ORIGINAL ARTICLE

Intralesional Methotrexate versus Intralesional Triamcinolone acetonide in Treatment of Resistant Localized Alopecia Areata

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Abstract

Background: ***Noncicatricial hair loss is the hallmark of the common autoimmune hair condition alopecia areata(AA). Although AA often manifests as isolated patches on the face and scalp, it can affect any part of the body that bears hair, potentially resulting in much more widespread involvement.***

Aim and objectives: ***To evaluate the efficacy of intralesional methotrexate against intralesional triamcinolone acetate in treating patients with localized resistant alopecia areata at the dermatology department.***

Patients and methods: ***The current study was conducted on 40-participants in the outpatient clinic of Dermatology and Venereology Departments of Al-Hussein University Hospitals, Al-Azhar University,Cairo from July 2021 to January 2023. Twenty patients were selected for each group. Intralesional injections in alopecia areata patches were administered to both groups using a 30-gauge needle attached to an insulin syringe. Each group had a maximum of four injections spaced three weeks apart.***

Results: ***Clinical Improvement, Density, and Hair Thickness were not significantly different between the two groups (p=0.776, 0.569, and 0.125, respectively). The pain sensation and the number of sessions were significantly lower in the methotrexate group, with p-values of<0.001&0.014, respectively.***

Conclusion: ***No statistical difference was found between the results for the groups receiving methotrexate and triamcinolone. Pain was major side effect, and higher number of sessions were needed in Triamcinolone group with statistically significant difference compared with Methotrexate group. As an alternative to intralesional triamcinolone, intralesional MTX shows promise as a treatment for localized resistant AA.***

Keywords: Methotrexate; Intralesional triamcinolone acetonide; Alopecia areata

1. Introduction

Alopecia areata (AA) is an autoimmune disorder that causes chronic inflammation of the hair follicles, leading to nonscarring hair loss. Although it typically manifests as patchy hair loss, alopecia can develop to alopecia totalis (AT), where the scalp hair becomes completely bald, or alopecia universalis (AU), where the hair on your entire body begins to fall out.[1]

In terms of the course of the condition, 34% to 50% of patients see hair regrowth after a year, whereas 15% to 25% experience AA totalis, which is the complete loss of scalp hair. The severity of AA is directly related to the prognosis in the long run. Current therapies can stimulate new growth, but they cannot alter the progression of the disease.[2]

One of the many medications used to treat skin disorders is methotrexate (MTX), an immunosuppressant folic acid antagonist. In recent studies, researchers looked at MTX for AA both alone and in combination with other treatments.[3]

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Adenosine, a mediator of many of MTX's anti-inflammatory properties, is built up when the enzyme AICAR (5-aminoimidazole-4-carboxamide ribonucleotide formyl transferase) is inhibited. The release of adenosine into the extracellular space has several anti-inflammatory effects, including preventing the buildup of white blood cells, reducing the production of TNF-α and IFN-γ, and blocking the activities of various monocytes, macrophages, and T-cells. This mechanism may account for MTX's impact on AA.[4]

For optimal local action with little systemic effect, injectable steroids with poor solubility are preferable because of their sluggish absorption from the injection site. The primary mode of action is by reducing immune system activity.[5]

Methotrexate inhibits DNA synthesis and reduces purine and pyrimidine synthesis as a result of its powerful inhibitory effect on dihydrofolate reductase, the rate-limiting enzyme in tetrahydrofolate biosynthesis. It is applied in the treatment of inflammatory diseases where a high turnover of inflammatory cells, such as T lymphocytes, in target tissues is rampant.[6]

Among multiple anti-inflammatory actions, it inhibits white blood cell accumulation, leads to a reduction in TNF-α and IFN-γ synthesis, and inhibits a variety of monocyte, macrophage, and T-cell activities. This action might explain the effect of MTX in AA.[4]

With folliscope follow-up, this study aims to examine the effectiveness of MTX and triamcinolone acetonide in treating refractory localized AA.

2. Patients and methods

The current study is a double-blind comparative clinical study conducted on 40 participants in the outpatient clinic of Dermatology and Venereology Departments of Al-Hussein University Hospitals, Al-Azhar University, Cairo, from July 2021 to January 2023. Two groups of twenty patients each were formed: Group A: Twenty patients with localized resistant alopecia areata that have not responded to other treatments will receive intralesional methotrexate. Group B: Twenty patients with localized resistant alopecia areata that have not responded to previous treatments will be given intralesional triamcinolone acetonide.

