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Report
Clinical study of effectiveness and tolerance of Loma Lux Acne tablets , manufactured by "Loma Lux Laboratories" , USA, as additional treatment to basic therapy of acne disease

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Report

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Results of clinical trial of therapeutic effectiveness and safety of Loma Lux Acne(tablets) are represented in the report. Loma Lux Acne is indicated for treatment of patients with acne vulgaris and rosacea.
Loma Lux Acne has good effectiveness and tolerance in treatment of mild and moderate acne vulgaris disease.

Acne is wide spread skin disease among 85% of young people of 12-25 age and among 11% of young people elder 25 y.o.

Acne may cause disfigurement and development of firm scars. Even mild case of disease may provoke emotional distress and have serious psychoemotional consequences. The latest studies improved understanding of this pathology and were the background for development of rational methods of treatment.

There are four interrelated factors of acne pathogenesis: pathological follicular hyperkeratosis, exceeded production of secret of sebaceous glands, reproduction of Propionibacterium acnes (P. acnes) and inflammation. Androgenes influence on the type of secretion and on hypersecretion of sebaceous glands, that plays certain role in pathogenesis of disease.

The most popular drugs for treatment of acne are the following: antibiotics (Clindamycine, Erythromycine, Tetracycline), that inhibit P. acnes [1,2,3,4], retinoids (tretinoin, isotretinoin), that posses comedolitic effect; oral contraceptives, decreasing high level of androgenes[4,5]. Benzoil peroxide in used locally, it posses keratolytic, drying and bacteriostatic effects. Azelainic acid decreases content of free fat acids , inhibits growth of P. acnes. Sulfur and Resoricne are used locally too[6,7,8].

Local therapy is usually used for treatment of mild acne. Moderate and hard forms of acne with papulo-pustular manifestation are treated orally. It should be mentioned, that extensive local treatment may provoke irritation and dermatitis.

Oral treatment, included antibiotics, isotretinoin, oral contraceptives may provoke side effects rather often[8,9]. It brings the necessity of dose decreasing. Decreasing the dose draws decreasing the effectiveness of therapy, limitation of sunburn or its abolition. That,s why new drugs for acne treatment are necessary.

Target of the investigation is to study effectiveness and tolerance of complex homeopathic drug for acne treatment - Loma Lux Acne, tablets, manufactured by "Loma Lux Laboratories", USA.

It posses anti-inflammatory and keratolitic activity. One tablet 300 mg contents Potassium bromide 1X(12), Sodium bromide 2X(1,2), Nikel sulfate 6X(0,02 mg), Sulfur 6X(0,02 mg), Calcareum 9X($2x10^{-8}$mg) and excipients: Lactose monohydrate, Magnesium stearate.

Targets of investigation

1) To study influence of test drug on disease;
2) To study tolerance and possible side effects;
3) To compare the results of treatment of patient in the main and control groups

Design of study

Open comparative parallel clinical study was carried on after registration of Loma Lux Acne, tablets(manufactured by "Loma Lux Laboratories", USA) in Ukraine. The study was carried on according to the State Pharmacological Center demand to clinical trials.

60 patients were included into the study at the clinics of Dermatovenerology Chair of National Medicinal University by A.A. Bogomoletz.
Patients were randomized in main (30 patients) and in control (30 patients) groups. Patients of both groups were compared by sex, age and duration of disease, manifestation of main signs. Every patient has randomized number. Randomized number was recorded in Individual Case Report Form.
Patient of main group have been treated with test drug Loma Lux Acne, tablets (manufactured by "Loma Lux Laboratories", USA). Patients of control group had have only basic treatment.
During the study every patient had physical examination and laboratory testing.
The results of examination and testing, as concomitant therapy, were recorded in Individual Case Report Form.

Labeling
On the label of test drug there were marks:
- name of test drug;
- manufacturer;
- batch number of test drug;
- storage condition;
- manufacturing date.

Delivering and account of test drug
Amount of drug, received by clinical center, should be mentioned in the act of delivering-acceptance, signed by Investigator.
Investigator records amount of given drug, date, time, number of patient in the Individual Case Report Form.

Storage condition
Test drug was stored in dry dark place at the temperature $+5^0$C to $+25^0$C, in closed room, where the only Investigator was allowed to enter.

