

A PROSPECTIVE STUDY TO DETERMINE THE EFFECTIVENESS OF CLINDAMYCIN (ALLOPATHY), BERBERIS AQUIFOLIUM (OREGON GRAPE-HOMEOPATHY) AND AZADIRACHTA INDICA (NEEM-AYURVEDIC) MEDICATIONS AGAINST THE MICROORGANISM CAUSING ACNE VULGARIS.

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ABSTRACT:

Context: Acne vulgaris is the most common psychologically distressing skin disorder which is treated with indiscriminate use of oral and topical antibiotics mainly targeted against the anaerobic organism *Propionibacterium acnes*, without much consideration given to other causative microorganisms.

Objectives: This study was therefore undertaken to isolate the probable aerobic organisms causing acne vulgaris and to demonstrate the resistance and sensitivity pattern to the commonly used antibiotic Clindamycin. Also traditional acne medications like *Berberis aquifolium* and *Azadirachta indica* which are supposed to have antimicrobial effects and are used as over the counter medications were tested against the isolated microbes to make a comparative study. This type of comparative study is first of its kind and shall help the dermatologists to select judiciously from the cafeteria of medications available for treating acne.

Design: prospective comparative study of three months duration.

Study setting: patients attending Dermatology OPD of Bowring and Lady Curzon Hospital

Patients presenting with pustular or nodulocystic acne, between 13 to 50 years of age.

Results: 40 patients were included in the study among which 70 % (28 patients) belonged to age group 20-29 year. Samples from 40% (16) patients showed growth of *Staphylococcus aureus* organism on aerobic culture. Followed by 32.5 % (13) samples isolating Coagulase negative *Staphylococcus aureus* (CONS). 68.8% of isolated *Staphylococcus aureus*

showed sensitivity to Clindamycin, 12.5% showed sensitivity to *Berberis aquifolium* and 18.8% showed sensitivity to Neem.

76.9%, 69.2% and 30.8% samples which grew Coagulase negative *Staphylococcus aureus* (CONS) showed sensitivity to Clindamycin, *Berberis aquifolium* and Neem respectively. Gram negative organisms showed resistance to all three medications.

Conclusion: This study shows that *Staphylococcus aureus* and CONS are most commonly isolated aerobic organism from acne. These are still sensitive to Clindamycin compared to medications of other systems of acne management like homeopathy and ayurveda. CONS showed significant sensitivity to homeopathic medication too. We suggest in vivo studies for better evaluation and comparison.

INTRODUCTION:

Acne vulgaris is common human skin disease characterized by areas of skin with multiple non inflammatory follicular papules or comedones and by inflammatory papules, pustules and nodules in its more severe forms. Although not a serious threat to general health, acne is one of the most socially distressing skin condition, especially for adolescents resulting in diminished self esteem, social withdrawal due to embarrassment and depression⁽¹⁾. Due to development of resistance in microorganisms causing acne to common antibiotics and the differences in species and strains of the microorganisms in different regions, a research in the method of therapy seems indispensable⁽²⁾.

Propionibacterium acnes an anaerobic pathogen, plays important role in the pathogenesis of acne and

many studies have been undertaken targeting this organism, but not many studies involving the aerobic microbes. The aerobic bacteria reported to cause acne are *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Micrococcus* spp.⁽³⁾

During the last 20 years, the number of topical and systemic drugs for the treatment of acne vulgaris has been enriched⁽⁴⁾. The indiscriminate use of antibiotics whether topically or orally has raised concerns globally about the development and spread of resistant organisms and the fears about resulting antibiotic resistance⁽⁵⁾. There are many products available for treatment of acne, however those treatments that are most effective tend to have greater potential for side effects, need a great degree of monitoring. A number of topical antibiotics have been tried in acne vulgaris, but erythromycin and clindamycin preparations are the most popular.