Inclusion criteria:

Patients whose localized alopecia areata has shown resistance to topical treatments(i.e., has not improved after three months), and men and women.

Exclusion criteria:

Patients suffering from widespread baldness(alopecia totalis and universalis), patients with alopecia who have infection or scarring, women who are expecting a child or who are nursing parents, and those who are immunocompromised or who have a history of chronic liver or blood disease.

Methodology:

Full history taking:

A patient's medical history, including their name, age, employment, marital status, and any other relevant habits. Health background: when symptoms first appeared, how they progressed, how long the condition lasted, how hair loss occurred, and any other related issues(such as itchy or burning scalp). Medications taken: the length of time someone has taken medication for alopecia areata, when they stopped, the effects, and any negative side effects, as well as any medications used for other medical issues. Medical background, including alopecia areata and surgical procedures performed in the past, and finally, hereditary factors of alopecia areata and related disorders.

Dermatological evaluation:

To confirm the presence of alopecia areata lesions, one must consider the following: Traditional bald spots caused by alopecia areata have smooth surfaces, round or oval shapes, and well-defined edges. The skin within the patch is perfectly normal, but it may seem somewhat pinkish. It is common to see exclamation mark hairs, which are small hairs that narrow at the tip and widen at the base, when viewed through a lens or at the patch's edge. We applied one patch up to three, not more than three patches. The washing period was 6 months before starting the treatment of our study. The dose of methotrexate in our study is based on previous work by Hamdino et al.[7]

According to Dai YX, et al.,[8] studies assessed the relation between cigarette smoking, alcohol consumption, and risk of AA. It was reported that current smokers had an increased risk of developing AA. We assess our improvement using the FollicleScope hair analyzer, which detects capabilities including the following: density of hair and thickness of the hair. The patients were assessed before treatment and three weeks after the last session. Score of hair density: (+):<30%, (++): 30-60%n and (+++):>60%. Score of hair thickness: (+):<0.05, (++):0.05-0.1, and (+++):>0.1.

Digital Follicle Exam:

Using a folliscope, the patients were examined. Unlike competing goods, the Dlite Folli scope comes with interchangeable points that provide fixed magnifications of 15, 30, 50, 100, 150, and 200x. Additionally, a thumb wheel allows you to zoom in or out between 10x-200x. The special accessories come with the Dlite Folliscope, which is

the only version of a handheld zoom camera.

Its detecting capabilities include the following: density of hair, thickness of the hair, the ratio of terminal hair to villus hair, and the patients were assessed once before treatment and three weeks after last session.

Evaluation of safety:

Patients were instructed to document any potential side effects, including redness, discomfort, ulceration, burning, ecchymosis, infection, post-inflammatory hyperpigmentation, skin atrophy, and any other complications.

Ethical considerations:

For maximum of 4-sessions, they were scheduled every three weeks. The patients were assessed once before treatment and three weeks after last session. Prior to the trial, all patients were apprised of the procedures and were asked to provide their written permission.

MTX Group:

A vial containing 25mg/ml of methotrexate was used. Intradermal injections of MTX were performed under strict aseptic conditions, with a volume of 0.02ml administered at 1-cm intervals. Each injection of insulin was limited to 0.1-0.2ml (2.5-5mg) and was administered using a 30-gauge needle connected to an insulin syringe.

TrA Group:

Intralesional steroids(kenacort® 40mg/ml) were first administered at a concentration of 40mg/ml. At 1-centimeter intervals, a volume of 0.05-0.1ml of diluted triamcinolone acetonide(10mg/ml TrA) was injected intradermally. The greatest volume administered per session is not more than 2ml(20mg) using a 0.5-inch long 30-gauge needle attached to an insulin syringe.

Statistical analysis:

After data collection, editing, and coding, IBM SPSS 20 was utilized for data input. Parametrically distributed quantitative data were shown as means, standard deviations, and ranges, whereas qualitative data were percentages and numbers. The center value of a set of discrete integers is the sum of all the values divided by the number. Standard deviation measures data dispersion. If the standard deviation is low, the data cluster around the mean; if high, they are widely spread.