Selection criterion
Criterion of including:
- men and women;
- age 18-35 y.o.;
- diagnosis: papulos-pustular acne of mild and moderate severity;
- written inform concern of participation in the study;
- ability of patient to adequate collaboration in the study.

Criterion of excluding
- pregnancy , lactation;
- history of known hypersensivity to the components of drug;
- competitive decompensate diseases or acute condition, that can influence on the results of study;
- participation in another clinical study.

Withdrawal from study

Withdrawals from study are the following:

- individual intolerance of test drug;
- appearance of hard and/or unexpected side effects;
- remarkable worsening of common status within the study;
- not following treatment regime;
- refuse of patient to participate the study.

Treatment scheme of test drugs

Patients of both groups with acne were received basic complex therapy included sulfur preparations, vitamins, tonics.

Besides this, patients of main group administered test drug Loma Lux Acne, tablets, manufactured by Loma Lux Laboratories, USA, during 6 weeks. Administered dose depended on body weight.

Body weight (kg)	Daily dose
23 – 45	1 tablet
46 – 68	2 tablets
69 – 91	3 tablets
more than 91	4 tablets

Drug was administered once a day, in the fasting state, drinking water. Eating and drinking were not recommended.

Concominant treatment

Patients were prohibited to administrate any other system and local antibacterial drugs.

All the drugs, used as concominant therapy, were recorded in Individual Case Report Form and patient history: dose, administration, frequency of administration, beginning and over of the treatment.

Scheme of examination of every patient

For estimation of therapeutic efficacy and tolerance of test drug patients were examined by following methods:

- objective examination(observation of skin of face, chest and back), account of inflammable and not inflammable rash elements);
- records of subjective complaints;
- testing of microbiocenosis of skin damage;
- evaluation of severity of acne.

Examination of skin

When skin examination special attention was paid to the type of rash, spread and localization of rash, inflammation, manifestation of seborrhea and comedons. Inflammable and not inflammable rash elements were accounted separatelly.

Records of subjective complaints of patient was carried on by following parameters:
-pain;
burning.

Degree of manifestation of signs was estimated by following score:

0 – absent of signs;
1 – mild degree of manifestation;
2 – moderate degree of manifestation;
3 – significant degree of manifestation.

Study of microbiocenosis of damaged skin

Cultivation of aerobic and anaerobic bacteria was carried on 5% blood agar by Gold depletion method. Amount of bacteria was expressed as cfu/ml.

Evaluation of degree of severity of acne disease was calculated by following scale

№	Name of criterium	Value of testing criterion	Score
1	Duration of disease	Less than 1 year 1 – 5 years 6 – 10 years More, than 10 years	1 2 3 4
2	Effect of previous therapy	Not carried on Was effective Was not effective	0 1 2
3	Hereditary factor	Is absent Is present	0 2
4	Psychoemotional factor	Not impaired impaired	0 2
5	Concomitant therapy	Not reviled Has relative patogenetic meaning Has immediate patogenetic meaning	0 1 4
6	Type of skin	normal Combine Fat problematic	0 2 3
7	Spread	Local dissemination	2 3
8	Hyperemia in nidus	Is absent mild Moderate extensive	0 2 3 4
9	Infiltration in nidus	Is absent mild moderate	0 2 3

		extensive	4
10	Pain in nidus	no yes	0 4
11	Amount of open comedones	Less than 20 20-50 51-100 more than 100	1 2 3 4
12	Amount of closed comedones	Less than 20 20-50 51-100 More than 100	1 2 3 4
13	Amount of papulae	absent Less, than 10 10-40 41-80 More, than 80	0 2 3 4 5
14	Amount of pustulae	Absent Less, than 10 10-40 41-80 More, than 80	0 3 4 5 6
15	Amount of deep elements (conglobat, phlegmonous, abscess)	absent 1-5 6-10 11-15 More, than 15	0 4 5 6 7
16	Seborrea	Absent mild moderate	0 3 4
17	Scars	no yes	0 3
18	Microbial contamination in nidus	Complies to norm Overcome of norm	0 4

Coefficient of severity is calculated by formula:

$$G = \sum_{i=1}^{n} Ki \cdot S$$

где G – coefficient of severity of acne disease of patient

K – scores of i - criterion;

n – amount of testing criterion of patient

S – coefficient of diffusion of dermatosis (equal to 1 for local form, equal to 1,2 for diffusion form)

Degree of severity was evaluated:

Less, than 35 scores – mild degree,

36 – 63 scores – moderate degree,

More, than 63 scores– hard degree.

