

Efficacy of Topical Ichthammol in Treatment of Mild Plaque Psoriasis

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Abstract: **Background:** Ichthammol, derived from shale oil, it is purported to have antimicrobial, anti-inflammatory, antipruriginous, and analgesic properties. It is also believed to promote blood flow and act as a decongestant. It has been employed in the therapy of psoriasis, eczematous dermatitis, leg ulcers, seborrheic dermatitis, and furuncles. **Objectives:** To evaluate the efficacy and safety of topical Ichthammol for treatment of mild plaque psoriasis. **Patients and methods:** This therapeutic interventional study was conducted in Baghdad training center of Dermatology and Venereology for period from April 2018 to May 2019. A total of 34 patients with mild plaque-type psoriasis were evaluated. They were 19 (56%) males and 15(44%) females. Their ages ranged from 7-65 years with Mean± SD (32±17.2). Split test used for each patient, each patient divided into right and left side and some patient divided into anterior and posterior parts according to psoriasis location, Ichthammol used to the right and anterior side and Vaseline used for left and posterior side. both Ichthammol and Vaseline were used twice daily. Assessment of drug efficacy was based on the reduction of PASI score. **Results:** The degree of response to total course of treatment with Ichthammol in comparison with Vaseline showing that 27 patients on Ichthammol had less than 25% clearance rate while 21 patients had clearance rate <25% with Vaseline, while 5 patients on Ichthammol and 7 patients on Vaseline had showed clearance between 25-50%. Also 2 patients on Ichthammol in comparison with 7 pts on Vaseline had showed 90% clearance rate. According to side effect Vaseline showed no side effect but ichthammol had showed burning sensation and irritation in 7 patients. **Conclusion:** Ichthammol is not a cost-effective non significant drug for psoriasis while Vaseline was significantly better.

Keywords: Ichthammol, Mild Plaque Psoriasis, and Vaseline.

INTRODUCTION

Part 1: Psoriasis

It is a common, chronic, disfiguring, inflammatory and proliferative condition of the skin in which both genetic and environmental influences have a critical role. The most characteristic lesions consist of red, scaly, sharply demarcated, indurated plaques, present particularly over extensor surfaces and scalp. The disease is variable in duration, periodicity of flares and extent [1]. The word "psora" derived from Greek, which means itch [2]. In most reviews, the prevalence of psoriasis is said to be 2% of the world's population [3].

Etiology

The following factors had been implicated:

A-Genetic factors B-Triggering factors: Trauma [4], Infection [3], Psychological factors [3], Drugs [1], Sun light [1, 5], Changes in the environment [6], Endocrine factors [3], Obesity [7], Alcohol and Cigarette smoking [1, 8], AID [3].

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***Immunology and Inflammation:**

- T-Lymphocytes in the pathogenesis of psoriasis [9, 10];
- TH1 Cytokines
- Dendritic cell/macrophage function [8, 9].

Clinical presentation:

*According to the morphology of psoriasis:

1. Chronic plaque psoriasis (psoriasis vulgaris) [3].
2. Guttate Psoriasis [1].
3. Small plaque psoriasis [11].
4. Erythrodermic psoriasis [11].
5. Pustular psoriasis: It can be either localized or generalized [3].

*According to location of psoriasis [1]:

Psoriasis of the scalp, Penis, Sebopsoriasis, Flexural psoriasis, Napkin psoriasis, Hands and feet, Psoriasis of the nail, Psoriatic arthritis [12], Atypical forms: these include digital, interdigital, verrucous, follicular, lichenoid [1], Linear and Zonal Lesions [1], and Mucosal.

