tissue of the patient, accompanied by tinea corporis-like and eczema-like inflammatory lesions, and can produce itching and other symptoms [5,6]. Vitiligo can affect the aesthetics of the patient's face and neck, and can lead to psychological problems in patients, for which early intervention is required.

308nm excimer ultraviolet light is a routine clinical treatment for refractory vitiligo. Its main function is to induce the apoptosis of activated T cells in the skin lesion area, effectively remove the infiltrating T lymphocytes in the skin area, and activate pseudoperoxidation. Hydrogenase induces the synthesis of vitamin D3, thereby accelerating the proliferation of melanocytes, increasing the level of melanin in skin tissue, reducing the area of leukoplakia, and effectively relieving related symptoms [7,8]. Long-term application of 308nm excimer ultraviolet light to patients with refractory vitiligo can produce plateau phenomenon, and increasing the treatment energy cannot effectively relieve related symptoms. The thickness of the skin tissue increases significantly, resulting in a decrease in the penetration of ultraviolet light which affects the therapeutic effect. Carbon dioxide fractional laser is based on the traditional carbon dioxide pulse laser treatment plan, adding computer graphics generator and other equipment, which can accurately treat the depth and avoid damage to the dermis [9]. Fractional carbon dioxide laser therapy can form tiny treatment holes on the skin surface, induce the migration of melanin in peripheral cells, promote the secretion of growth factors and cytokines, accelerate the division and proliferation of melanocytes, and reduce the area of leukoplakia [10]. Fractional carbon dioxide laser therapy can effectively remove superficial epidermal tissue and excessively thick stratum corneum in the lesion area, improve the penetration of ultraviolet light, avoid the plateau period of 308nm excimer ultraviolet light, and improve the treatment effect [11].

The combination of 308nm excimer ultraviolet light and carbon dioxide fractional laser treatment has a significant effect on patients with refractory vitiligo, which can reduce the vitiligo area. This may be because 308nm excimer ultraviolet light has a strong penetrating power, which can induce the apoptosis of T lymphocytes in the skin lesion area, induce the synthesis of vitamin D3, block the production of cytokines, accelerate the proliferation of melanocytes, and then reduce the area of leukoplakia. Carbon dioxide fractional laser treatment can form vertical microscopic treatment holes in the leukoplakia area of the skin tissue, resulting in damage to the barrier function of the skin tissue, allowing 308nm excimer ultraviolet light to penetrate the epidermal tissue, increasing the total amount of local energy absorption, and strengthening the therapeutic

effect [12]. Fractional carbon dioxide laser therapy can also inhibit the synthesis and secretion of inflammatory factors, regulate the function of the immune system, restore the balance of T cells, and increase the level of melanocytes, thereby reducing the area of leukoplakia and improving the treatment effect of the disease [13]. The results of this study showed that IgG levels in the study group were lower than those in the control group after treatment. Analysis shows that tyrosinase is a typical oxidase, and its main function is to regulate melanin synthesis. The combination of IgG and tyrosine in the human body can produce an immune response, which in turn affects the synthesis of melanin, leading to an increase in the area of leukoplakia and hindering the recovery process of patients. During the treatment of refractory vitiligo, it is necessary to control the IgG level, increase the activity of tyrosinase, and increase the synthesis of melanin to improve related symptoms [14]. The combined application of 308nm excimer ultraviolet light and carbon dioxide fractional laser treatment can achieve synergy between the two treatment options, induce T cell apoptosis *in vivo*, reduce IgG levels, increase tyrosine activity, and increase melanin synthesis. The results of this study show that the incidence of adverse reactions in the study group is lower than that in the control group. The reason is that long-term application of 308nm excimer ultraviolet light can lead to increased skin thickness and hyperkeratosis, which can easily induce adverse reactions in skin tissues. Combined with carbon dioxide fractional laser treatment, it can remove excessively thick stratum corneum, and can ensure that the treatment accuracy is limited to the superficial layer of the skin and effectively protect the dermis, thus the treatment is relatively safe [15].

In summary, the combined application of 308nm excimer ultraviolet light and carbon dioxide fractional laser treatment for patients with refractory vitiligo has a significant effect. It can reduce the leukoplakia area and IgG levels, and has high treatment safety, which can be a valuable treatment option.

Disclosure statement

The author declares no conflicts of interest.

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Research on the Application of Mini Facelift in Facial Plastic Surgery

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Abstract: *Objective:* This paper aims to study the clinical effect of mini facelift in patients undergoing facial plastic surgery. *Methods:* The study period was from January 2021 to January 2023. One hundred cases were selected from patients with facial plastic surgery at our hospital. They were divided according to the two-color ball method into control group and study group. 50 cases in the control group underwent routine major facelift and skin flap surgery, while 50 patients in the study group underwent mini facelift surgery. The items to be compared between the two groups were clinical effects, psychological conditions, and satisfaction. *Results:* Based on the results, it was determined that the study group had shorter operation time and swelling period than the control group, and the difference between the groups was significant, $P < 0.05$. By comparing the Hamilton Anxiety Scale (HAM-A) score and the Hamilton Depression Scale (HAM-D) score, no preoperative symptoms were found in the two groups ($P > 0.05$). After surgery, the two scores in the study group decreased, and the difference between the study group and the control group can be expressed by $P < 0.05$. Moreover, it was determined that the study group had higher satisfaction than the control group, and there is a significant difference between them, $P < 0.05$. *Conclusion:* The application of mini facelift in facial plastic surgery can shorten the operation time and swelling period, improve satisfaction, and relieve negative emotions, hence it is suitable for comprehensive clinical application.

Keywords: Plastic surgery; Face; Mini facelift

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1. Introduction

Plastic and cosmetic surgery in clinical settings specifically refers to departments that repair and reshape the patient's appearance and the shape of different human body parts through medical devices or drug surgery. In addition, surgeons using surgical skills or other medical technology to achieve the above purposes are also included in this discipline. After plastic surgery, the external beauty of the human body can be enhanced, and its distinctive feature lies in its strong artistic, technical, and scientific quality [1]. In recent years, with the introduction and application of mini facelift surgery, the development of plastic surgery has been further promoted. This article selected 100 cases of facial plastic surgery patients in our hospital from January 2021 to January 2023 for research.

2. Materials and methods

2.1. General information

From January 2021 to January 2023, 100 cases of patients with facial plastic and cosmetic surgery in our hospital were selected. The patients were divided into the control group and the study group by two-color ball method, each with 50 cases. The control group had 18 male patients (36.00%) and 32 female patients (64.00%), the age range was 20–70 years old, with a mean age of 38.5±5.7 years old. The study group had 17 male patients (34.00 %) and 33 female patients (66.00%), the age range was 21–69 years old, with a mean age of 38.3±5.6 years old. After statistical comparison, there is no significant difference between the two groups in the general information, indicated by $P > 0.05$, which is fair and comparable.

The inclusion criteria included patients consistent with the indications for facial plastic surgery, patients over 18 years old and under 70 years old, and patients who voluntarily participate in this research and sign the informed consent.

The exclusion criteria were patients with severe systemic diseases who are not suitable for facial plastic surgery, patients suffering from blood infectious diseases, patients with cognitive or mental disorders, and women who are pregnant or breastfeeding.

2.2. Methods

Preoperative preparations for the two groups of patients are as follows. It is necessary to determine whether the patients have underlying diseases such as hyperglycemia and hypertension through a comprehensive examination and to carry out appropriate control. Female patients are required to undergo surgery during non-menstruation period. If patients need to take anticoagulant drugs, such as aspirin, they should stop taking it within 7 to 10 days before the operation to prevent intraoperative bleeding or postoperative hematoma.

The mini facelift surgery was performed on patients in the study group. The detailed operation content is as follows. The incision must be designed before the operation. The length of the minimally invasive small incision made within the temporal hairline needs to comply with the 2cm standard and the specific range of lacunar separation requirements. It is defined from four aspects including upper, medial, lower, and lateral. The upper edge of the temporalis muscle is the upper range standard, the outer edge of the orbital bone is the medial range standard, and the upper edge of the zygomatic bone and zygomatic arch is the lower range standard. After the incision, the standard of the outer range is about 1cm from the edge. The method of implanting absorbable threads was used to lift the distal subcutaneous tissue, skin, and superficial musculoaponeurotic system (SMAS) fascia layer in the cavity at three points, and knotting and fixation was performed in the cavity. At the hairline edge (three points), imported polydioxanone (PDS) absorbable sutures can be used to fix the points, precisely the lowest point of the hairline, the upper edge of the zygomatic arch, and the outer edge of the orbital bone. After the galea aponeurosis layer at the posterior edge of the distal incision was fixed and sutured, the hairline can be lifted again. The scalp tissue with a width of about 2cm needs to be removed inside the incision, and the skin is locked again.

Patients in the control group underwent conventional major facelift and skin flap surgery. Detailed operation content is as follows. The patient was given local anesthesia, and an incision was made about 1–2mm below the eyelashes of the lower eyelid. After reaching the lateral canthus, incision was done along the crow's feet. A 5mm extension operation was performed, the skin, subcutaneous tissue, and orbicularis oculi muscle were incised in sequence, the potential gap between the orbicularis oculi muscle and the orbital septum fascia was separated, and the orbicularis oculi muscle was cut to the infraorbital rim. Incision of the medial separation is specifically the orbital subperiosteal and superficial periosteal surface, with the standard of 0.5cm, the lateral

separation is specifically the prezygomatic space, to the starting point of the zygomatic major muscle, Wang's ligament, and the orbicularis oculi limiting ligament. For adequate release, the wound must be fully hemostatic, and the lower edge of the orbital septum must be opened to release the orbital fat and moved downward until it reaches the lowest position of the tear trough and palpebral groove deformity. 5-0 absorbable sutures were used to sew the lower part of the orbital septum and the deep orbital fat, and it was fixed at the periosteum of the orbital rim. Appropriate trimming is required if the patient has a thick orbicularis oculi muscle. The myocutaneous flap was stretched upward and it was observed whether the nasolabial fold has been improved and lifted. The myocutaneous flap was fixed on the periosteum of the lateral canthus through No. 1 silk thread. The patient was asked to look at his head with his eyes open and the occurrence of lower eyelid ectropion was judged, the excess skin was removed, and the skin was sutured using a 7-0 cosmetic thread. Within 24 hours after surgery, the lower eyelids and cheekbones must be kept under pressure bandage, the surgical site must be kept clean, and a series of essential treatments such as swelling and hemostasis should be given. Spicy and irritating food must be prohibited, and the suture removal time is 5–7 days after operation.