Records of examination of patients were carried on as following

Days of study	0	7	14	21	35	42
Visits (points of examination)	1	2	3	4	5	6
Medical history and previous evaluation of compliance to criterion inclusion/exclusion	*					
Written informed concern	*					
Objective examination, included evaluation of degree of severity	*	*	*	*	*	*
Microscopical examination	*			*		*
Record of subjective complaints of patient	*		*	*	*	*
Revel and record of possible side effects		*	*	*	*	*
Evaluation of effectiveness and tolerance						*

Evaluation of effectiveness

Criterion of effectiveness:
- degree of reduction of main clinical manifestation of acne disease by objective examination and microbiological testing;
- reduction of characteristic complaints of patient.

Evaluation of effectiveness of test drug was carried on the basis of above mentioned criterion by following scale

High effectiveness	**Patient status is characterized as "significant improvement" at the end of treatment course(significant reduction or disappearance of clinical signs of acne disease; normalization of microbiocenosis of damaged skin, absent of complaints of patient)**
Moderate effectiveness	**Patient status is characterized as "improvement" at the end of treatment course(reduction of clinical signs of acne disease; tendency to normalization of microbiocenosis, absent of complaints of patient)**
Low effectiveness	**Patient status is characterized as "non-significant improvement" at the end of treatment course(non-significant positive dynamics of clinical signs of acne disease; non-significant tendency to improvement at microbiological testing of nidus, patient complaints are not changed**

Evaluation of tolerance

Tolerance of drug has been evaluated on the basis of subjective symptoms and sensation, reported by patient, objective data of investigator during the treatment. Dynamics of laboratory tests and frequency of side effects were taken into account too.

Tolerance of drug was evaluated by investigator (objective data) and patient(subjective data) according to the following scale

Good	**Side effects are absent**
Satisfactory	**Non-significant side effects, that does not cause serious problems of patient and withdrawal of drug is not necessary**
Unsatisfactory	**Undesirable side effect is present, it affects the patient status significantly, and withdrawal of drug and special medical measures are necessary**

Study design and discussion of the results of study

Common description of patients included in study

Main and control groups included patients with acne disease at the age from 18 to 35 y.o.. Main group included 11 men and 19 women. Control group included 30 patients, 16 men and 14 women among them. Duration of disease history of patients of the main group was from 3 months to 12 years, and patients of control group – from 1 month to 10 years.

Concominant pathology was reveled at 10(33,3%) patients of main group and at 12(40%) patients of control group.

4 patients(13,3%) of main group had pathology of gastrointestinal tract(chronic gastritis, colitis, cholecystitis, diskinesia of bile-excreting tract), 1 patient(3,3%) had bordered psoriasis, 2 patients (6,6%) had foot mycosis and 2 patients(6,6%) had lichen versicolor. In control group 10 patients(33,3%) had pathology of gastrointestinal tract (chronic gastritis, cholecystopancreatitis, chronic colitis), 2 patients(6,6%) had bordered psoriasis, 2 patients (6,6%) had foot mycosis and 1 patient (3,3%) had lichen versicolor.

Diagnosis, sex, age of patients of main and control groups are represented in tables 1 and 2.

Table 1.

Diagnosis, sex, age of patients of main group

Diagnosis	Patients	Sex		Age (years)					
		m	f					m	
Acne disease (mild degree) (till 35 scores)	19 (63,3%)	4 (13,3%)	15 (50%)	2 (6,6%)	7 (23,3%)	2 (6,6%)	5 (16,6%)	-	3 (10%)
Acne disease (moderate degree) (36-63 scores)	11 (36,6%)	2 (6,6%)	9 (26,6%)	1 (3,3%)	4 (13,3%)	1 (3,3%)	3 (10%)	-	2 (6,6%)
Total	30 (100%)	6 (20%)	24 (80%)	3 (10%)	11 (36,6%)	3 (10%)	8 (26,6%)	0 (0%)	5 (16,6%)

Table 2.