Treatment of Psoriasis:

1. **Topical therapy [21]:** *Topical corticosteroids* [3], *Vitamin D analogues* [11], *Coaltar* [13], *Topical calcineurin inhibitors* [13], *Tazarotene* [14], *Salicylic acid (SA)* [3], *Zinc* [15], *Topical Podophyllin 5%* [3], *Petrolatum (Vaseline):* White (bleached) and yellow soft paraffins are purified mixture of semisolid mixture of hydrocarbons obtained from petroleum (crude oil). It appears as white or pale yellow, soft, unctuous odorless mass. To prevent oil separation, soft paraffin's may contain a suitable stabilizer. It's practically insoluble in water and ethanol; soluble in chloroform, ether, and most fixed and volatile oils. It is categorized as ointment base. It should be kept in a well-closed container. In a thin layer or when melted, both paraffins show a slight fluorescence. Melting point lies within 38-60 °C [16].
2. **Phototherapy:** *Narrow band ultraviolet B light* [13], *Psoralen and Ultraviolet A Light* [11], *Targeted phototherapy:* The 308 nm excimer laser [13].
3. **Systemic therapy:** *Methotrexate* [13], *Ciclosporin A* [13], *Oral retinoid* [3], *Oral antimicrobial therapy* [12], *Azathioprine* [1], *Sulfasalazine* [1], *Dapsone* [12], *Biological therapies:-* Alefacept [17], Biologics that Target TNF:- Adalimumab [18], Etanercept [19], Infliximab [19], Golimumab [19], nCertolizumab Pegol [19]. Anti-IL-23:- Targeting the p40 subunit of IL-12 and: Ustekinumab and briakinumab, Targeting the p19 subunit guselkumab, risankizumab, tildrakizumab. Anti-IL-17 agents:- Secukinumab, ixekizumab. Anti-IL-22: e.g. fezakinumab. Apremilast.

Part 2: Ichthammol

Ichthammol is known by a number of colloquial terms such as drawing salve, black ointment, black drawing grease, bear grease, and herbal clay. Scientific names include ammonium bituminosulfonate, ammonium ichthosulfonate, and sodium shale oil sulfonate [20].

Sulfonated shale oil (SSO) refers to ichthammol proper and ichthyol, typically considered separate entities derived from different methods of production. It is organic matter produced by anaerobic bacterial degradation of phytoplankton during the Jura period of the Mesozoic era (208–146 million years ago) and deposited in sedimentary rock is termed sulfur rich oil shale. The dry distillation of this rock while excluding air (low temperature carbonization) at 480 °C results in the production of shale oil [20]. Further distillation removes particulate matter and high molecular weight molecules such as polycyclic aromatic hydrocarbons. Ichthyol or pale sulfonated shale oil (PSSO) is derived when light acids are employed. Depending on the base used for neutralization, ammonium, calcium, or sodium salts are produced. Both products have a high hydrogen to carbon ratio and are low in nitrogen. They are comprised of sulfur (10%), ammonium sulfate (5–7%), hydrocarbons, nitrogenous bases, acids, and thiophene derivatives [21]. Unlike crude shale oil which is known to be carcinogenic, mutagenic and a photosensitizer, ichthammol, and ichthyol have been found to be safe in short- and long-term topical use.

Mechanism of Action: Ichthammol is purported to have antimicrobial, anti-inflammatory, anti-pruriginous, and analgesic properties [20, 22, 23].

PATIENTS AND METHODS AND /OR MATERIAL AND METHODS

This therapeutic interventional study was conducted in Baghdad training center of Dermatology and Venereology for period from April 2018 to May 2019. Formal consent was taken for each patient before starting the therapy, after full

explanation about the nature of the disease, course, the procedure of treatment, follow up, prognosis and the need for pre and post treatment photographs.

Inclusion criteria: Mild plaque- type psoriasis which is defined as PASI score of less than 10.

Exclusion criteria from history, physical examination and investigations, the following population were excluded:

- Pregnant or lactating women,
- Those with hepatic, renal, haematological or other systemic disorders,
- Immunosuppression,
- Diabetes mellitus,
- Peripheral neuropathy,
- Poor peripheral circulation,
- Previous use of systemic medication like methotrexate, cyclosporine and others,
- Patients with lesions on the following sites: Scalp, face, hands and feet,
- Patients with pustular and guttate psoriasis were also excluded.