The median cuts the data set in half from highest to lowest. The median is less impacted by outliers than the mean, which is its main advantage. The Paired t-test compared the two groups using quantitative data and a parametric distribution. We set a 5% error margin and a 95% confidence interval. This is why the p-value was significant: A p-value over 0.05 is insignificant. A p-value is significant if <0.05(95% confidence interval), P<0.001:very important.

3. Results

Table 1. Demographic data of patients in methotrexate group.

METHOTREXATE		N	%
AGE	Range	17-55	
	Mean±SD	36±10.453	
SEX	Female	14	70.0
	Male	6	30.0

It was found that patients had an average age of 36±10.453 years. Regarding sex, 6-male patients(30%) and 14-female patients(70%) were included in our study,(table 1).

Table 2. Smoking among Methotrexate group.

METHOTREXATE		N	%
SMOKING	No	13	65.0
	Moderate smoker	3	15.0
	Heavy smoker	4	20.0

The majority of our patients 13(65%) were not smokers, 4-patients(20%) were heavy smokers, while 3-patients(15%) were moderate smokers,(table 2).

Table 3. Summary of results regarding Triamcinolone Acetonide.

TRIAMCINOLONE ACETONIDE		N	%
AGE	Range	18-50	
	Mean±SD	32.25±9.141	
SEX	Female	14	70.0
	Male	6	30.0
SMOKING	No	17	85.0
	Mild smoker	1	5.0
	Moderate smoker	2	10.0

It was found that patients had an average age of 32.25±9.141 years. Regarding sex, 6-male patients(30%) and 14-female patients(70%) were included in our study,(table 3).

Table 4. Comparison between Methotrexate and *Triamcinolone* Acetonide regarding Density of hair by folliscope

		GROUP				TOTAL	
		Methotrexate		Triamcinolone Acetonide			
		N	%	N	%	N	%
DENSITY OF HAIR BY FOLLISCOPE	(-)	5	25.0%	5	25.0%	10	25.0%
	(+)	1	5.0%	3	15.0%	4	10.0%
	(++)	5	25.0%	5	25.0%	10	25.0%
	(+++)	9	45.0%	7	35.0%	16	40.0%
TOTAL		20	100.0%	20	100.0%	40	100.0%
MANN-WHITNEY TEST	Mean Rank	21.50		19.50			
	Z	-0.569					
	P-value	0.569					

Group-A:9-patients(45%) showed improvement by(+++) score table. Only one-patient(5%) showed improvement by(+) score, no improvement was reported among 5-patients(25%). Group B:7-number of patients improved by(+++) score, 3-patients(15%) improved by(+) score, no improvement was reported among 5-patients(25%). There was no discernible variation between the two sets of data,(table 4).

Table 5. Comparison between Methotrexate and Triamcinolone Acetonide regarding Thickness of hair by folliscope

		GROUP				TOTAL	
		Methotrexate		Triamcinolone Acetonide			
		N	%	N	%	N	%
THINCKNESS OF HAIR BY FOLLISCOPE	(-)	5	25.0%	5	25.0%	10	25.0%
	(+)	3	15.0%	9	45.0%	12	30.0%
	(++)	9	45.0%	6	30.0%	15	37.5%
	(+++)	3	15.0%	0	0.0%	3	7.5%
TOTAL		20	100.0%	20	100.0%	40	100.0%
MANN-WHITNEY TEST	Mean Rank	23.20		17.80			
	Z	-1.536					
	P-value	0.125					

Group-A:45%(n=9) of improved by score(++), 25%(n=5) did not show improvement followed by 15%(n=3) improved by(+++)&(+) score. Group-B:45%(n=9) had (+) score, 30%(n=6)&25%(n=5) had(++)&(-) scores, respectively, none of our patients had(+++) score. The difference between each group wasn't significant, where P-value=0.125,(table 5).

Table 6. Comparison between Methotrexate and Triamcinolone Acetonide regarding pain.

		GROUP				TOTAL	
		Methotrexate		Triamcinolone Acetonide			
		N	%	N	%	N	%
PAIN	No	16	80.0%	5	25.0%	21	52.5%
	Painful	4	20.0%	15	75.0%	19	47.5%
TOTAL		20	100.0%	20	100.0%	40	100.0%
LIKELIHOOD RATIO	X2	12.842					
	P-value	<0.001*					

Group-A:80%(n=16), did not experience pain throughout the treatment. Group-B:75%(n=15), had experienced pain throughout the treatment. The difference between the groups was statistically significant, where P-value<0.001*,(table 6).