Diagnosis, sex, age of patients of main group

Diagnosis	Patients	Sex		Age (years)					
		m	f	18-20		21-30		31-35	
				m	f	m	f	m	f
Acne disease (mild degree) (till 35 scores)	18 (60%)	4 (13,3%)	20 (66,6%)	2 (6,6%)	15 (50%)	1 (3,3%)	4 (13,3%)	1 (3,3%)	1 (3,3%)
Acne disease (moderate degree) (36-63 scores)	12 (40%)	2 (6,6%)	4 (13,3%)	1 (3,3%)	1 (3,3%)	1 (3,3%)	2 (6,6%)	-	1 (3,3%)
Total	30 (100%)	6 (20%)	24 (80%)	3 (10%)	16 (53,3%)	2 (6,6%)	6 (20%)	1 (3,3%)	2 (6,6%)

It is clear from tables above, that most patients had acne disease of mild degree: 63,3% (19) of patients of test group and 60% (18) of control group. Most patients of both groups were women – 80%(24).Most of women were 18-20 y.o. : 46,6% (14) of women of test group and 53,3% (16) of women of control group.

Less part of patients were in age 31-35 y.o.: 16,6% (5) of patients of test group, and 9,9% (3) of patients of control group. Thus, patients of test and control group were comparative by sex, age and diagnosis. They had similar pathology.

All the patients had complaints on acne rash on the face. Patients of main and control groups had moderate pain and burning in the rash area.

Table 3

Dynamics of subjective score of patients of main and control group

Complaints	Score	Main group (n=30)				Control group (n=30)			
		Before treatment		After treatment		Before treatment		After treatment	
		p	%	p	%	p	%	p	%
Burning	0	-	-	20	66,7	-	-	5	16,7
	1	3	10,0	8	26,7	5	16,7	13	43,3
	2	14	46,7	2	6,6	13	43,3	10	33,3
	3	13	43,3	-	-	12	40,0	2	6,6
Pain	0	3	10	24	80,0	2	6,7	6	20,0
	1	13	43,3	6	20,0	12	40,0	15	50,0
	2	10	33,3	-	-	11	36,6	5	16,7
	3	4	13,4	-	-	5	16,7	4	13,4

Analysis of dynamics of subjective status of patients of main and control groups (table 3) shown, that patients of both groups had complaints and burning of skin before treatment (p>0,05). In main group before treatment 43,3% patients had intensive burning, 46,7% patients had moderate burning and 10,0% of patients had mild burning, after treatment only 6,6% of patients had intensive burning, 26,7% of patients had mild burning, and burning stopped at 66,7% of patients.

In control group before treatment 40,0% of patients had intensive burning, 43,3% patients had moderate burning and 16,7% of patients had mild burning; after treatment only 6,6% of patients had intensive burning, every third patient had moderate burning, 43,3% of patients had mild burning and burning stopped at 16,7% of patients.

90,0% of patients of main group and 93,3% patients of control group had complaints on pain in nidi; there was no significant difference(p>0,05) between groups.

In the main group 13,4% of patients had intensive pain, every the third patient had moderate pain and 43,3% patients had mild pain before treatment; but after treatment only every fifth patient had mild pain in nidus, and pain disappeared at 80,0% of patients.

In the control group 16,7% of patients had intensive pain, 36,6% of patients had moderate pain and 40,0% patients had mild pain before treatment; but after treatment 13,4% of patients had intensive pain, 16,7% of patients had mild pain in nidus, and pain disappeared at every fifth patients.

Most of patients had hyperemia in acne area, open and closed camedones, separate pustules.

Table 4.

Dynamics of objective clinical signs of patients of main and control group

Clinical data	Score	Main group (n=30)				Control group (n=30)			
		Before treatment		After treatment		Before treatment		After treatment	
		p	%	p	%	p	%	p	%
Erithema	0	-	-	19	63,3	-	-	6	20,0
	1	6	20,0	10	33,3	5	16,7	9	30,0
	2	10	33,3	-	-	10	33,3	10	33,3
	3	14	46,7	1	3,4	15	50,0	5	16,7
Infiltration	0	-	-	22	73,3	-	-	8	26,7
	1	10	33,3	7	23,3	9	30,0	13	43,3
	2	15	50,0	1	3,4	16	53,3	5	16,7
	3	5	16,7	-	-	5	16,7	4	13,3
Pustulisation	0	-	-	23	76,7	-	-	11	36,7
	1	7	23,3	7	23,3	8	26,7	10	33,3
	2	10	33,3	-	-	9	30,0	4	13,3
	3	13	43,4	-	-	15	50,0	5	16,7

Analysis of objective examination of patients of main and control groups (table 4) shown, that patients of both groups had erythema of different degree, there was no significant difference between groups ($p>0,05$). In main group before treatment 46,7% of patients had intensive erythema in nidus, every third patient had moderate erythema and every fifth patient had mild erythema, after treatment only one patient (3,4%) had intensive erythema, 63,3% of patients didn,t had erythema, and the third part of patients had mild erythema.