Pre-Treatment Assessment:

Before starting treatment, a full history was taken from the patients including age, address, occupation, duration of disease, associated itching, history of previous treatment and family history of psoriasis. Physical examination was performed carefully to each patient including size, site, erythema, as well as scale and thickness of the psoriatic plaques. Determination of the extent and severity of psoriasis and their response to treatment was done according to two parameters **PASI** and **BSA** scores.

- **PASI** score can be calculated as following:

Table 1.1: Calculation of the psoriasis area and severity index

<i>Severity of psoriasis lesions</i>				
0=none, 1=slight, 2=moderate, 3=sever, 4=very sever				
	Head	Trunk	Upper limb	Lower limb
Erythema	0 to 4	0 to 4	0 to 4	0 to 4
Induration	0 to 4	0 to 4	0 to 4	0 to 4
Scaling	0 to 4	0 to 4	0 to 4	0 to 4
Total score=1	Sum of above	Sum of above	Sum of above	Sum of above
<i>Area of psoriatic involvement</i>				
0=none, 1=less than 10%, 2= from 10% to 30%, 3=from30% to 50%, 4=from 50% to70%, 5=from 70% to 90%, 6=from 90% to 100%				
Degree of involvement=2	0 to 6	0 to 6	0 to 6	0 to 6
Multiply 1x2	1x2	1x2	1x2	1x2
Correction factor=3	0.1	0.3	0.2	0.4
1x2x3	A	B	C	D
A+B+C+D= total PASI				

In PASI scoring, 72 is considered as the highest score, while 0 is considered as the lowest score.

- **BSA (Body Surface Area):** The surface of the patient's one palm is equal to (1%) and each (10) thumbs is equal to (1%) that was roughly method to measure the body surface area of involvement.

Treatment protocol

A total of 36 patients with mild plaque-type psoriasis were evaluated but only 34 patients completed the study (both the treatment and follow up period). The patients defaulted due to sever irritation and burning sensation that caused by ichthammole. Split test used for each patient, each patient divided into right and left side and some patient divided into anterior and posterior parts according to psoriasis location, ichthammole used to the right and anterior side and Vaseline used for left and posterior side.

- **Right and anterior side:**
 - ❖ **Ichthammol Ointment**
 - **Usage:** For upper and lower limbs and trunk. The drug was used twice daily.
 - **Ingredient:** Ichthyole, vitamin E, vitamin F (essential fatty acid), Salicylic acid, chlorophyll.



Figure 1.1: Ichthammol Ointment

❖ **Ichthammol gel**

- **Usage:** For flexural areas. Apply the gel on a wet skin and hair and rub in circular motion until foam appears then rinse with water twice daily.
- **Ingredient:** Ichthyol, piroctoneolamine, white willow.

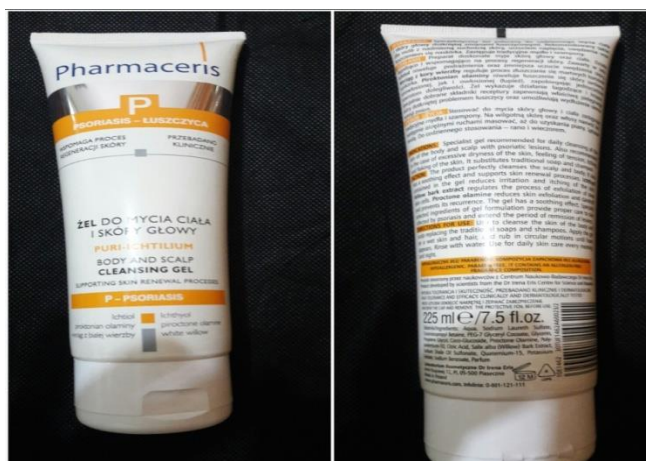


Figure 1.2: Ichthammol gel

• **Left and posterior parts:-**

- ❖ **Vaseline:** Patients treated with Vaseline only kept in a plastic container at room temperature in the hospital twice daily.

