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A COMPARATIVE STUDY ON THE EFFICACY OF THREE GALENIC PREPARATIONS FOR TOPICAL USE

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Abstract

Background: Atopic dermatitis, eczema, psoriasis are an important challenge for dermatology doctors. In order to have the best result in shorter time of treatment, it is necessary a collaboration with clinical pharmacists to have the right product, for the right type of skin, in the right amount according to the affected surface. It is very important to decide first which NSAID to use as topical therapy, second the type of formulation to use having at disposal Galenic preparations such as lotion, cream and unguent

Objective: To study the efficacy and compliance of patients on three Galenic preparations.

Method: A randomized, open group controlled trial. 198 patients were included in this trial to be treated either with lotion of 0.1%, cream of 0.1% or unguent 0.1% mometasone furoate (MF). The data were analyzed with chi-square test.

Results: About 118 (59.6%) of patients were males and 80 (40.4%) were females. The male/female ratio was 1:0.67. After 28 days of treatment quite all patients were improved or had no signs of illness (lotion 97.6% improved, cream 80% absence of signs, unguent 63.0 % improved).

The results after statistical analysis shows that there are much more possibility to become absent from signs using cream, rather than lotion or unguent [cream vs lotion 157 folds (P= 0.002) while unguent vs lotion 25 folds (P<0.001)].

There were not noticed any treatment-related irritation from all three formulations.

Conclusion: All three formulations can improve the health status of patients with eczema, dermatitis or psoriasis. However cream gives faster and better clinical improvements compared to unguent or lotion. All three galenic preparations were well tolerated.

Keywords: Formulation, topical formulation, eczema, efficacy

Introduction

This trial is part of a wider study focused on the best practices in hospital pharmacy in Albania. The first part of the study was focused on formulation, preparation, stability and quality control of topical drugs. Pharmacists' involvement with use of topical drugs consists on a close collaboration with medical doctors to prescribe the best medicine for individual patients. Topical corticosteroids, especially mometasone furoate, are used usually to treat eczema, atopic dermatitis or more rarely psoriasis (Valencia IC et al 2003).

The second part is the clinical trial to prove the efficacy. The cutaneous tolerance and cosmetic acceptability is an organic part of the efficacy of a topical preparation (Freeaman S. et al. 2002). So it is very important to evaluate that as well.

Ministry of Health in Albania is aiming to reduce the cost of medicines at "Mother Teresa" hospital and what better way can do than using all human capacity of professionals working there. No other healthcare professional is better equipped to formulate, prepare and monitor in collaboration with prescribers and consumers the best medicine for individual needs of patients. We're aiming to create multidisciplinary teams of physicians and pharmacists for improving quality and safety in medication use.

Patients, materials and methods

The study was a randomised, open clinical trial. The main diagnosis included in this study are eczema, atopic dermatitis and psoriasis.

Inclusion Criteria: at least 1 week without medication with corticosteroids and absence of secondary bacterial infections. The area to be treated should be quite the same, same skin type.

Exclusion criteria: the presence of another illness such as heavy renal or cardiovascular disease, or polyvalent allergy.

Patients were included after giving written consent. They have been divided in 3 groups:

1st group was going to be treated with unguent 0.1% mometasone furoate (MF) from 14 - 28 days; 2nd group was going to be treated with

cream 0.1% mometasone furoate (MF) from 14 - 28 days; 3rd group with lotion 0.1% mometasone furoate (MF) from 14 - 28 days.

For each group has been evaluated the effect, patient's compliance and safety for 2-4 weeks of treatment.

The data has been registered as in a rutine clinic documentation, in an approved format. There were recorded demographic data, signs of illness and their severity grading them according to the following scale: mild=0, moderate=1, severe=2. After 2 weeks of treatment we added also grade absent=3. The situation has been evaluated the day in which the patient came first to the clinic (day 0) and then in day 14 and day 28 of the treatment. It has been investigated the efficacy of lotion compared to cream or unguent prepared with the same concentration of MF treating eczema, atopic dermatitis or psoriasis. After 14 days of treatment the response to it was recorded as moderate, improved or absent. At the end of 28 days treatment patients were asked to give their opinion on the formulation regarding acceptability (feeling, staining skin or clothes, stickiness, spreadability).