Stoughton and Resh did the first definitive work with topical clindamycin in acne vulgaris. It has been found to be as effective as systemic tetracyclines, topical erythromycin and topical benzoyl peroxide. Clindamycin penetrates the skin and retains its biological activity against *P. acnes* even in contact with skin. The concentration of clindamycin in the comedonal material is more than sufficient to suppress the growth of *P. acnes*. There is a concurrent reduction in the free fatty acid levels on the skin surface⁽⁶⁾. Since acne vulgaris is a recurrent condition repeated use of antibiotics is not recommended because of the side effects and is also not cost effective for patients.

The development of antibiotic resistance and the emergence of 'super bugs' is a serious worldwide problem, caused primarily by the misuse and overuse of antibiotics. Antibiotic resistance of the resident cutaneous bacterial flora is a well recognized consequence of systemic antibiotic therapy⁽⁷⁾. Therefore we must broaden our view of how to prevent and treat microbial infections to include alternatives that are not centered upon standard antibiotic therapy or we risk the possibility of eventually having no defense against these microbes. While many natural products claim to have antimicrobial properties, very little research has been conducted to investigate their claims.

Berberis aquifolium, also known as mountain grape or oregon grape is extensively used by homeopaths in treatment of acne. The specific action of this agent is in scaly, pustular and other skin diseases due to the disordered condition of the blood. It is the most reliable alternative when the influence of the dyscrasia is apparent in the skin. It is given freely during the treatment of skin diseases where an alternative is considered an essential part of the treatment⁽⁹⁾.

Neem or *Azadirachta indica* is a large, evergreen tree and has strong health maintaining properties. The antibacterial, antifungal & blood purifying properties of neem are useful in skin disorders and keep the skin healthy. Neem is implicated in effectively killing the bacteria that cause acne and studies prove that neem will reduce inflammation. It cleanses the skin and also helps in clearing acne scars.

Hence this study was undertaken to identify the commonest aerobic organism causing acne in our hospital and also to evaluate the efficacy of commonest used antibiotic clindamycin against these organisms in comparison with alternative traditional preparations like *Berberis aquifolium* (Oregon grape) and *Azadirachta indica* (Neem) powder which are reported to have nourishing, anti-inflammatory, anti-microbial activities which in turn help to control acne.

To the best of our knowledge this is the first such comparative study that has been undertaken in India.

OBJECTIVES:

1. To identify aerobic bacteria that causes acne.
2. To compare the antibiotic sensitivity and resistance pattern of commonly used allopathic (clindamycin), homeopathic (*Berberis aquifolium*), ayurvedic (Neem) medicines against the isolated bacteria.

MATERIALS AND METHODS:

Study Design: A Prospective Comparative study

Study setting: Study was conducted in the Department of Microbiology in B & LCH over a period of three months.

SOURCE OF DATA

Samples obtained from nodulocystic and pustular skin lesions of acne patients attending OPD of Dermatology in Bowring and Lady Curzon Hospital.

SAMPLE SIZE- n 1 = 40. 40 patients were enrolled in the study

INCLUSION CRITERIA:

1. Those patients who had acne at least for one week duration.
2. Patients between 13yrs to 50 yrs.

EXCLUSION CRITERIA:

1. Patients having bleeding in the acne.
2. Patients who are more than 50 yrs.

MEHODLOGY

The samples (pus from acne) were collected in the dermatology department with sterile precautions by using sterile cotton swabs. Swabs were placed in sterile container and transported to lab immediately. Aerobic culture were done on Macconkey agar, Blood agar and Chocolate agar and were incubated at 37 °C, for 18 hours and if there is no growth, then up to 48 hours. The isolated organisms were identified using standard identification techniques. Antibiotic sensitivity was done using standard Kirby Bauer's Method using CLSI^[10-13] guidelines.