Case presentation:

Case(1):

Twenty-seven years old female, clinical examination showed good improvement. Examination by folliscope showed marked increase in hair density and moderate increase in thickness of hair.

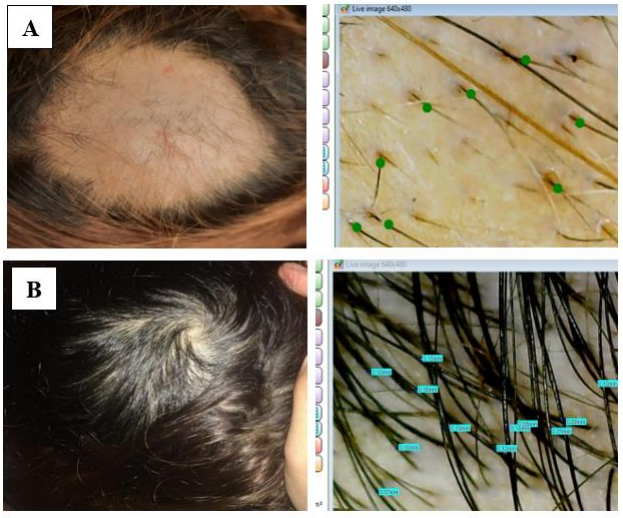

Figure 1. A)Before treatment by Triamcinolone, B)After treatement by Triamcinolone.

Case(2):

Forty-nine years old female, clinical examination showed good improvement. Examination by showed marked increase in hair density and moderate increase in thickness of hair folliscope.

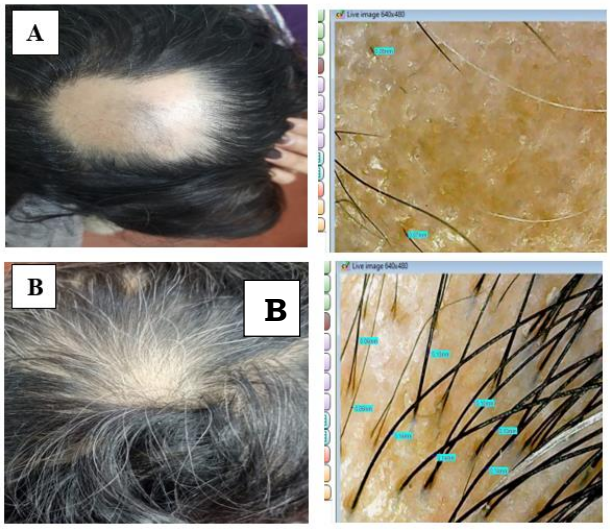

Figure 2. A)Before treatment by methotrexate, B) After treatment by methotrexate.

Case(3):

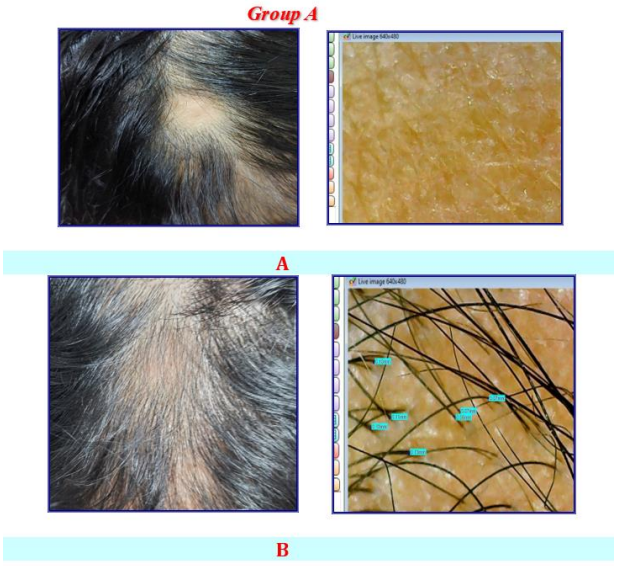

Figure 3. A) Before treatment by methotrexate, B) After treatement by methotrexate. 51 years old female, clinical examination showed good improvement after 2 sessions Examination by folliscope showed moderate increase in hair density and moderate increase in thickness of hair.