2.3. Observation indicators

The indicators below were observed in the two groups.

(1) The operation time and swelling period of the two groups of patients are recorded.

(2) Hamilton Anxiety Scale (HAM-A) and the Hamilton Depression Scale (HAM-D) are used to evaluate the changes in the psychological status of the two groups of patients at two different periods before and after surgery. The higher the score is, the more it indicates that the patient's mental condition is poor [2].

(3) A self-made satisfaction questionnaire is used to evaluate the satisfaction of the two groups of patients. The total score is 100 points. A score of 80–100 proves that the standard is very satisfactory. A score of 60–79 proves that the standard is relatively satisfactory. A score below 60 points prove unsatisfactory.

2.4. Statistical analysis

The statistical software SPSS22.0 was used to process the two data sets in the study. The counting data were described as percentages (%), and the χ^2 test was used for comparison. The measurement data were described as mean ± standard deviation (SD), and the *t*-test was used for comparison. When $P < 0.05$, the data are statistically different.

3. Results

3.1. Clinical comparison of operation time and the swelling period

The operation time and swelling period were compared between the groups, and there were statistically significant differences in the data, that is $P < 0.05$, as shown in **Table 1**.

Table 1. Clinical comparison of operation time and swelling period between two groups of patients (mean ± SD)

Group	Operation time (minutes)	Swelling period (days)
Control group (n = 50)	184.38±56.31	7.55±2.46
Study group (n = 50)	42.20±12.37	2.63±1.40
t	17.4383	12.2911
P	0.0000	0.0000

3.2. Clinical comparison of the improvement of mental status

When comparing the HAM-A score and the HAM-D score between the groups before surgery, the difference was insignificant, $P > 0.05$. In the comparison of the two scores after surgery, the study group was lower than the control group, and there was a significant statistical difference, $P < 0.05$, as presented in **Table 2**.

Table 2. Clinical comparison of the improvement of mental status between the two groups of patients (mean ± SD)

Group	HAM-A score		HAM-D score	
	Before surgery	After surgery	Before surgery	After surgery
Control group (n = 50)	24.24±3.50	19.97±2.34	26.03±3.68	21.45±2.16
Study group (n = 50)	24.17±3.47	11.53±1.71	25.97±3.70	10.82±1.94
t	0.1004	20.5919	0.0813	25.8896
P	0.9202	0.0000	0.9354	0.0000

3.3. Clinical comparison of patient satisfaction

The satisfaction rate of patients in the control group was 86.00% (43/50), of which 7 cases were unsatisfactory, 18 cases were relatively satisfactory, and 25 cases were very satisfactory. The satisfaction rate of patients in the study group was 98.00% (49/50), of which 1 case was unsatisfactory, 22 cases were relatively satisfactory, and 27 cases were very satisfactory. By comparing the satisfaction of the two groups of patients, it was found that the study group had higher satisfaction. The difference between the groups can be expressed by $P < 0.05$, which means it is statistically significant.

4. Discussion

As the name suggests, plastic surgery aims to help patients in need to achieve the goal of enhancing their external beauty. In recent years, with the continuous development of surgical technology, minimally invasive surgery has been widely used in plastic and cosmetic surgery, and the growth trend is pronounced. During diagnosis and treatment, whether patients can undergo correct and effective minimally invasive surgery application plays a vital role. If surgical techniques are misused, it will impact the patient's recovery, even worsen the condition, or cause severe complications.

Traditional cosmetic surgery mainly uses threads to pass through the lower layer of the skin. Then, the spinous processes on the threads hook onto the fat tissue, thereby lifting sagging skin. Although the lifting effect is average compared to surgery, it does not require a lengthy recovery period after surgery, thus it is clinically called a simple lifting surgery. The patients who are suitable for facelift surgery are those with loose neck, chin, and corners of the mouth, and those with nasolabial folds, face, and forehead wrinkles. Face lifting surgery mainly uses relatively advanced endoscopic technology to lift the sagging tissues of the nasolabial folds and cheeks, thereby quickly eliminating the nasolabial folds, effectively lifting the facial skin, tightening the skin and the pores, and finally restoring the skin to its original fairness, delicateness, elasticity, and luster as much as possible. The entire facelift surgery process will not cause significant trauma or severe edema.

The postoperative recovery can be rapid, and the overall effect is ideal. Facelift surgery will not impact their everyday work and life [3]. Mini facelift mainly combines traditional wrinkle removal surgery and thread carving. During the operation, the scope of the incision is significantly reduced through precise local operations, which reduces the degree of wound damage and drastically shortens the operation time to avoid surgical stress trauma such as different kinds of nerve injury. Mini facelift surgery does not require suturing and removal,

and there will be no permanent scars on the patient's cheeks. The blood supply to the hair follicles will not be affected and can be maintained for a long time. After the surgery, the skin will be shiny and elastic, and the face expression will be natural. The recovery speed is high, and patients can work and live normally [4]. In addition, mini face lifting surgery takes oriental facial aesthetic standards as one of the reference standards. It provides a comprehensive and detailed design plan based on the different conditions of each patient to ensure that the final solution is genuinely customized, it also ensures compliance with international aesthetic standards, and promotes the satisfaction of patients [5].

This study aimed to evaluate the effect of mini facelift in facial plastic surgery patients. The results showed that the study group had shorter operation time and swelling period than the control group ($P < 0.05$). The study group had lower HAM-A score and HAM-D score after surgery compared to the control group ($P < 0.05$). The study group had higher satisfaction than the control group ($P < 0.05$), which is enough to show that the application of mini facelift in facial plastic surgery can shorten the operation time and swelling period, improve satisfaction, and relieve negative emotions. This method is suitable for comprehensive clinical application.

Disclosure statement

The author declares no conflict of interest.

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Analysis of the Therapeutic Efficacy of Mucopolysaccharide Polysulfate Cream Combined with Desonide Cream in the Treatment of Chronic Eczema

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Abstract: *Objective:* This paper aims to analyze the therapeutic efficacy of mucopolysaccharide polysulfate cream combined with desonide cream in the treatment of chronic eczema. *Methods:* A sample of 70 patients with chronic eczema admitted from April 2022 to April 2023 were randomly divided into groups. Mucopolysaccharide polysulfate cream combined with desonide cream was applied in group A, and desonide cream was used in group B. The treatment efficacy was analyzed in both groups. *Results:* The curative effect on chronic eczema in group A was better than that in group B, $P < 0.05$. The target skin lesion area of group A was smaller than that of group B, and the skin lesion area score was lower than that of group B, $P < 0.05$. The skin lesion-symptom score of group A was lower than that of group B, $P < 0.05$. The treatment satisfaction of group A was higher than that of group B, $P < 0.05$. *Conclusion:* Patients with chronic eczema treated with mucopolysaccharide polysulfate cream combined with desonide cream can promote the regression of skin lesions and enhance the therapeutic efficacy.

Keywords: Chronic rash; Desonide cream; Polyiodic acid polysaccharide cream

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1. Introduction

Eczema is common among skin diseases, which is related to infection and inflammation of the epidermis and dermis. It is characterized by itching and symmetry, with a high recurrence rate. After the acute onset of eczema, if the diagnosis and treatment are poor, it can turn into chronic eczema, inducing severe itching and even leading to local skin inflammatory infiltration, which is manifested as skin thickening, moss-like and rough lesions, which can reduce the patient's quality of life. Therefore, attention should be paid to rash treatment. In clinical practice, skin rashes are mostly treated conservatively with drugs. Glucocorticoids are commonly used, which can inhibit the proliferation of skin lesions, fight inflammation, and improve skin physiological functions. However, glucocorticoids have a high risk of side effects and cannot restore the physiological functions of the damaged skin. Some scholars suggest combining the treatment with mucopolysaccharide polysulfate cream to

enhance the curative effect. This article selected 70 chronic eczema patients treated from April 2022 to April 2023 as samples to explore the therapeutic efficacy of mucopolysaccharide polysulfate cream combined with desonide cream.

2. Materials and methods

2.1. General information

A sample of 70 patients with chronic eczema admitted from April 2022 to April 2023 were randomly divided into groups. There was no difference in the data of patients with chronic eczema in groups A and B, $P > 0.05$. The details are shown in **Table 1.**

Table 1. Analysis of the data of patients with chronic eczema

Group	Gender		Age (years)		Duration of disease (years)		Skin lesion area proportion (%)	
	Male	Female	Range	Mean	Range	Mean	Range	Mean
Group A (n = 35)	21 (60.00)	14 (40.00)	20–77	50.14 ± 0.84	1–9	4.24 ± 0.85	1–5	2.79 ± 0.25
Group B (n = 35)	22 (62.86)	13 (37.14)	21–78	50.17 ± 0.86	1–8	4.21 ± 0.87	1–6	2.84 ± 0.27
χ^2/t	0.0589		0.1476		0.1459		0.8039	
P	0.8083		0.8831		0.8844		0.4243	

2.2. Inclusion and exclusion criteria

Inclusion criteria included patients who can follow the doctor's instructions and apply the medicine, patients who give informed consent, and patients who do not carry out chronic eczema treatment independently.

Exclusion criteria were patients with chronic eczema in the acute phase, patients with other skin diseases such as acne and psoriasis, patients with organ lesions, and patients with rashes in the perianal and vulvar areas.

2.3. Treatment methods

To clean the local skin of chronic eczema and severe itching, loratadine tablets (Bayer Pharmaceuticals Co., Ltd.) were given, a single dose of 10mg, once a day.

Group A was treated with desonide cream (Chongqing Huabang Pharmaceutical Co., Ltd.) and mucopolysaccharide polysulfate cream (Mobilat Produktions GmbH). Desonide cream was applied evenly on the lesion area, followed by massaging for 2–5 minutes, and then mucopolysaccharide polysulfate cream was applied and massaged again for 2–5 minutes until the cream is completely absorbed. The treatment was done 2 times per day for one month.

Group B was treated with desonide cream, and the regimen was the same as group A, with the treatment done for one month.

2.4. Observation of therapeutic effect

If the skin area decreases by 60–94%, it will be considered markedly effective. If it decreases by 20–59%, it will be considered effective. If the skin area decreases by less than 20%, it will be considered ineffective.