Preparation of disk solution

Commercially available Clindamycin(Hi-mediadisc) with a concentration of 2 microgram/ml disk were used. The modified paper disc diffusion was employed to determine the antibacterial activity of solvent extract of ayurvedic and homeopathic preparations. For antibacterial properties, 0.1 ml bacterial suspension of 10⁵CFU ml⁻¹ was uniformly spread on Nutrient Agar plate to form lawn cultures. The methanol extracts were prepared in such a manner that ultimate amount (in dry form) in each disc came to 1mg in Azadirachta indica and 2 microgram in Berberis aquifolium. The blotting paper discs (10mm diameter) were soaked in various diluted extract, dried in oven at 60 degree C to remove excess of

solvent and tested for their antibacterial activity against bacterial pathogens by disc diffusion technique. After incubation for 24 h at 37°C, zone of inhibition of growth was measured in mm.

The Antibiograms obtained were statistically compared and data analysed.

RESULTS OF THE STUDY:

40 patients were included in the study among which 70%(28 patients) belonged to age group 20-29 years, 25% (10 patients) belonged to 14-19 years age group and 5%(2 patients) belonged to age group 30 and above. 57.5% (28 patients) were males and 42.5% (17 patients) were females.

57.5% (23) patients had duration of disease between 1 to 5 years. 35%(14 patients) had duration of disease less than 1 year and 7.5% (3) patients had duration of disease for more than 5 years.

Organisms isolated: (table 1)

Samples from 40% (16) patients showed growth of Staphylococcus aureus organism on aerobic culture. Followed by 32.5%(13) samples isolating Coagulase negative Staphylococcus aureus (CONS), 12.5%(5) samples isolating Pseudomonas species, 7.5%(3) samples isolating Klebsiella spp and 2.5%, (1) Pseudomonas aeruginosa and 2.5%(1) each of multiple isolates of Klebsiella with Pseudomonas spp and Staphylococcus aureus with Klebsiella spp.

Sensitivity and resistance of the organisms to Clindamycin (allopathic), Oregon grape (Homeopathic) and Neem (ayurvedic) drugs: (table 2)

68.8% of isolated Staphylococcus aureus showed sensitivity to Clindamycin, 12.5% showed sensitivity to Oregon grape and 18.8% showed sensitivity to Neem.

76.9%, 69.2% and 30.8% samples which grew Coagulase negative Staphylococcus aureus showed sensitivity to Clindamycin, Berberis aqua folium and Neem respectively.

20% of Pseudomonas patients showed sensitivity only to Neem and none were sensitive to Clindamycin and Oregon grape.

Samples which isolated *Klebsiella* spp, *Klebsiella* with *Pseudomonas* and *Pseudomonas aeruginosa* were 100% resistant to all these groups of drugs.

Sample that isolated *Staphylococcus aureus* and *Klebsiella* showed 100% sensitivity to Clindamycin and none to Oregon grape and Neem.

DISCUSSION:

Acne has many psychiatric and psychological implications than most other dermatological conditions. Acne vulgaris is a common skin disease with potential complications that are more than skin deep. The past two decades have seen a worldwide upsurge in the use of traditional medicine (TM) and complementary and alternative medicine (CAM) in both developed and developing countries. In India the corresponding figure is 65%. Herbal preparations are widely used as self-medication for acute conditions; practitioners of herbal medicine tend to concentrate on treating chronic conditions.¹⁴¹ Western allopathic medicine emphasizes the use of antibiotics and other medicines and approaches to defend against "germs" or microbes. Therefore the present study was conducted to investigate antibacterial properties of Ayurvedic and homeopathic preparations, which is less studied and used in Indian traditional Medicine in comparison with commonly used allopathic drugs in acne.

In our study 70% of patients were in the age group of 20-29 years which suggest that hormonal influence of that particular age group play major role in causation of acne. 57.5% were males and this suggests no significant difference in occurrence of acne in males and females. Significant difference was seen in the duration of disease between patient group, patients with disease duration of 1-5 years were 57.5% compared to 35% < 1 year and 75% > 5 year of disease duration, which shows that in spite of therapeutic intervention acne vulgaris is a chronic condition.