The statistical analysis was chi-square test.

The clinical trial has been considered finished in the moment we had enough cases so that we could draw a conclusion.

This clinical trial was approved by National Committee of Bioethics, Ministry of Health in Albania.

Results

There has been included 198 patients in this study. In this study participated 118 male and 80 female patients as it is illustrated in Figure 1.

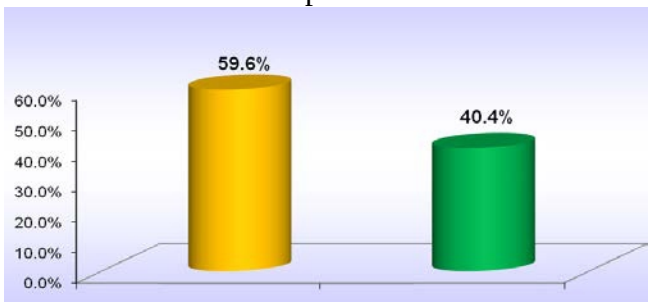

Fig. 1. Spreading of patients according to gender

The main diagnosis included in this study are eczema (48.5%), atopic dermatitis (26.3%) and psoriasis (25.3%). The decision to choose such group of illnesses was made based on two facts: these are the target group treated with glucocorticosteroids, part of which is MF the active ingredient of our galenic formulations and we could have enough patients to get a significant

result from statistical point of view. Data regarding diagnosis and kind of treatment of the patients included in the study are shown in Table 1.

Table 1. Spreading of patients in base of diagnosis and treatment

Variable	Number (n)	Percentage (%)
Diagnosis		
Dermatitis	52	26.3
Eczema	96	48.5
Psoriasis	50	25.3
Treatment		
Lotion	84	42.4
Cream	60	30.3
Unguent	54	27.3
Total	**198**	**100.0**

Fig.2 shows that the majority of patients included in this study suffered eczema (48.5%) while those suffering atopic dermatitis or psoriasis were quite the same (26% and 25.3% respectively).

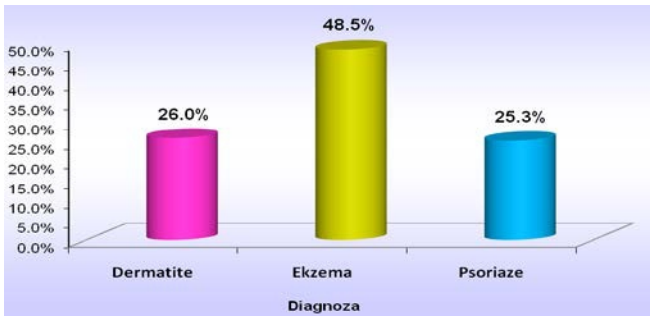

Fig. 2. Spreading of patients in base of diagnosis

In Fig. 3 it is shown the distribution of patients in each group of treatment. So it can be noticed that patients suitable to be treated with lotion were 42.4%, those treated with cream 30.3% and those with unguent 27.3%.

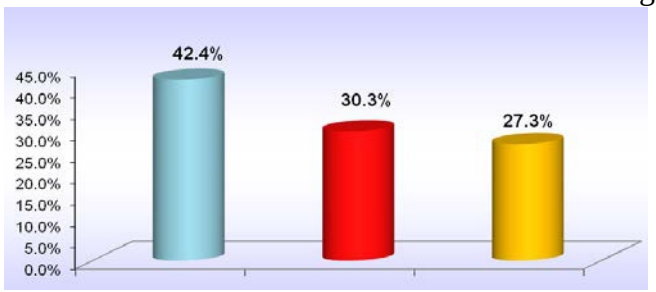

Fig. 3. Spreading of patients in base of treatment

The assessment of severity of symptoms in day 0, 14 and 28 is shown in Table 2.