2.5. Statistical analysis

The data of chronic eczema patients were processed with SPSS21.0. Chronic rash count data were recorded in %, and χ^2 test was performed. Chronic rash measurement data were recorded in mean ± standard deviation (SD) and t test was performed. $P < 0.05$ indicates that there is a statistical difference.

3. Results

3.1. Comparison of therapeutic effects on chronic eczema

The curative effect on chronic eczema in group A (97.14%) was higher than that in group B, which was 80.00%, $P < 0.05$. The results are shown in **Table 2**.

Table 2. Comparison of therapeutic effects on chronic eczema [n (%)]

Group	Markedly effective	Effective	Ineffective	Effective rate
Group A (n = 35)	29 (82.86)	5 (14.29)	1 (2.86)	97.14%
Group B (n = 35)	20 (57.14)	8 (22.86)	7 (20.00)	80.00%
χ^2	-	-	-	5.0806
P	-	-	-	0.0242

3.2. Comparison of target skin lesion area and skin lesion area score

After treatment, the target skin lesion area and skin lesion area score of patients with chronic eczema in group A were smaller and lower than those of group B, $P < 0.05$. Before treatment, the target skin lesion area and skin lesion area score of group A were no different from those of group B, $P > 0.05$. The results are presented in **Table 3**.

Table 3. Comparison of target skin lesion area and skin lesion area score (mean ± SD)

Group	Target skin area (cm^2)		Skin lesion area score (points)	
	Before medication	After medication	Before medication	After medication
Group A (n = 35)	51.87 ± 2.43	12.42 ± 1.05	2.95 ± 0.43	0.61 ± 0.11
Group B (n = 35)	51.89 ± 2.49	33.19 ± 1.43	2.96 ± 0.42	1.18 ± 0.23
t	0.0340	69.2619	0.0984	13.2267
P	0.9730	0.0000	0.9219	0.0000

3.3. Comparison of skin lesion-symptom scores

After treatment, the scores of itching degree, skin color, skin elasticity, and skin lesion thickness of patients with chronic eczema in group A were all lower than those of group B, $P < 0.05$. Before treatment, there was no difference in the skin lesion-symptom scores of group A and group B, $P > 0.05$. The results are shown in **Table 4**.

Table 4. Comparison of skin lesion-symptom scores (mean ± SD)

Group	Degree of itching (minutes)		Skin color (minutes)		Skin elasticity (minutes)		Skin lesion thickness (minutes)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication	Before medication	After medication
Group A (n = 35)	2.42 ± 0.85	0.73 ± 0.25	2.74 ± 0.78	0.71 ± 0.26	2.69 ± 0.78	0.69 ± 0.25	2.78 ± 0.88	0.67 ± 0.23
Group B (n = 35)	2.46 ± 0.87	1.32 ± 0.36	2.73 ± 0.79	1.33 ± 0.38	2.67 ± 0.81	1.42 ± 0.39	2.81 ± 0.89	1.41 ± 0.36
t	0.1946	7.9638	0.0533	7.9663	0.1052	9.3227	0.1418	10.2479
P	0.8463	0.0000	0.9577	0.0000	0.9165	0.0000	0.8877	0.0000

3.4. Comparison of satisfaction with chronic eczema treatment

Based on **Table 5**, the satisfaction rate of chronic eczema treatment in group A was 97.14%, which was higher than that in group B (77.14%), $P < 0.05$.

Table 5. Comparison of satisfaction with chronic eczema treatment [n (%)]

Group	Satisfied	Basically satisfied	Not satisfied	Satisfaction rate
Group A (n = 35)	26 (74.29)	8 (22.86)	1 (2.86)	97.14%
Group B (n = 35)	15 (42.86)	12 (34.29)	8 (22.86)	77.14%
χ^2	-	-	-	6.2477
P	-	-	-	0.0124

4. Discussion

The pathogenesis of chronic eczema is unknown, and histological changes are apparent. Typical features of chronic eczema are cell infiltration and exudation. Summary analysis shows that chronic eczema has no specific onset group, and the onset time is not seasonal. Based on the analysis of clinical practice, chronic eczema is related to the combined influence of external and internal factors, that is, it develops under the influence of bacterial infection, poor living habits, endocrine disorders, unclean diet, and other factors [1]. Relevant literature reports that the patient's allergic constitution is the main factor inducing chronic eczema. Under the influence of the above factors, type IV delayed allergic reaction occurs and manifests as skin lesions [2]. In addition, chronic eczema has a long course of disease and is often protracted and difficult to heal, thus it requires early diagnosis and treatment. Currently, most clinical treatments for chronic eczema use external hormones to promote the regression of skin lesions and reduce the area of skin lesions. However, chronic eczema has a high recurrence rate with prolonged repeated skin lesions, that require continuous external hormone treatment, which can cause many hormones to accumulate in the local skin, leading to skin atrophy and dullness. Hormones treatment reduces the skin's moisture content and increases skin dryness. Therefore, exploring efficient combination regimens for treating chronic eczema is essential.

This article selected desonide cream to treat chronic eczema. It is a glucocorticoid drug that can inhibit inflammation. It can reduce swelling and itching symptoms when applied to the external skin. It can also optimize the skin color, reduce skin itching, and adjust the skin texture. Relevant literature reports that chronic eczema in infants and young children can be treated with desonide cream, which can quickly control the eczema condition [3]. However, it should be noted that the typical pathological characteristics of chronic eczema are metabolic dysfunction, skin keratosis, inflammatory infiltration, and skin barrier dysfunction. Treatment with glucocorticoids can optimize the function of stratum corneum and restore the skin's physiological functions. However, eczema often recurs without healing, thus the long-term application of external glucocorticoids has specific toxic side effects, which can affect the treatment efficacy. In addition, when desonide cream is applied externally, the concentration of the cream absorbed by the skin lesion area is high in the early stage, which can quickly alleviate the symptoms of skin lesions. However, after external application for some time, the physiological functions of the local skin are enhanced, thus the concentration of the absorbed cream is reduced, resulting in a prolonged administration period. Moreover, long-term external application of glucocorticoids can act on cuticle cells, causing the loss of cuticle differentiation enzyme activity, thereby damaging the stratum corneum structure and reducing the number of new cells, which is manifested as a reduction in skin thickness in the damaged area [4]. At the same time, the long-term application of desonide cream can also affect lipid components and cause local skin acid-base disorders. Therefore, external application of desonide cream alone is required in order to improve skin functional indicators such as oil and stratum corneum effectively.

Some scholars suggest that patients with chronic eczema should be given mucopolysaccharide polysulfate

cream after applying desonide cream. It is a low-molecular-weight heparin that is rich in polyiodic acid mucopolysaccharide. It can moisturize the skin, reduce swelling and inflammation, and inhibit exudation. Through the analysis of clinical practice, polyiodic acid mucopolysaccharide has strong permeability, it can penetrate the dermis and the subcutaneous tissue in a short time, inhibit the synthesis of prostaglandins in the skin lesion area, and block the diffusion of hyaluronidase, thereby stimulating local blood supply, reducing swelling and inflammation [5]. In addition, after the mucopolysaccharide polysulfate cream is applied externally, the medicinal ingredients can act on the intercellular area, improve intercellular permeability, stimulate cell and connective tissue metabolism, and promote cell regeneration, which help to moisturize the skin and avoid skin cracks and dryness. In the literature involving patients with chronic eczema treated with external application of mucopolysaccharide polysulfate cream, it reported that it can reduce the area of skin lesions, suppress itching, and improve skin color. The synergistic effect of mucopolysaccharide polysulfate cream combined with desonide cream can promote the drugs to penetrate deeply into the skin tissue, which enhances the eczema treatment effect [6].

Based on the data analysis in this article, the treatment efficacy of chronic eczema in group A was 97.14%, which was higher than that in group B, which was 80.00%, $P < 0.05$. The addition of mucopolysaccharide polysulfate cream can improve the treatment efficacy of chronic rash. Simple treatment with desonide cream, a glucocorticoid drug, can achieve anti-inflammatory, anti-itching, and anti-allergic effects and stimulate vasoconstriction. If it is applied according to medical instructions, it can promote local swelling symptoms caused by inflammatory infiltration. It can also lower the temperature of the skin lesion area, and adding mucopolysaccharide polysulfate cream can increase skin permeability and enhance the efficacy of desonide cream [7]. The results also showed that the target skin lesion area of group A (12.42 ± 1.05 cm^2) was smaller than that of group B, and the score of skin lesion area of group A (0.61 ± 0.11) was lower than that of group B, $P < 0.05$. In group A, the degree of itching, skin color, skin elasticity, skin lesion thickness, and other scores were all lower than those in group B, $P < 0.05$. It can be seen that the addition of mucopolysaccharide polysulfate cream can promote the regression of skin lesions and reduce the symptoms of eczema. This may be because the main active ingredients of mucopolysaccharide polysulfate cream are polysulfonic acid-based mucopolysaccharides, which are heparin-like substances with significant anti-inflammatory effects. After external application, they can penetrate the subcutaneous tissue quickly and optimize the local blood, as well as enhance the skin's water-locking function [8]. Moreover, the addition of this drug can also stimulate the metabolism of the skin lesion area, which is beneficial to cell regeneration. It is a safe non-hormonal drug that can also shorten the administration cycle and dosage of hormonal drugs such as desonide cream [9]. The last data set showed that chronic eczema treatment satisfaction in group A was 97.14%, which was higher than that of group B, which was 77.14%, $P < 0.05$. It can be seen that the addition of mucopolysaccharide polysulfate cream can enhance the treatment satisfaction of patients with chronic eczema. This may be due to that the drug is administered according to the external application method. The active ingredients take effect directly in the skin lesion area without being metabolized by the viscera, which can reduce adverse drug reactions. The local blood concentration of the drug is high, and the effect is quick, thus the patient's treatment satisfaction is high. In addition, when applying external drugs to treat chronic eczema, the following matters need to be considered. Patients need to return to the hospital for review every 2–4 weeks so that the doctor can adjust the dosage plan. Patients should avoid contact with irritating substances and allergic substances. Patients should maintain positive and stable emotions and avoid mental stress. Doctors should actively diagnose and treat the primary disease, and if it is combined with other skin diseases, they should also actively diagnose and treat it accordingly [10].