Patients were assessed at 4 visits during the treatment period (at week zero, week 2, week 4, week 6) to record the clinical response, cure and any local or systemic side effects. After the cessation of treatment, all patients were followed up every 4 weeks for 8 weeks during which relapse and any local or systemic side effects were recorded.

Efficacy Evaluations

Pre, during and post treatment, photographs were taken by using Samsung Galaxy J7 with rear camera 13 mega pixels, in the same place with fixed illumination and distance. Assessment of drug efficacy was based on the reduction of PASI score. Patients were considered as good responders if the reduction in PASI score was 50% or more [24], partial responders if the reduction in PASI score was 25-49% and poor responders if the reduction in PASI score was <25%. Complete clearance was considered when there was a reduction in PASI score of $\geq 90\%$.

Relapse is defined as loss of 50% of PASI improvement from baseline in patients who achieved at least 50% reduction in PASI score [25].

Statistical Analysis

Data presented as mean \pm SD MIC for three independent experiments and analyzed by two-way ANOVA for Gaussian or Kruskal-Wallis for non-Gaussian data followed by Dunnett's multi-comparison post-hoc test comparing to base PASI (before treatment) * p<0.05, ** p<0.01 and *** p<0.001.

RESULTS

Thirty-four patients were evaluated by age, gender, and history of disease followed at least 1 year. In the present study, the results showed that 19 (56%) of males and 15 (44%) of females had mild plaque-type psoriasis. The age ranged from 7-65 years (32 ± 17.2); whereas, the duration of illness ranged from one month to 20 years with (6.8 ± 6.2). There base line PASI score ranged from 0.3 to 9.6 (2.8 ± 1.6) as shown in Table 1.2.

Table 1.2: The Socio-demographic information of Study group

Age (years)	Range	7-65
	Mean± SD	32±17.2
Gender	Male N(%)	19 (56%)
	Female N(%)	15(44%)
PASI score at baseline	Range	0.3-9.6
	Mean	2.8
	SD	1.6
Duration of illness (days)	Range	0.1 - 20
	Mean± SD	6.8±6.2

Vaseline demonstrated highly effective results and degree of response rates after the total course of treatments, vasalinehad good response in 7 pts with clearance rate more than 50% while only 2 pts on ichthammole showed good response. Patients with partial response were 5 on ichthammole and 6 on vasaline with clearance rate 25%-49%, and those with poor response were 27 patients on ichthammole and 21 patients on vasaline with clearance rate less than 25% (Table 1.3).

Table 1.3: The total response and clearance rate at 6wks

Treatment Category	Clearance rate at 6 wks									
	No.	<25%	No.	25-49%	No.	50-75%	No.	75-89%	No.	<90
Ichthammol	27	79.4	5	14.7	0	0	0	0	2	5.9
Vaseline	21	61.7	6	17.7	2	5.8	0	0	5	14.8
<i>P</i> -value= 0.001										

Finally, according to the duration of treatment, this research investigated the linear correlation between the actions of both treatments. The results showed that the actions of both treatments had a linear correlation ($r=0.9$, $p<0.001$) after two weeks. Both treatments started their actions on the selected patients significantly with a different values of response rates.



Figure 1.3: Right Side: Effect of Ichthammol before Treatment, after 2 and 6 weeks; Left Side: Effect of Vaseline before Treatment, after 2 and 6 weeks



Figure 1.4A: Effect of Vaseline Before Treatment, 2,4,6 weeks



Figure 1.4B: Effect of Ichthammol Before Treatment, 2,4,6 weeks

DISCUSSION

Psoriasis is a common chronic, non-infectious, inflammatory skin disorder. It can have a profound impact on physical, psychological and social well-being [26]. Although recent advances in biological therapy has revolutionized outcome for persons with severe Psoriasis, little attention was paid to topical treatment, which have form the cornerstone

of the treatment for most of patients with psoriasis [27]. This study compared the effect of Ichthammol and Vaseline Petroleum Jelly on selected patients with psoriasis.