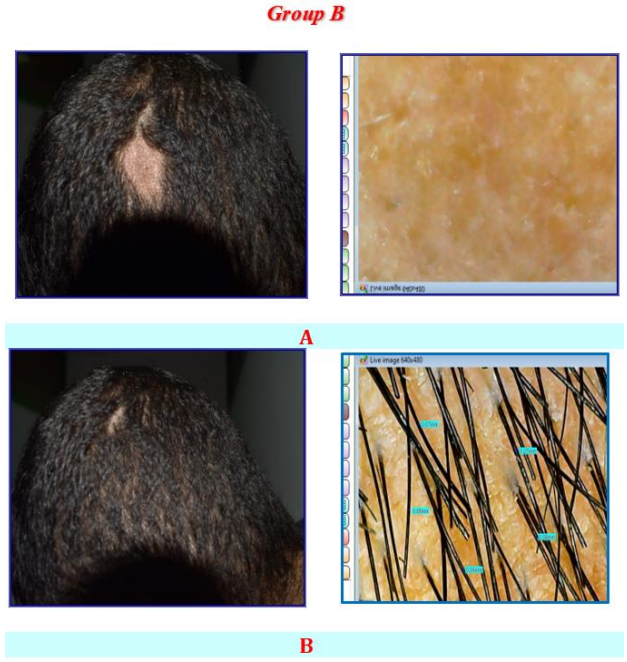

Figure 4. A) Befor treatment by Triamcinolone, B) After treatement by Triamcinolone. 35 years old male, clinical examination showed good improvement. after 3 sessions Examination by folliscope showed marked increase in hair density and moderate increase in thickness of hair.

4. Discussion

After looking at the gender breakdown of the two types of participants, out of the total number of patients enrolled, 6 were male(30%) and 14 were female(70%). With a p-value of 1, there is no statistically significant difference in the distribution of genders between the two groups.

Our findings are consistent with Uzuncakmak et al.,[9] that patients with AA are mostly female.

The average age of patients in group-A was 36.000±10.453 years, whereas the average age of patients in group-B was 32.250±9.141 years when we compared Methotrexate with Triamcinolone Acetonide based on age. An independent sample t-test revealed no significant difference in the mean patient age between the two groups(p=0.178).

Uzuncakmak et al.,[9] found that people under the age of 40 had a higher prevalence of AA, which is in line with our findings. Whereas, according to the age group of 20-29years old had the highest prevalence of AA, with a median age of 29.86±14.48.

The same findings were reported by Tan et al.,[10] who found that the age group ranging between 21-40years old was the biggest, followed by those between 1-20years old, those between 41-60years old, and those between 61-80years old. It has also been shown that the 30-59 and 31-35age groups had the highest rates of AA visits.

Adults as a whole were shown to have a lower prevalence of AA compared to younger age groups MacLean & Tidman,[11] which runs counter to our findings. Possible causes for these discrepancies in outcomes include genetics, environment, and race. It is possible that the gradual progression of AA to AU over time is associated with the older median age of AA.

In our research, we compared the two groups' clinical improvement rates. Of the patients in group B, 9(or 45%) had significant improvements in their clinical status. Of the patients that were evaluated, 25%(n=5) showed moderate to no improvement. Mild improvement was seen in only one patient(0.5%). On the other hand, 7 patients (35%) in group B exhibited excellent improvement, which is somewhat lower than that of group A; 5 patients (25%) in group B showed moderate improvement, and 5 patients showed no change at all. Three patients(15%) showed a little improvement. Clinical improvement was not substantially different between the two groups(p=0.776).

Similarly, Kuldeep et al.,[12] found that, at the 3-month follow-up after treatment, the MTX group had better symptom improvement than the TrA group(65% vs. 50%), although there was no statistically significant difference between the two groups.

Our research analyzed hair density using a follicle scope. Surprisingly, group A had the largest

number of patients showing improvement, with 9 patients (45%) achieving a(+++) score, while just one patient(5% of the total) achieved a(+) score. Among the five patients (about 25%), no improvement was seen. In group B, 7 patients improved by a(+++) score, whereas 3 patients improved by a(+) score, according to the data. There was no discernible variation between the two sets of data. After the folliscope thickness assessment, 45%(n=9) of group A showed an improvement with a score of(++), 25%(n=5) showed no improvement, and 15%(n=3) showed an improvement with a score of(+++) and(+). Among our group B patients, 45%(n=9) had a(+) score, 30%(n=6) had a(++) score, and 25%(n=5) had a(-) score. At least one patient did not have a(+++) score. There was no statistically significant difference between the two groups(P=0.125).