In summary, chronic eczema patients treated with mucopolysaccharide polysulfate cream combined with

desonide cream can promote the regression of local skin lesions, reduce eczema symptoms, and improve the treatment satisfaction of eczema patients. This treatment method has high clinical application value.

Disclosure statement

The author declares no conflict of interest.

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A Prospective Open-Label Study of the Antifungal Activity of External Forms of Activated Zinc Pyrithione in the Treatment of *Malassezia*-Associated Skin Diseases

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Abstract: *Background:* There are insufficient data on the antifungal activity of active zinc pyrithione, which is widely used in practice. Considering the reported role of *Malassezia* spp. in the pathogenesis of several dermatologic diseases, it is of scientific and practical importance to investigate this issue. *Aim:* To evaluate the antifungal activity of external forms of activated zinc pyrithione in the treatment of psoriasis, seborrheic dermatitis, and pityriasis versicolor. *Method:* An open-label prospective study was conducted between March and July 2022. Patients with psoriasis, seborrheic dermatitis, and pityriasis versicolor were treated with external forms of activated zinc pyrithione for 21 days. Skin scales and circular prints from lesion foci, as well as from skin areas without clinical manifestations before and after therapy were studied. A quantitative assessment of skin colonization by micromycetes of *Malassezia* was performed using microscopic and cultural methods of examination. Clinical efficacy and drug safety of the therapy was assessed using the Dermatological Symptom Scale Index, by recording adverse events at weeks 0, 1, 2, and 3. *Results:* 64 patients aged 18 to 65 years with diagnoses of psoriasis, seborrheic dermatitis, and pityriasis versicolor were included. 60 patients completed the study, 4 were excluded due to failure to adhere to the schedule. In patients with seborrheic dermatitis and pityriasis versicolor in the lesion foci after therapy, a significant decrease was observed in the colonization level according to the results of microscopic and cultural studies. In psoriasis patients, a significant decrease in the colonization level was obtained only based on the results of microscopic examination. In all groups, significant differences in comparison to the initial level were observed at the 1st week of treatment. There was no adverse events observed. *Conclusion:* Activated zinc pyrithione in the form of cream and aerosol showed moderate antifungal activity against micromycetes of the genus *Malassezia*.

Keywords: Activated zinc pyrithione; *Malassezia*; Psoriasis; Seborrheic dermatitis; Pityriasis versicolor

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1. Introduction

Malassezia spp., lipophilic (excluding *M. pachydermatis*) yeast fungi, as part of the normal skin microbiome, account for over 90% of the fungal population in different skin regions [1]. *Malassezia* spp. is mainly limited to subcutaneous areas and rarely found on limbs and genitalia. Three species (*Pityrosporum orbiculare*, *P. ovale*, and *P. pachydermatis*) were identified over a long period of time and merged into *Malassezia*. In 1995, a total of 7 species have been classified into the *Malassezia* genus (*M. furfur*, *M. obtusa*, *M. globosa*, *M. sloofiae*, *M. sympodialis*, *M. pachydermatis*, *M. restricta*) based on molecular analysis. There are currently 14 species identified [2].

The prevalence of different *Malassezia* species depends on age, localization, and geographic location. In healthy individuals in Canada and Korea, *M. globosa* is found in children under 14 years of age, and *M. sympodialis* is found in the elderly [3,4]. *M. globosa* is mainly found on the head, and *M. sympodialis* is found on the trunk [3]. According to other data, *M. restricta* is detected on the head, while *M. globosa* is found on the chest [4]. *M. sympodialis* is most commonly found in Spain and Sweden [5,6], *M. restricta* is found commonly in Japan [7]. *M. restricta* localizes mainly in the external part of the ear canal, in the behind-the-ear folds, and in the bridge of the nose, while *M. globosa* localizes mainly on the back, occipital region, and inguinal folds [8].

Malassezia spp. are opportunistic microorganisms that cause dermatologic and systemic diseases. They become pathogens when immune balance is disturbed and interact with the skin by two mechanisms: direct and indirect. In direct exposure, specific metabolites of *Malassezia* are the cause of irritant reactions. Lipases break down triglycerides into fatty acids that cause flaking and release arachidonic acid, which is involved in the development of inflammation. Indirect exposure leads to the activation of immune and allergic reactions leading to the development of inflammation [1,2].

Pedrosa *et al.* distinguish three groups of dermatoses associated with *Malassezia* spp. First group is classical dermatoses (papillary rash and *Malassezia* folliculitis); Second group is dermatoses in which *Malassezia* play a role (seborrheic dermatitis); Third group includes dermatoses that may be associated with *Malassezia* (psoriasis, fusion reticular dermatosis, atopic dermatitis) [2].

Malassezia spp. are the cause of pityriasis versicolor. The specific association of *M. globosa* with pityriasis versicolor has been established in various studies in Greece, Spain, and Iran, but in Canada, *M. sympodialis* was most often identified as the cause of the disease [2]. Nevertheless, no correlation with the number of the pathogen was observed. It was found that sebum induces the formation of hyphae that promote the penetration of the pathogen into the skin. *Malassezia* spp. may be the cause of hypo- or hyperpigmented spots, affecting melanocytes in pityriasis versicolor [2].

In seborrheic dermatitis, *M. globosa* and *M. restricta* have been detected in the majority of cases [2]. Seborrheic dermatitis is currently considered as a chronic inflammatory dermatosis [9,10]. Grice and Dawson, and Theelen *et al.* believed that *Malassezia* are the cause of the development of seborrheic dermatitis [11,12], but it should be noted that their elimination does not lead to the cure of the disease. Apparently, it is more appropriate to consider *Malassezia* metabolites as triggers of seborrheic dermatitis. Karakadze *et al.* identified 11 gene mutations associated with seborrheic dermatitis. Most of the encoded proteins play a role in both immune response and epidermal differentiation dysfunction. These dysfunctions lead to the proliferation of *Malassezia*, their spread into the dermis, and the response of innate immunity, which causes inflammation [13].

In recent years, more and more data on the role of *Malassezia* spp. in psoriasis have become available [14]. It was found that the microbiome can influence the course and exacerbations of different psoriasis subtypes [15,16]. Several authors have shown that *M. japonica* and *M. furfur* are associated with psoriasis vulgaris, and other *Malassezia* are associated with guttate psoriasis and scalp psoriasis [17-19]. *M. globosa* is found predominantly

in scalp psoriasis, *M. furfur* and *M. sympodialis* were found less frequently; however, considering that these species exist normally on the above-mentioned areas, it is difficult to explain their role in psoriasis. At the same time, it should be noted that patients with psoriasis have antibodies to *Malassezia* spp. and their antigens [20].

In psoriasis, interleukin-23 (IL-23/Th17) is known to play a key role in the pathogenesis of the disease [21]. *Malassezia* can induce the production of cytokines associated with T helper 1 (Th1) cells in peripheral blood [22], as well as influence keratinocyte proliferation and production of pro-inflammatory cytokines involved in the pathogenesis of inflammation [23]. According to various data, topical and systemic antifungal preparations can have a significant therapeutic effect in the treatment of psoriasis [24-27]. According to Hurabielle *et al.*, in these cases, *Malassezia* spp. play the role of a factor exacerbating the disease, but they are not its cause, which explains the positive results of antifungal therapy. Undoubtedly, additional studies are required to understand the role of *Malassezia* spp. in the pathogenesis of psoriasis [16].

The treatment of dermatoses associated with *Malassezia* is based on antifungal and anti-inflammatory therapy (when involved in the pathogenesis of inflammation). Oral terbinafine is ineffective in prune-like psoriasis, but effective in moderate forms of seborrheic dermatitis. Oral itraconazole has a pronounced clinical effect in treating seborrheic dermatitis and reduces the number of *Malassezia* spp., but these data are few [2]. Topical (antifungal agents, corticosteroids, pimecrolimus, tacrolimus, zinc pyrithione, keratolytics) and systemic (imidazoles, terbinafine, isotretinoin) drugs are recommended in the treatment of seborrheic dermatitis [9].

In recent years, there has been renewed interest in zinc preparations, which have the following pharmacologic properties: they influence the differentiation of keratinocytes, have anti-inflammatory, antifungal, and antibacterial effects [28]. Thus, zinc preparations may act pathogenetically on dermatoses associated with *Malassezia*.

Activation of zinc pyrithione molecule leads to strengthening of intramolecular bonds, which results in activated zinc pyrithione becoming 50 times more stable in comparison with standard zinc pyrithione. Activated zinc pyrithione can bind to phospholipids and chelate metal cations, activate apoptosis, and inhibit regeneration. The antimicrobial and antifungal actions are based on the ability of this drug to disrupt the integrity of cell membranes [29]. In a comparative study of the anti-inflammatory activity of zinc pyrithione in a laboratory model of psoriasis, it was found that the anti-inflammatory effect of activated zinc pyrithione was insignificantly inferior to betamethasone and superior to zinc pyrithione [30,31].

To date, there are very few studies on the antimycotic activity of activated zinc pyrithione in the treatment of skin diseases. New data on the drug in this aspect will allow the expansion of the range of indications for use and better understanding of the pathogenesis of dermatoses.

The aim of the study is to evaluate the antifungal activity of external forms of activated zinc pyrithione in the treatment of psoriasis, seborrheic dermatitis, and pityriasis versicolor. Secondary objectives were to evaluate the clinical efficacy and safety of the drug application.

2. Methods

2.1. Inclusion and exclusion criteria

This paper conducted a prospective, open-label, interventional study. Inclusion criteria were men and women of any race between the ages of 18 and 65; signed informed consent; outpatients and/or inpatients; an established clinical diagnosis of psoriasis, seborrheic dermatitis, or pityriasis versicolor. Exclusion criteria were widespread forms of psoriasis (skin lesion area more than 10%); the need for systemic antimycotic therapy (for pityriasis versicolor); hypersensitivity to any component of external forms of activated zinc pyrithione; topical or systemic use of antifungal drugs within 3 months prior to the date of inclusion of the patient in the study; pregnancy or breastfeeding; expected violation of the drug regimen by the patient. The following criteria were also excluded:

withdrawal of informed consent; failure of the patient to comply with the visit schedule; development of serious adverse events or medical conditions/diseases for which, in the opinion of the investigator, continuation of the study treatment is not feasible, or is dangerous to the patient, or is not in the interest of maximizing the patient's welfare and safety.