At the same time half of patients of control group before had intensive erythema before treatment, 33,3% patients had moderate erythema and 16,7% of patients had mild erythema, after treatment erythema disappeared only at every the fifth patient, 16,7% of patients had intensive erythema, every third patient had moderate burning, 30,0% of patients had mild erythema.

Before treatment there was infiltration of different degrees among the patients of main and control group (table 5), but difference between groups($p>0,05$) was not significant. In the main group 16,7% of patients has extensive infiltration,

half of patients had moderate infiltration, and every the third patient had mild infiltration. After treatment 73,3% of patients of this group didn,t have infiltration, 23,3% of patients had mild infiltration and only one patient had moderate infiltration.

In the control group 16,7% of patients has extensive infiltration, 53,3% of patients had moderate infiltration, and 30,0% patients had mild infiltration. After treatment only 26,7% of patients of this group didn,t have infiltration,13,3% of patients had extensive infiltration in nidus, 16,7% of patients had moderate infiltration, and 43,3% of patients had mild infiltration.

There was pustulisation in nidus of different degree at the patients of both groups before treatment(table 5), but there was not difference between groups ($p>0,05$).

In the main group 43,4% of patients had extensive pustulisation, every third patient had moderate pustulisation. After treatment in this group most of patients didn,t have pustulae(76,7%) and 23,3% of patients had mild pustulisation.

In the control group half of patients had extensive pustulisation, 30,0% of patients had moderate pustulisation and 26,7% of patients had mild pustulisation. After treatment in this group 16,7% of patient had extensive pustulisation, 13,3% of patients had moderate pustulisation, and pustulae were regressed at 36,7% of patients.

Analysis of data, represented in the tables 3 и 4, shown, that subjective and objective evaluation of patients status was similar before treatment, there was no significant difference between groups($p>0,05$), but after treatment of Loma Lux Acne subjective signs were regressed significantly more($p <0,05$) in the main group, than in control group (Tinctura Calendulae), normalization of clinical signs was more significant in main group($p<0,05$), than in control group.

Coccus contamination of pustule and surrounding skin was revealed under microscopical examination.

Staphylococus epidermidis и Propionibacterium acnes were eliminated by microbiocenosis test. After 6 weeks of treatment by test drug normalization of microbiocenosis occurred at 16 patients.

Evaluation of effectiveness

17 patients had positive dynamics of skin process after 4 weeks of treatment.
One could see decrease of hyperemia in nidus, pain and burning, regress of papulae rash, absent of fresh elements
There was clinical improvement at 16 (53,3%) of patients at the end of treatment by test drug, 5 (23,3%) patients had clinical remission. 9(30%) patients didn,t have any positive clinical dynamics.

Criterion of effectiveness

- Degree of decreasing of main clinical manifestation of acne rash;
- Normalization of biocenosis of damaged skin;
- Diminish of characteristics patient's complains.

Table 5

Evaluation of effectiveness of test and reference drugs in the main and control group

Score	Main group (n=30)		Control group (n=30)	
	p	%	p	%
Low effectiveness	9	30%	12	40,0
Moderate effectiveness	5	16,6%),	7	23,3
High effectiveness	16	53,3%	6	20,0

Analysis of effectiveness of treatment(table 5) shown, that data of main group are much better, than data of control group. So, there is high effectiveness at16 (53,3%) patients of main group and only at 20,0% of patients of control group, moderate effectiveness at 5 (16,6%) patients of main group and at 23,3% of patients of control group. At 30% (9 patients) of courses effectiveness was evaluated as low.

Tolerance of drug

Tolerance was evaluated on the basis of objective and subjective data.
All the patients, treated with Loma Lux Acne didn,t have side effects.
All 30 patients(100%) had good tolerance.
Test drug Loma Lux Acne, manufactured by Loma Lux Laboratories, USA, is effective and could be used in treatment of mild and moderate degree of acne disease at young patients. It posses anti-inflammatory and keratolitic effects. Drug is well tolerated. It is recommended for introduction into dermatological practice for treatment of acne vulgaris disease.

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