Staphylococcus aureus (40%) and CONS (32.5%) were the most commonly isolated aerobic microorganisms isolated from pus of acne Patients. A similar study⁽¹⁾ showed aerobic organisms, *Staphylococcus aureus*, *Staphylococcus*

epidermidis, and *Micrococcus* spp as the commonest aerobic organisms. Among the isolated *Staphylococcus aureus* of which 60% were Methicillin resistant (MRSA) but Clindamycin sensitive and CONS were significantly more sensitive to Clindamycin compared to ayurvedic and homeopathic drugs. In addition these gram positive organisms were relatively sensitive to ayurvedic and homeopathic drugs. Gram negative organisms showed 100% resistance to these ayurvedic and homeopathic drugs. Though neem and Oregon grape are reported to have antimicrobial properties our study shows that they were effective only against few gram positive organisms and had no effect against gram negative organisms. *Klebsiella* spp and *Pseudomonas* spp were 100% resistant to all three groups of drugs, which shows that Clindamycin which is widely used for acne is not effective in cases which yield in gram negative microorganism.

In discriminate use of antibiotics over prolonged period results in development of antibiotic resistance. While many herbal and homeopathic products claim to have anti microbial properties, very little research has been conducted to investigate their claims. This study shows these products have very limited anti microbial activity especially against gram negative microorganism.

LIMITATIONS:

1. Anaerobic organisms were not isolated and therefore the sensitivity pattern of these organisms against the study medications were not evaluated.
2. Since this is an invitro study regarding sensitivity of micro organisms to the study medications the other pathomechanisms in causing acne were not addressed and the healing properties of the study medications other than antimicrobial effects were not evaluated.

CONCLUSION:

This study shows that *Staphylococcus aureus* and CONS are most commonly isolated aerobic organism from acne patients. These are still sensitive to

Clindamycin compared to other system of acne management like homoeopathy and ayurveda .CONS showed significant sensitivity to homeopathic medication too. Allopathic drugs usually provide effective therapy for bacterial infections, but there is an increasing problem of antibiotic resistance like development of MRSA and a continuing need for new solutions. Hence now herbal and homeopathic drugs are preferred to allopathic drugs. But careful clinical discretion and testing of antimicrobial sensitivity patterns are recommended before initiating treatment of acne.

Organisms isolated	Number of patients(n=40)	%
1.Staphylococcus aureus	16	40.0
2.CONs	13	32.5
3.Pseudomoas spp	5	12.5
4.Klebsiella spp	3	7.5
5.Klebsiella spp+Pseudomonas spp	1	2.5
6.Pseudomoas aeruginosa	1	2.5
7.Staphylococcus aureus + Klebsiella spp	1	2.5

Table 1: Organisms isolated

1. Staphylococcus aureus	16	5(31.3%)	11(68.8%)	14(87.5%)	2(12.5%)	13(81.3%)	3(18.8%)
2. CONS	13	3(23.1%)	10(76.9%)	4(30.8%)	9(69.2%)	9(69.2%)	4(30.8%)
3. Pseudomoas spp	5	5(100%)	0(0%)	5(100%)	0(0%)	4(80%)	1(20%)
4. Klebsiella spp	3	3(100%)	0(0%)	3(100%)	0(0%)	3(100%)	0(0%)
5. Klebsiella spp + Pseudomonas spp	1	1(100%)	0(0%)	1(100%)	0(0%)	1(100%)	0(0%)
6. Pseudomoas aeruginosa	1	1(100%)	0(0%)	1(100%)	0(0%)	1(100%)	0(0%)
7. Staphylococcus aureus+ Klebsiella spp	1	0(0%)	1(100%)	1(100%)	0(0%)	1(100%)	0(0%)

Table 2. Organisms isolated and sensitivity report of Clindamycin, Bereberis aquifolium and Azadirachta indica

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