2.2. Study methods

The study was carried out at the clinical base of the Department of Skin and Venereal Diseases of the Kirov Military Medical Academy of the Ministry of Defense of the Russian Federation, laboratory support by Research Institute of Medical Mycology named after P.N. Kashkin (Research Institute of Mycological Monitoring and Fungal Biology). Duration of the study was from March to July 2022.

All included patients were treated with topical forms of activated zinc pyrithione (psoriasis and seborrheic dermatitis in the form of a cream, pityriasis versicolor in the form of an aerosol) for 21 days. The drug was applied to the lesion foci 2 times a day. Control examinations were performed on weeks 0 (visit 1), 1 (visit 2), 2 (visit 3), and 3 (visit 4). At visits 1, 2, 3, and 4, basic physical data were recorded, the dermatologic index of the symptom scale was determined, and adverse events were recorded. Laboratory examination (microscopic and culture tests) was performed at visit 1 and 4.

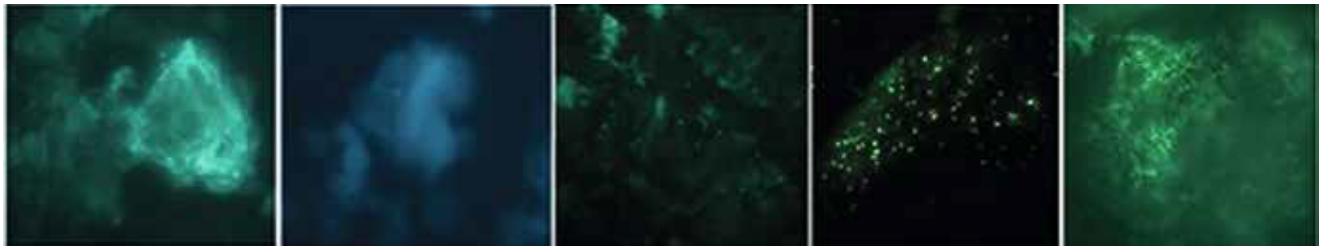
2.3. Observation indicators

The colonization of skin by *Malassezia* micromycetes in the lesions before and after application of the study drug was observed, as well as the clinical efficacy and safety of the investigational drug.

Microscopic study was one of the indicators observed in this study. The material was skin scales from lesions and skin areas without clinical manifestations (control), taken with surgical adhesive tape. The number of samples studied was 248 (128 before treatment and 120 after treatment).

Microscopic examination of preparations was performed using light-field and luminescent microscopy. When making native temporary micropreparations according to the "crushed drop" type, the samples were enclosed in a mounting solution of KOH (potassium hydroxide) at a concentration of 10% wt. in 40% vol of DMSO (dimethyl sulfoxide) with the addition of methylene blue. Additionally, a solution of Calcofluor white with Evans blue was added to the pre-preparation before examination as a fluorescent label for chitin and cellulose of the fungal cell wall. Microscopy of preparations from the samples of Object No.1 with subsequent photofixation of the results was carried out using a Leica DM LB2 microscope with a Leica DFC320 camera at magnification ratios of ×200 and ×400.

The results of microscopic examination were evaluated using a 5-point scale developed by us: 0 – absence of cells, 1 – single cells, 2 – moderate number of cells (up to 20 cells in the field of view), 3 – significant number of cells (from 20 to 100 cells in the field of view), 4 – abundance of cells (more than 100 cells in the field of view). Visualization of the score evaluation of microscopy results is presented in **Figure 1**.



No cells (0 points) | Single cells (1 point) | Moderate number of cells (2 points) | Significant number of cells (3 points) | Abundance of cells (4 points)

Figure 1. Visualization of the scale of the degree of colonization of samples under the microscope

Furthermore, culture study is another indicator observed. Material was taken from lesions and skin areas without clinical manifestations (control) in two variants: with the help of adhesive tape with the size of the working area 3.5 cm × 1.5 cm, the number of samples studied was 248 (128 before treatment and 120 after treatment); circular prints taken by the method of contact cups (bacterial prints with elective lipid-containing nutrient medium), the number of samples studied was 248 (128 before treatment and 120 after treatment).

Dense (agarized) lipid-containing elective nutrient medium, modified Leeming-Notman agar (mLNA), was used for isolation and cultivation of lipid-dependent micromycetes of the genus *Malassezia*. Composition of mLNA medium includes distilled water (1 liter), fermentative peptone (10 g), glucose (10 g), yeast extract (2 g), dry bovine bile (8 g), glycerol (10 ml), glycerol monostearate (0.5 g), Tween 60 (5.0 ml), olive oil (20 ml), and agar (15 g). To inhibit bacterial growth, an anti-antibiotic, chloramphenicol at a concentration of 40 mg/L, was added to the mLNA medium. One batch of mLNA medium produced in the laboratory was used to fulfill the entire scope of work.

Samples from adhesive tapes, fixed on the slides, before inoculation on nutrient media were pre-treated from the outside of the slide, as well as from its back side by successive progressive movements with a cotton swab soaked in 95% ethyl alcohol to avoid contamination of the inoculation by fast-growing mycelial (filamentous) micromycetes. Samples on adhesive tapes were removed from the slides with sterile tweezers and inoculated in pairs (from the lesions and control) on nutrient medium in Petri dishes.

The incubation of Petri dishes and contact cups (bakpechatka) was carried out in the incubator at 32 ± 2°C for 10 days. After the end of culturing, the counting of the grown colonies of micromycetes in each Petri dishes and contact cups was carried out with photofixation of the results. The results were expressed as the number of colonies per 1 dm^2 (CFU/dm^2).

Since *Malassezia* micromycetes are representatives of the human skin normobiota and the degree of colonization by these fungi varies considerably in the human population, for laboratory assessment of antifungal treatment efficacy, we additionally took into account the initial degree of colonization of healthy skin without clinical manifestations for each patient individually.

To assess the degree of skin colonization in the foci of *Malassezia* micromycetes infection before and after treatment, patients were ranked into groups based on the results of microscopic and culture studies. For microscopy, patients were ranked into groups (n = 5) according to the results, namely according to the number of scores (0–4). For culture studies, ranking by groups (n = 8) was carried out according to the value of CFU/dm^2: 0; 1...100; 101...200; 201...400; 401...800; 801...1600; 1601...3200, and more than 3200.

To determine the clinical efficacy of the drug, the modified dermatologic symptom scale index (DSSI) was used, as well as the physician's overall assessment of the patient's clinical condition (physician global assessment, PGA scale) (**Table 1**). Skin itching, erythema, scaling, infiltration, pigmentation, excoriations, cracks, and crusts were taken into account when calculating the DSSI. The severity of symptoms was graded as follows: none (0 points), mild (1 point), moderate severity (2 points), and significant severity (3 points). The total DSSI score is the sum of the values for each indicator and can range from 0 to 24.

2.4. Ethical review

The study was approved by the independent ethical committee of I.I. Mechnikov FGBOU VO NWSMU, protocol No. 2 of 16.02.2022.

2.5. Statistical analysis

Preliminary calculation of sample sizes was not performed. Statistical processing of the results of the study was carried out using the licensed software package STATISTICA v.10.0 (StatSoft, USA) and StatTech v. 2.8.8

(StatTech LLC, Russia). Culture results (CFU/dm^2) were evaluated for conformity to normal distribution using the Shapiro-Wilk criterion. Quantitative data were described using median, and lower and upper quartiles (Q1–Q3). The Wilcoxon (*W*) test was used to compare quantitative indices of skin colonization from the lesion and control skin areas at visits 1 and 4. Comparison of two independent groups was performed using the non-parametric Mann-Whitney criterion (*U*-test). Correlation analysis was performed using the non-parametric Spearman correlation coefficient. Differences were considered statistically significant at $P < 0.05$.

Table 1. Overall physician assessment of the patient's clinical condition (Physician Global Assessment, PGA)

Point	Degree of severity	Description	Response to therapy
0	Complete clearance	No signs of illness (100% improvement)	Complete response
1	Almost complete clearance	Very significant improvement (≥ 90%, < 100%), only traces of disease remain	Partial response
2	Marked improvement	Significant improvement (≥ 75%, < 90%), only isolated signs of disease remain	Partial response
3	Moderate improvement	Condition intermediate between marked minor improvement (≥ 50%, < 75%)	Partial response
4	Slight (weak) improvement	Some improvement (≥ 25%, < 50%), significant signs of disease remain	Disease stable
5	No change	No change from baseline (± 25%)	Disease stable
6	Worsening	Disease worsened from comparison to baseline by ≥ 25% or more	Disease progression

3. Results

3.1. Participants of the study

At the screening stage, 64 patients aged 18 to 65 years with diagnoses of limited psoriasis (16 males, 8 females, mean age 32.6 ± 16.8), seborrheic dermatitis (20 males, mean age 27.7 ± 10.1), and pityriasis versicolor (19 males, 3 females, mean age 27.8 ± 12.1) meeting the inclusion/exclusion criteria were examined. Sixty patients completed the study, four patients (2 psoriasis and 2 pityriasis versicolor) were excluded due to non-compliance with the visit schedule.

3.2. Main results of the study in psoriasis patients

In the microscopic and culture studies, micromycetes of the genus *Malassezia* were detected in 95% of patients (19/20). No *Malassezia* fungi were detected in the study material from one patient (No. P10 in the database) obtained at the 1st visit; therefore, it was not included in the analysis of the results in this group for the above-mentioned indicators.

In microscopic study, *Malassezia* micromycetes were detected in samples from foci in 16 patients (84.2%) before the start of antimycotic therapy, and in 11 patients (57.9%) after completion. After treatment, a decrease in the degree of colonization was observed: the majority of samples, 8 (42.1%), were in the 2nd rank group (1 point), 2 (10.5%) in the 3rd rank group (2 points), and another 1 (5.3%) in the 4th rank group. Group 5 did not include any of the studied samples either before or after therapy. The number of patients in whom *Malassezia* was not detected microscopically in the foci increased from 3 (15.8%) to 8 (42.1%). Complete elimination of the tested pathogen in samples from the foci after treatment occurred in 5 (26.3%) patients (**Table 2**). The differences between the related groups (before and after treatment) were statistically significant (**Table 3**). On healthy skin (control), *Malassezia* micromycetes were detected at the beginning of the study (visit 1) in 13 patients (68.4%) and at the end (visit 4) in 14 patients (73.7%); no significant differences between the related groups were found in this case (**Table 3**).