Table 2. Spreading of patients based on results per each period of the treatment.

Variable	Period of treatment					
	Day 0		Day 14		Day 28*	
	Number	Percentage	Number	Percentage	Number	Percentage
Health status						
Severe	198	100.0	6	3.0	-	-
Improved	0	0.0	192	**97.0**	126	**67.0**
Absent	-	-	-	-	62	**33.0**
Total	198	100.0	198	100.0	188	100.0

*10 subjects didn't return to the clinic

At the end of 14 days of treatment the efficacy of different formulations is showed in Table 3.

Table 3. Percentage of healing according to the formulation used for 14 days.

Variable	Type of formulation			
	Lotion	Cream	Unguent	P†
Health Status				
Improved	82 (97.6)*	12 (20.0)	34 (63.0)	
Absent	2 (2.4)	48 (80.0)	20 (37.0)	<0.001
Total	84 (100.0)	60 (100.0)	54 (100.0)	

* Number of subjects and percentage in brackets

† The overall value of P (statistical significance) according to chi-square test.

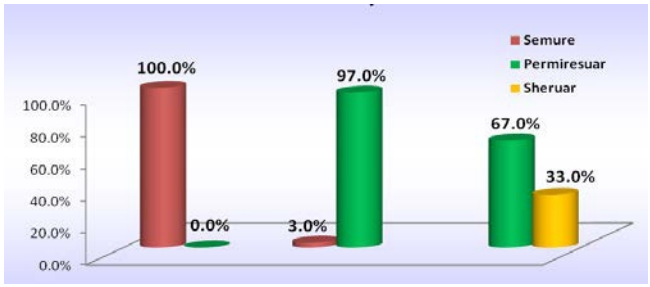

Fig. 4. Spreading of patients based on results of the treatment per each period.

It can be noticed that in cream group the situation is much better, comparing to 2 other groups 20% is improved, while 80% had no more signs in the skin; in unguent group 63% is improved while 37% had no more signs; for the group of lotion the result is less optimistic 97.6% of patients treated with lotion are only improved, while 2.4% it can be said that had no more signs (P<0.001) (Fig. 6.)

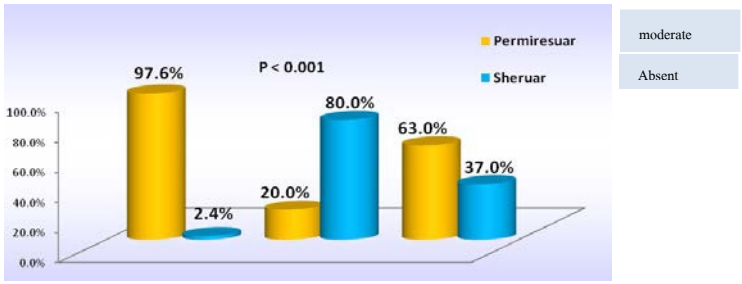

Fig.5. The assessment of the efficacy of each formulation by "moderate" or "absent", after 28 days of treatment.

After controlling the age effect, subjects that use unguent has 25 folds more possibility to heal all signs, rather than those treated with lotion, while subjects treated with cream has 157 folds more possibility to heal all sign in the skin, rather than those treated with lotion (Table 4). In both cases the result is very significant (P=0.002 dhe P<0.001, respectively).

Table 4. The evaluation of health status and type of formulation after 28 days of treatment; The value of OR controlled per age through models of binary logistic regression.

Variable 2	Univariant		Limits 95% CI	
	OR	P*	Lower	Upper
Type of formulation				
Lotion	1.00 (reference)			
Cream	**156.6***	< 0.001	17.070	1436.275
Unguent	**24.6**	0.002	2.895	208.884

* The result is statistically significant (P < 0.05)

After concomitant control of age effect, type of formulation, diagnosis and gender there can be noticed important differences in the results (Table 5).