When it comes to methotrexate, our findings align with those of Alsufyani et al.,[13] who found that when MTX was administered to patients with severe types of AA(multifocal, universalis, totalis, and diffuse), it had a positive impact(>50% regrowth in 67.7% of cases) with minimal side effects.

Our findings are in line with those of the study by Hamdino et al.,[7] which found statistically significant improvements in both the MTX and TrA-groups at the end of the 12-week session, as well as at the 1-month, 2-month, and 3-month follow-ups, allowing for more objective evaluations of treatment efficacy.

According to Hamdino et al.,[7] it was found that the MTX-group had better results after AA at the injection site improvement compared to the TrA-group. Additionally, during treatment and follow-up, two patients in the MTX-group developed new lesions, while five patients in the TrA-group did.

This is in line with the results of Srivastava et al.,[14] who established that there was a cumulative improvement in hair regrowth as measured by the regrowth score and distinctive trichoscopic observations at all follow-up intervals after intralesional TrA.

While we focused on localized patchy AA in the scalp, Rafique et al.,[15] tested intralesional MTX vs TrA. After 12 weeks of sessions, the regrowth scale showed a considerably larger clinical improvement in the TrA-group compared to the MTX-group. This is because, after sessions, only 20% of patients in the MTX-group attained the desired score of 4(regrowth≥75%), whereas 40% of patients in the TrA group did so.

In the TrA-group, we found results that are consistent with those of Ganjoo et al.,[16] which found that 47% of patients experienced complete hair regrowth(>75%) 12-weeks after receiving an intralesional injection of 5mg/ml of TrA spaced 4-weeks apart.

Our analysis of the mean treatment duration for the two groups revealed the following:50%(n=10) of patients in group A had only 2 sessions, while 25%(n=5) had 3 or 4 sessions. In group-B, none of our patients improved after 2-sessions, and the majority(56%, or 13-patients) had 3-sessions, while 35%, or 7-patients, had 4-sessions. The results showed a statistically significant difference between the two sets of data(P=0.014*).

We found that MTX showed promise in treating adult AA, and according to Hamdino et al.,[7] there was no statistically significant difference between the two groups in terms of patient satisfaction or the number of sessions needed.

In a study conducted by Rafique et al.,[15] it was found that Group-A(methotrexate) required an average of 3.30+/-0.52 sessions of therapy, whereas Group-B (triamcinolone) required an average of 3.34+/-0.48 sessions. These results were similar to our own findings.

Our research on methotrexate side effects found that only four individuals (20%) reported pain after therapy, whereas sixteen patients (80%) reported no pain at all. Although, 14-individuals did not have thinning hair after therapy, 6(30%) showed signs of white hair. Only four-patients had erythema as a post-injection response; the rest of the patients did not.

Regarding the adverse effects of triamcinolone therapy, we noticed that 15-patients(or 75% of the total) had pain after treatment, whereas only 5-patients(or 25% of the total) did not. After receiving our therapy, not a single one of our patients showed signs of white hair. Only five individuals, or 25% of the total, had erythema as a post-injection response; the other seventy-five percent did not.

In our research, we compared methotrexate with triamcinolone acetonide for pain. We found that the two groups were significantly different, with the lowest number of patients experiencing pain in group A. The difference was statistically significant, with a P-value of less than 0.001*.

Similar to what Hamdino et al.,[7] found, all of the negative side effects seen by participants in both groups during sessions were short-lived and went away throughout the course of the follow-up. Hyperpigmentation affected nine individuals in the MTX group, erythema two, and erosions one; hypopigmentation two, erythema one, and atrophy one in the TrA group were side events. The research found that individuals may safely use intralesional MTX for AA without worrying about the potential systemic side effects of the drug.

4. Conclusion

The results of intra-lesional therapy with methotrexate and triamcinolone were not significantly different from one another. There was a statistically significant difference in the

percentage of patients reporting pain between the two groups; 75% of those on triamcinolone and 25% of those using methotrexate reported pain.

The results of intra-lesional methotrexate were comparable to those of conventional therapy, suggesting that it might be a new, safe, and effective way to treat lesions. This has the potential to enhance the way patients with lesions are treated in our healthcare facilities.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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There are no conflicts of interest.

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