Table 2. Results of microscopic examination of samples from psoriasis patients at visits 1 and 4 (n = 19)

Rank groups	Number of points	Analyzed samples, abs. (%)			
		Foci		Control	
		Visit 1	Visit 4	Visit 1	Visit 4
1	0	3 (15.8%)	8 (42.1%)	6 (31.6%)	5 (26.3%)
2	1	6 (31.6%)	8 (42.1%)	12 (63.1%)	14 (73.7%)
3	2	4 (21%)	2 (10.5%)	1 (5.3%)	0 (0%)
4	3	6 (31.6%)	1 (5.3%)	0 (0%)	0 (0%)
5	4	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 3. Analysis of skin colonization dynamics in psoriasis patients (scores for microscopy, CFU/dm^2 for culture studies) at visits 1 and 4 (Median, Q1–Q3)

Focal point of the lesion						Healthy skin					
Microscopy		Adhesive tape		Contact cups (bak-pechatka)		Microscopy		Adhesive tape		Contact cups (bak-pechatka)	
Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4
1.0 (1.0–2.8)	0.5 (0–1.0)	228 (57–676)	38 (8–112)	20 (0–188)	0 (0–10)	1.0 (0–1.0)	1.0 (0–1.0)	61.5 (0–229)	30 (0–76)	0 (0–0)	0 (0–22)
P = 0.019*		P = 0.053		P = 0.06		P = 1.0		P = 0.198		P = 0.575	

*significant differences between related groups ($P < 0.05$)

In culture study, before antimycotic therapy, micromycetes of the genus *Malassezia* were isolated from adhesive tape in 17 (89.4%) patients and from contact cups samples in 10 (52.6%) patients. After treatment, *Malassezia* micromycetes were isolated from adhesive tape samples in 14 (73.7%) patients and from contact cups samples in 6 (31.6%) patients. There was a decrease trend of the degree of skin colonization in the foci of *Malassezia* spp. lesions in psoriasis patients under the background of treatment according to the culture results of samples on both adhesive tape and contact cups, and no significant differences between the related groups were revealed (**Table 3**).

After exposure to the investigated drug, most of the tested samples on adhesive tape entered the rank groups with the lowest level of colonization: 5 (26.3%) in the 1st (0 CFU) and 7 (36.9%) in 2nd (1...100 CFU/dm^2). The number of patients in groups 5 (401...800 CFU/dm^2) and 6 (801...1600 CFU/dm^2) decreased from 3 (15.8%) to 0%, while the number of patients in group 3 (101...200 CFU/dm^2) increased by 10.5%. Regarding the results of contact cups cultures, the number of patients with the highest level of skin colonization from group 8 (more than 3200 CFU/dm^2) decreased from 3 (15.8%) to 1 (5.3%). The number of samples in group 2 (1...100 CFU/dm^2) increased by 10.5%, from 2 to 4. At the same time, none of the studied samples entered groups 3 (101...200 CFU/dm^2) and 7 (1601...3200 CFU/dm^2). Complete elimination of the pathogen from the focus after treatment according to the culture results of samples occurred in 4 (21%) patients.

3.3. Additional results of the study in psoriasis patients

Analysis of the dynamics of DSSI in the course of treatment showed the following results: Median $_{\text{week 0}}$ = 7.5 (6.5; 11.0) points, Median $_{\text{week 1}}$ = 6.0 (5.0; 9.0) points, Median $_{\text{week 2}}$ = 5.0 (3.0; 7.0) points, Median $_{\text{week 3}}$ = 3.0

(2.0; 4.5) points, significant differences between related groups were obtained at the 1st week of treatment ($P < 0.001$). 15% of patients (3/20) achieved complete or almost complete clearance on the PGA scale (physician global assessment) and 45% (9/20) achieved marked improvement (**Figure 2**).

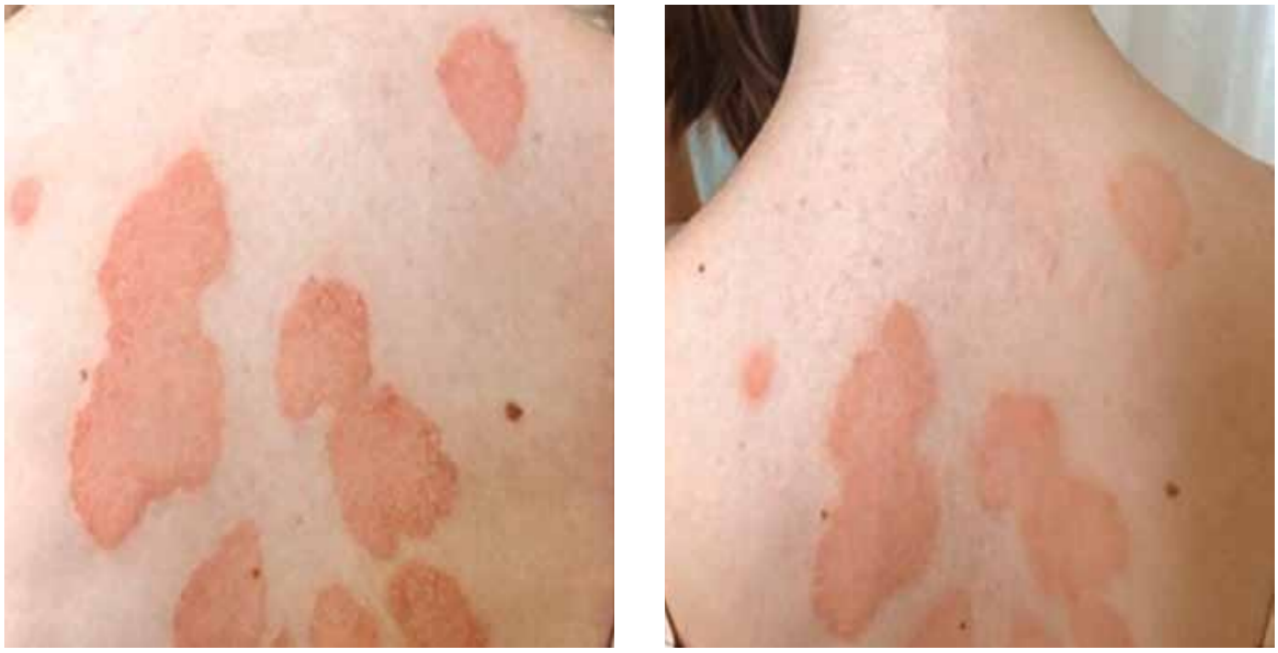


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Figure 2. Assessment of clinical effectiveness of the study drug (patient 19 years old, psoriasis, number P09 in the database): а — visit 1, DSSI — 10 points; б — visit 4, DSSI — 3 points, overall physician's evaluation — 2 points (marked improvement, partial response)

3.4. Main results of the study in patients with seborrheic dermatitis

In microscopic and culture studies, *Malassezia* micromycetes were detected in 100% of patients (20/20). In microscopic study, *Malassezia* micromycetes were detected in samples from foci in 19 patients (95.0%) before antimycotic therapy and in 17 patients (85.0%) after treatment. After treatment, a decrease in the degree of colonization was observed: most of the samples, 12 (60.0%), entered the 2nd rank group (1 point) and another 5 (25.0%) entered the 3rd group (2 points), while none of the studied samples entered the 4th and 5th groups. The number of patients in whom micromycetes of the genus *Malassezia* were not detected microscopically in the foci increased from 1 (5.0%) to 3 (15.0%). Complete elimination of the tested pathogen in samples from the foci after treatment occurred in 2 (10.0%) patients (**Table 4**). The differences between the related groups (before and after treatment) were statistically significant (**Table 4**). *Malassezia* micromycetes were detected on healthy skin areas at the beginning of the study (visit 1) in 14 patients (70.0%) and at the end of the study (visit 4) in 11 patients (55.0%); no significant differences between the related groups were found in this case (**Table 5**).

Table 4. Results of microscopic examination of samples from patients with seborrheic dermatitis at visits 1 and 4 ($n = 20$)

Rank groups	Number of points	Analyzed samples, abs. (%)			
		Foci		Control	
		Visit 1	Visit 4	Visit 1	Visit 4
1	0	1 (5%)	3 (15%)	6 (30%)	9 (45%)
2	1	9 (45%)	10 (50%)	10 (50%)	10 (50%)
3	2	4 (20%)	5 (25%)	4 (20%)	0 (0%)
4	3	4 (20%)	0 (0%)	0 (0%)	1 (5%)
5	4	2 (10%)	0 (0%)	0 (0%)	0 (0%)

Table 5. Analysis of skin colonization dynamics in patients with seborrheic dermatitis (points for microscopy, CFU/dm^2 for culture studies) at visits 1 and 4 (Median, Q1–Q3)

Focal point of the lesion						Healthy skin					
Microscopy		Adhesive tape		Contact cups (bakpechatka)		Microscopy		Adhesive tape		Contact cups (bakpechatka)	
Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4
1.5 (1.0–3.0)	1.0 (1.0–1.5)	828 (124–1796)	48 (0–181)	885 (44–2094)	0 (0–10)	1.0 (0–210)	1.0 (0–1.0)	112.5 (38–333)	9.5 (0–66.5)	0 (0–118)	0 (0–10)
$P = 0.027$*		$P = 0.001$		$P = 0.002$*		$P = 0.606$		$P = 0.023$*		$P = 0.228$	

*significant differences between related groups ($P < 0.05$)

Before antimycotic therapy, *Malassezia* micromycetes were culturally isolated from adhesive tape samples in 18 patients (90.0%) and from contact cups samples in 19 patients (95.0%). After treatment, *Malassezia* micromycetes were isolated from adhesive tape samples in 14 patients (70.0%) and from contact cups samples in 9 patients (45.0%). There was a statistically significant decrease in the degree of skin colonization with *Malassezia* spp. in patients under the background of treatment according to the culture results of samples on both adhesive tape and on contact cups (**Table 5**).