Table 5. Concomitant evaluation of type of formulation with health status after 28 days treatment; OR controlled with age effect, type of formulation, diagnosis and gender through binar logistic regression models.

Variable			Limits 95% CI	
	OR	P*	Lower	Upper
Age	1.02	0.175	0.988	1.071
Type of formulation				
Lotion	1.00 (reference)	-	-	-
Cream	**404.2***	< 0.001	27.791	5879.998
Unguent	**72.83***	0.001	5.518	961.322
Diagnosis				
Dermatitis	1.00 (reference)	-	-	-
Eczema	**11.715***	0.015	1.620	84.703
Psoriasis	1.502	0.599	0.330	6.825
Gender				
Male	1.00 (reference)	-	-	-
Female	0.364	0.180	0.083	1.594

* the result is statistically significant (P < 0.05)

After the control of all these variables it can be noticed that patients treated with cream has much more possibilities to be healed comparing to those treated with lotion (OR = 404).

Discussion

This study compared the efficacy of up to 4 weeks treatment with mometasone furoate 0.1% cream versus unguent or lotion prepared in a galenic laboratory. The study was a randomised open group evaluation. The study was conducted in "Mother Teresa" Universitary Hospital-Tirana, Albania and was included a total of 198 patients. Only 12 patients didn't return to the clinic after 2 weeks of treatment.

Baseline showed that three treatment groups were well balanced in respect of number per group, age, gender, severity of signs and symptoms. However there were more cases of eczema than atopic dermatitis or psoriasis. Overall, all of three formulations were clinically effective and showed no irritability in anyone of the patients included in this study. Also it is clear that the possibility to be healed using unguent is also increased, but not as much as those with cream. Cream is obviously much more superior (OR = 404).

At the end of the treatment 80% of patients in cream group were healed, whilst in unguent group only 37% and from lotion group only 2.4% ($P<0.001$). This result lead us to the decision to carry on the treatment of patients in unguent and lotion group of patients, but the following data are not included in this study.

The fact that cream gives better results than lotion or unguent is explained by different reasons:

First of all from the formulation point of view, the prepared cream is emulsion type O/W. After application it inverts, because of the evaporation of the water. So cream and unguent create a continuous oil film layer on the skin which contains the active ingredient as suspension. The water phase hydrates the corn layer of the skin, making it more easy to be penetrated by the other phase along with the active ingredient. In the mean time the oily phase can mix easily with the oil of the skin itself, taking along the way the lipophyle drug. The unguent having no water will penetrate more slowly the skin layers, while the lotion can hydrate very well the corn layer of the skin, but then it is stopped by the lipostructure of the other layers of the skin. [11]

Secondly the penetration ability and as a consequence the medical effect of a formulation it is affected also by its viscosity and the diffusion coefficient of the drug. The prepared cream has lower viscosity than the unguentm and so it penetrated more easily and it showed a better efficacy in shorter time.

It is very interesting the fact that patients with eczema has more possibility to be healed, around 11.7 folds (P=0.015), compared to patients with atopic dermatitis.

So as a conclusion we can say that the efficacy of formulation cream is comparable with unguent, but patients compliance is much higher. In the other hand formulation cream produced a significantly more rapid clinical improvement than unguent or lotion. Meanwhile the formulation lotion was much more acceptable from cosmetic point of view, compared to cream or unguent (P<0.05), but showed slower clinical improvements.

Our results support the view that cream formulation for topical use is much more superior to unguent or lotion one.

This is the first study in Albania to compare three galenic preparations for topical use in the same time.

We recommend to continue this study with pharmaco-economic evaluation. These two evaluations together would be of great help for the pharmacy of "Mother Teresa" Hospital Center and the strategy of MoH to low down the treatment costs. We recommend as well a continuous collaboration between medical doctors and pharmacists to optimise the treatment of patients in Albania.

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This is the first study in Albania, where an attempt to evaluate the efficacy of three galenic preparations at once was done.

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