Ichthammol is known by a number of colloquial terms such as drawing salve, black ointment, black drawing grease, bear grease, and herbal clay. Scientific names include ammonium bitumino-sulfonate, ammonium ichthosulfonate, and sodium shale oil sulfonate. Sulfonated shale oil refers to ichthammol proper and ichthyol, typically considered separate entities derived from different methods of production. Ichthammol is purported to have antimicrobial, anti-inflammatory, antipruriginous, and analgesic properties. It is also believed to promote blood flow and act as a decongestant. Regarding the trunk and upper limbs, this study revealed a statically significant improvement was noted on both Ichthammol and Vaseline Petroleum Jelly in these patient's sites. Those effects may be due anti-inflammatory and anti-pruriginous properties of Ichthammol at these sites [28], and to Moisturizers properties of Vaseline Petroleum Jelly as it had been found that these moisturizers increase the clearance of plaques of psoriasis [29] as it cause occlusive and emollient effect. While, lower limb and axilla the site of the patients that given Vaseline Petroleum Jelly demonstrated a statistically significant improvement compared with the site on Ichthammol use which shows no improvement at these site. The improvement in trunk and upper limbs on both Vaseline and Ichthammol, with no improvement in lower limbs and axilla might be due to that sensitive area like axilla are folded (friction area) so lead to irritation on Ichthammol application. While non-significant result of Ichthammol application on lower limbs may be due to genetic variation or type of the skin that differ from patients to another. A lot of European articles, particularly from Germany, continue to widespread use of Ichthammol in treatment of psoriasis [28]. From these result the researchers cannot predict which patients respond better regarding the site of psoriatic lesion accordingly the use of Ichthammol on Iraqi patients seem to be not a cost effective drug and time consuming for the patients and the physicians.

Regarding the sex differences in response to treatment, this can be explained by that; the differences of response to Ichthammol application between sex might be due to lesser disease severity in women as female had significant lower disease activity in comparison with male across all ages [26].

While regarding the differences of response to treatment in different age groups, might be to genetic factor, there is no specific reason for this differences.

Vaseline demonstrated highly effective results and a better degree of response rates as compared to Ichthammol after the total course of treatments. This might be explained by that; Vaseline significantly reduced the erythema that induced by the exposure to small dose of radiation of UVB, and that Vaseline increase the clearance of plaques of psoriasis [29]. Therefore Unna in her study, did not suggest the use of Ichthammol in treatment of psoriasis [28].

Regarding side effect, Vaseline has acceptable safety profiles and no side effect. However, Ichthammol caused burning sensation and irritation in some patients. This agrees with the Lawrence study [30] as the most common side effect of Ichthammol was skin irritation. This disagrees with Cholcha *et al.*, study, as Ichthammol had found to be safe in short and long term topical use [31].

CONCLUSIONS

From this study researcher can conclude that:

1. Ichthammol has reduced the PASI score in some site significantly
2. Vaseline also has similar effect and not in all types of psoriasis.
3. Both Ichthammol and Vaseline failed to improve some site & lesion significantly.
4. Ichthammol is not a cost-effective drug for this reason the researchers don't recommend to use this drug in Iraqi patients.
5. Compared with Ichthammol Vaseline seems to be a cost-effective drug because it safer less irritant cheaper than and as effective as Ichthammol.

RECOMMENDATION

1. Since Ichthammol used effectively in large number of European countries the researchers recommend repeating the study for a longer time with different remedies.
2. Prolong the follow-up period to show the relapse rate of both Ichthammol and Vaseline. A possibility that Ichthammol group relapse slower that Vaseline group.

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