Most of the samples on adhesive tape, 11 (55.0%), were included in the 2nd rank group (1...100 CFU/dm^2), the number of patients in the 6th group (801...1600 CFU/dm^2) decreased from 5 (25.0%) to 2 (10.0%), and none of the samples entered the groups 5, 7, and 8 after exposure to the drug. The number of samples belonging to the 6th (801...1600 CFU/dm^2) and 2nd (1...100 CFU/dm^2) rank groups decreased by 15% according to the results of contact cups cultures. At the same time, none of the studied samples belonged to group 7 (1601...3200 CFU/dm^2). The number of patients with the highest level of skin colonization from group 8 (more than 3200 CFU/dm^2) decreased from 3 (15.0%) to 1 (5.0%). Complete elimination of the pathogen from the foci after treatment according to the culture results of samples on adhesive tapes and contact cups occurred in 4 (20.0%) and 10 (50.0%) patients, respectively. The number of samples belonging to high ranks in terms of colonization degree decreased significantly (by more than 50%).

3.5. Additional results of the study in patients with seborrheic dermatitis

Analysis of the dynamics of DSSI in the course of treatment showed the following results: Median $_{week\ 0}$ = 5.5 (4.0; 7.0) points, Median $_{week\ 1}$ = 3.0 (3.0; 4.5) points, Median $_{week\ 2}$ = 2.0 (2.0; 3.0) points, Median $_{week\ 3}$ = 1.0 (0.0; 2.5) points, significant differences between related groups were obtained at the 1st week of treatment ($P < 0.001$). 75% of patients (15/20) achieved complete or nearly complete clearance on the PGA scale (physician global assessment), as shown in **Figure 3**.

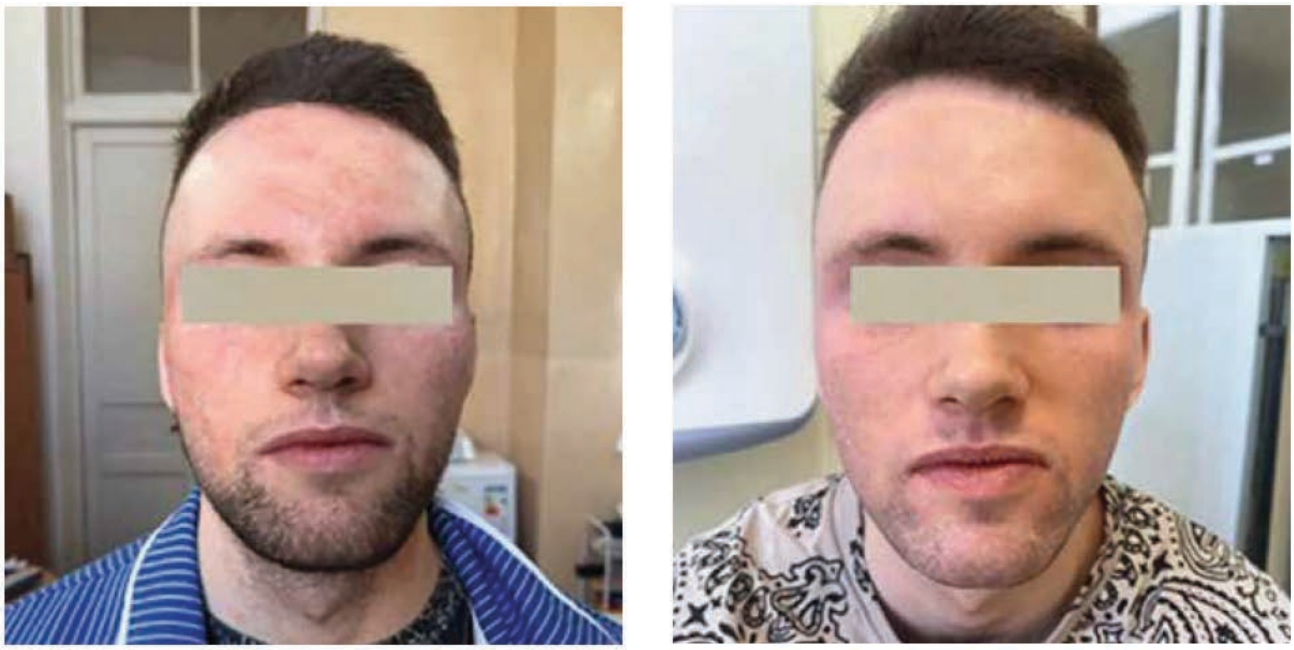

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Figure 3. Assessment of clinical efficacy of study drug (patient 20 years old, seborrheic dermatitis, number C05 in the database): a — visit 1, DSSI — 7 points; б — visit 4, DSSI — 1 point, overall physician score — 1 point (almost complete clearance, partial response)

3.6. Main results of the study in patients with pityriasis versicolor

Laboratory diagnosis of pityriasis versicolor was confirmed in almost all patients of this group, with the exception of subject O19, who, despite the presence of a clinical picture of the disease, positive results of culture and microscopic studies, did not have a typical tissue form of *Malassezia* micromycetes characteristic for the diagnosis of pityriasis versicolor. Therefore, the results for this patient were not taken into account in the subsequent group analysis.

Malassezia micromycetes were detected microscopically in samples from all 19 patients (100%), both before and after antimycotic therapy. After treatment, a decrease in the degree of colonization of the patients' skin was observed: most of the samples, 9 (47.4%), entered the 2nd rank group (1 point), 5 samples (26.3%) in the 3rd group (2 points), and 4 samples (21%) in the 4th group. The most significant decrease in colonization was observed in rank group 5, which included samples with an abundance of *Malassezia* spp. cells, from 15 (78.9%) to 1 (5.3%). Complete elimination of the tested pathogen in the samples from the lesions after treatment did not occur in any of the patients (**Table 6**). The differences between the related groups (before and after treatment) were statistically significant (**Table 7**). *Malassezia* micromycetes were detected on healthy skin areas at the beginning of the study (visit 1) in 14 patients (70.0%), and at the end of the study (visit 4) in 11 patients (55.0%); no significant differences between the related groups were found in this case (**Table 7**).

Table 6. Results of microscopic examination of samples from patients with pityriasis versicolor at visits 1 and 4 ($n = 19$)

Rank groups	Number of points	Analyzed samples, abs. (%)			
		Foci		Control	
		Visit 1	Visit 4	Visit 1	Visit 4
1	0	0 (0%)	0 (0%)	2(10.5%)	5 (26.4%)
2	1	0 (0%)	9 (47.4%)	13 (68.5%)	12 (63.1%)
3	2	1 (5.3%)	5 (26.3%)	4 (21%)	2 (10.5%)
4	3	3 (15.8%)	4 (21%)	0 (0%)	0 (0%)
5	4	15 (78.9%)	1 (5.3%)	0 (0%)	0 (0%)

Table 7. Analysis of skin colonization dynamics in patients with pityriasis versicolor (points for microscopy, CFU/dm^2 for culture studies) at visits 1 and 4 (Median, Q1–Q3)

Focal point of the lesion						Healthy skin					
Microscopy		Adhesive tape		Contact cups (bakpechatka)		Microscopy		Adhesive tape		Contact cups (bakpechatka)	
Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4	Visit 1	Visit 4
4.0 (3.5–4.0)	2.0 (1.0–3.0)	648 (296–1188)	38 (19–104)	155 (0–510)	0 (0–44)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	38 (19–114)	19 (0–76)	0 (0–22)	0 (0–11)
$P < 0.001$*		$P < 0.001$*		$P = 0.033$*		$P = 0.593$		$P = 0.17$		$P = 0.415$	

*significant differences between related groups ($P < 0.05$)

It was noted that microscopy of samples from patients after drug therapy (visit 4) revealed *Malassezia* spp. cells predominantly with a destructive cell wall (**Figure 4**). Thus, despite a moderate number of cells of this micromycetes in some samples, most of the cells detected were damaged and therefore incapable of growth and multiplication, i.e., of sustaining the infection process.

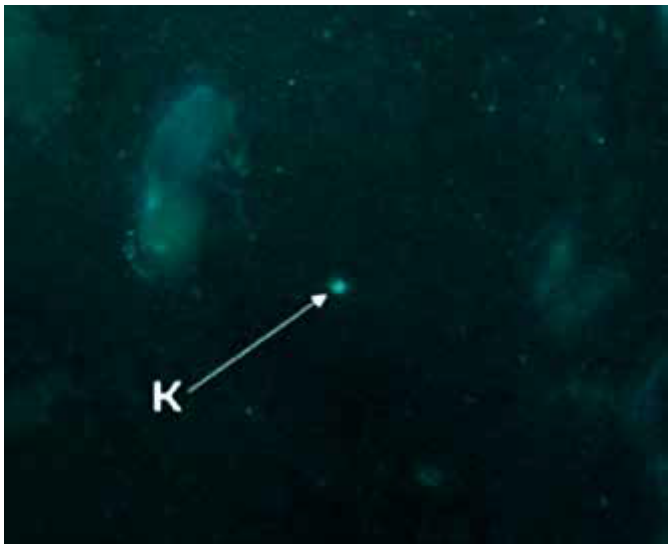

Figure 4. *Malassezia* sp. cell (K) with a destructive cell wall (Magnification ×400)

In culture study, prior to antimycotic therapy, micromycetes of the genus *Malassezia* were isolated from adhesive tape of patient samples in 19 (100%) and from contact cups samples in 10 (52.7%) patients. After treatment, *Malassezia* micromycetes were isolated from adhesive tape samples in 15 (78.9%) patients and from contact cups samples in 5 (26.3%) patients of this group. There was a statistically significant decrease in the degree of skin colonization by *Malassezia* spp. in patients under the background of treatment according to the culture results of samples on both adhesive tape and on contact cups (**Table 7**).

Most of the samples on adhesive films, 10 (52.7%), were included in the 2nd rank group (1...100 CFU/dm^2), the number of patients in the 8th group (more than 3200 CFU/dm^2) decreased from 3 (15.8%) to 1 (5.3%), groups 3 and 4 included 2 (10.5%) patients each, and groups 5, 6, and 7 did not include any of the samples after exposure to the tested preparation.

When evaluating the results obtained on contact cups, the number of samples in Group 1 increased from 9 (47.4%) to 14 (73.7%). The number of samples in the 3rd rank group (101...200 CFU/dm^2) decreased by 10.5%, from 3 (15.8%) to 1 (5.3%). In groups 5 and 7, the number of samples remained unchanged (5.3%). At the same time, none of the tested samples entered groups 4 (201...400 CFU/dm^2), 6 (801...1600 CFU/dm^2), and 8 (more than 3200 CFU/dm^2). Complete elimination of the pathogen from the foci after treatment according to the culture results of samples on adhesive tapes and contact cups occurred in 4 (21.0%) and 5 (26.3%) patients respectively. The number of samples belonging to high ranks in terms of colonization degree decreased significantly (by more than 50%).

3.7. Additional study findings in patients with pityriasis versicolor

The analysis of the dynamics of DSSI during treatment showed the following results: Median $_{week\ 0}$ = 4.0 (3.5; 5.5) points, Median $_{week\ 1}$ = 3.0 (2.0; 4.0) points, Median $_{week\ 2}$ = 2.0 (2.0; 3.0) points, Median $_{week\ 3}$ = 1.0 (1.0; 2.0) points, significant differences between related groups were obtained at the 1st week of treatment ($P < 0.001$). 50% of patients (10/20) achieved complete or nearly complete clearance on the PGA scale (physician global assessment) and 25% (5/20) achieved marked improvement (**Figure 5**).

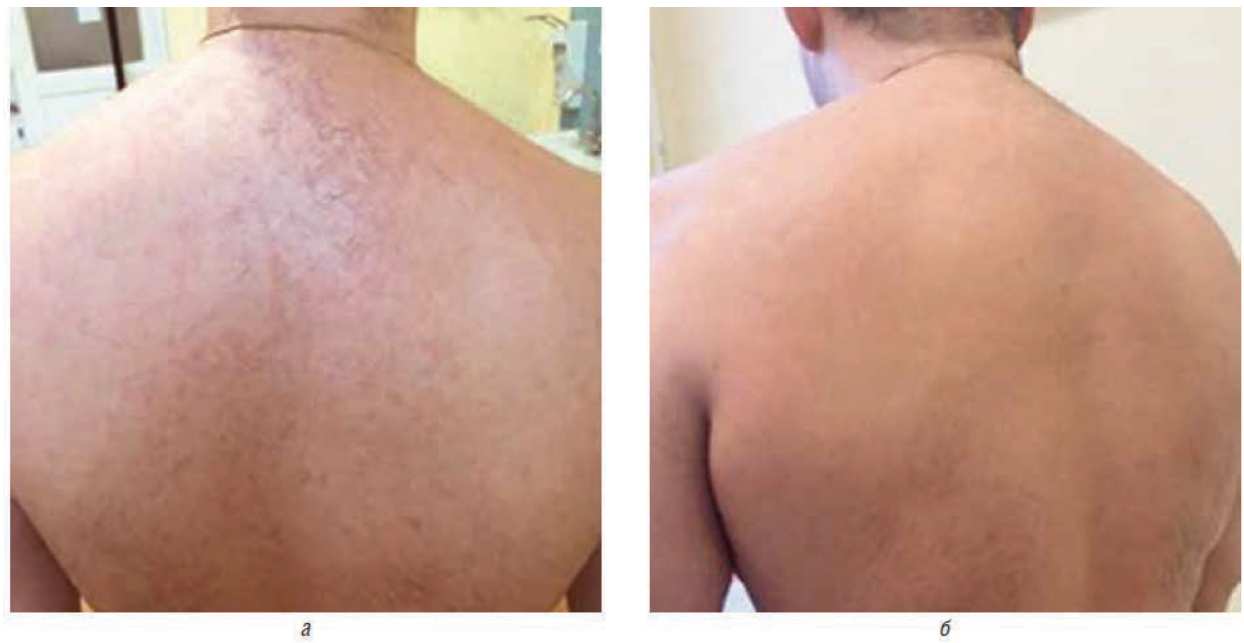

Figure 5. Assessment of clinical efficacy of study drug (patient 32 years old, pityriasis versicolor, number O06 in database): а — visit 1, DSSI — 4 points; б — visit 4, DSSI — 1 point, overall physician evaluation — 1 point (almost complete clearance, partial response)

3.8. Adverse events

No adverse events, including those associated with the use of activated zinc pyrithione, have been reported.

4. Discussion

The obtained results showed a high prevalence of *Malassezia* fungi in patients with psoriasis and seborrheic dermatitis. In the case of psoriasis, according to the results of three variants of investigations (microscopy, inoculation with adhesive tape, inoculation with a contact cup), *Malassezia* spp. were isolated in 95% of patients (19/20), and 100% (20/20) of patients in the case of seborrheic dermatitis. Quantitative indicators of colonization according to the culture data in the foci of psoriasis lesions and on control areas (healthy skin) testify to ambiguous results. No significant differences were obtained when inoculated from adhesive tapes (Median $_{foci}$ = 228 CFU/dm^2, Median $_{healthy}$ = 66 CFU/dm^2, P = 0.103), while the differences from contact cups inoculation were statistically significant (Median $_{foci}$ = 20 CFU/dm^2, Median $_{healthy}$ = 0 CFU/dm^2, P = 0.031). In patients with seborrheic dermatitis, colonization by fungi of the genus *Malassezia* in the lesion foci was significantly higher in both cases compared to the control (adhesive tape: Median $_{foci}$ = 828 CFU/dm^2, Median $_{healthy}$ = 113 CFU/dm^2, P = 0.032; contact cups: Median $_{foci}$ = 825 CFU/dm^2, Median $_{healthy}$ = 0 CFU/dm^2, P < 0.001).

The correlation analysis between the level of *Malassezia* spp. colonization in the lesions and DSSI in psoriasis did not reveal any correlation (adhesive tape: R = -0.34, P = 0.156; contact cups: R = -0.06, P = 0.816). The opposite results were observed in patients with seborrheic dermatitis, where a direct moderate correlation between the degree of severity of dermatosis (DSSI) and the level of colonization of *Malassezia* spp. in the lesions (adhesive tape: R = 0.48, P = 0.03; contact cups: R = 0.53, P = 0.017) was found. Thus, we can conclude about the involvement of yeast fungi in the pathogenesis of seborrheic dermatitis, while this issue requires further study for psoriasis.

The use of activated zinc pyrithione led to a decrease in the colonization of *Malassezia* spp. in the lesions in all studied dermatoses, which indicates a moderate antifungal effect, since it was not possible to achieve complete elimination of *Malassezia* spp. in the foci of lesions in most cases. In psoriasis and seborrheic dermatitis, the decrease in the contamination can be associated with the anti-inflammatory effect of the drug, but in pityriasis versicolor, such mechanism is impossible by definition. An important fact registered in the course of the study that should be considered is the detection of *Malassezia* spp. cells with destructive cell wall, i.e., incapable of growth and multiplication, and, therefore, incapable of maintaining the infectious process.

5. Limitations

The sample of psoriasis patients was not large enough, and therefore no statistically significant reduction in skin colonization was obtained. To obtain accurate conclusions on this issue, it is necessary to conduct an additional study with the inclusion of a larger number of patients.

6. Conclusion

Activated zinc pyrithione in the form of cream and aerosol showed a moderate antifungal activity against *Malassezia* micromycetes. The use of the drug confirmed its high clinical efficacy and safety in the treatment of psoriasis and seborrheic dermatitis.

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Disclosure statement

The authors declare no conflict of interest.

Author contributions

A.V.P., T.S.B., and T.V.B. were involved in the concept and design of the study. A.V.P., A.Y.A., and T.V.B., were involved in collection and processing of material. X.O. A.V.P., K.O.C., T.V.B., and A.Y.A. were involved in text writing. A.V.S. and N.V.V. were involved in editing.

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Integrated Services Platform of International Scientific Cooperation

Innoscience Research (Malaysia), which is global market oriented, was founded in 2016.Innoscience Research focuses on services based on scientific research. By cooperating with universities and scientific institutes all over the world, it performs medical researches to benefit human beings and promotes the interdisciplinary and international exchanges among researchers.

Innoscience Research covers biology, chemistry, physics and many other disciplines. It mainly focuses on the improvement of human health. It aims to promote the cooperation, exploration and exchange among researchers from different countries. By establishing platforms, Innoscience integrates the demands from different fields to realize the combination of clinical research and basic research and to accelerate and deepen the international scientific cooperation.

Cooperation Mode

Clinical Workers

In-service Doctors

Foreign Researchers

Hospital

University

Scientific institutions

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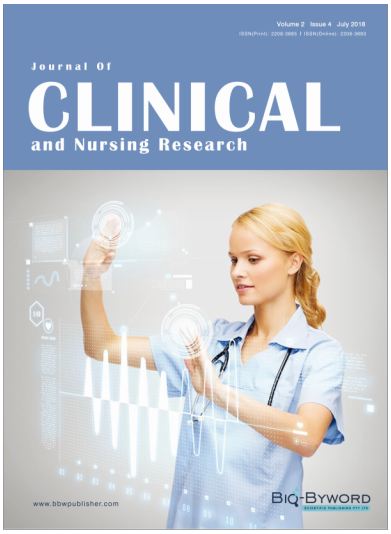
OUR JOURNALS

The *Journal of Architectural Research and Development* is an international peer-reviewed and open access journal which is devoted to establish a bridge between theory and practice in the fields of architectural and design research, urban planning and built environment research.

Topics covered but not limited to:

- Architectural design
- Architectural technology, including new technologies and energy saving technologies
- Architectural practice
- Urban planning
- Impacts of architecture on environment



Journal of Clinical and Nursing Research (JCNR) is an international, peer reviewed and open access journal that seeks to promote the development and exchange of knowledge which is directly relevant to all clinical and nursing research and practice. Articles which explore the meaning, prevention, treatment, outcome and impact of a high standard clinical and nursing practice and discipline are encouraged to be submitted as original article, review, case report, short communication and letters.

Topics covered by not limited to:

- Development of clinical and nursing research, evaluation, evidence-based practice and scientific enquiry
- Patients and family experiences of health care
- Clinical and nursing research to enhance patient safety and reduce harm to patients
- Ethics
- Clinical and Nursing history
- Medicine

Journal of Electronic Research and Application is an international, peer-reviewed and open access journal which publishes original articles, reviews, short communications, case studies and letters in the field of electronic research and application.

Topics covered but not limited to:

- Automation
- Circuit Analysis and Application
- Electric and Electronic Measurement Systems
- Electrical Engineering
- Electronic Materials
- Electronics and Communications Engineering
- Power Systems and Power Electronics
- Signal Processing
- Telecommunications Engineering
- Wireless and Mobile Communication