



DRUG UTILIZATION STUDY OF MEDICATIONS USED FOR ACNE VULGARIS IN A TERTIARY CARE HOSPITAL

¹*Dr. Sneha Agarwal, ²Dr. Ajita Pillai, ³Dr. Anil P. Singh, ⁴Dr. Reena Pareek, ⁵Dr. Neela V. Bhuptani

^{1,4}MD Pharmacology, PDU Govt. Medical College, Rajkot, Gujarat.

²Associate Professor, Department of Pharmacology, PDU Govt Medical College, Rajkot, Gujarat.

³Professor and Head, Department of Pharmacology, PDU Govt Medical College, Rajkot, Gujarat.

⁵Professor and Head, Department of Skin and Veneral disease, PDU Govt Medical College and Hospital, Rajkot, Gujarat.

***Corresponding Author: Dr. Sneha Agarwal**

MD Pharmacology, PDU Govt. Medical College, Rajkot, Gujarat.

Article Received on 04/09/2016

Article Revised on 25/09/2016

Article Accepted on 15/10/2016

ABSTRACT

Objective: To evaluate drug utilization pattern of medications used for Acne vulgaris, so as to facilitate the rational use of drugs in population. **Materials and Methods:** This prospective study was carried out for a period of 14 months in Dermatology, Venereology & Leprosy department of a tertiary care teaching hospital. Data was collected from physicians' records and documented in predesigned case record form. **Results:** Among the total of 1164 prescriptions analysed 72 drugs were prescribed which included 28 (38.8%) single oral drug formulations, 41(56.9%) topical preparations and 3 (4.2%) fixed dose combinations (FDCs). Vitamins were the most commonly prescribed oral drug. Among the topical preparations 55 % had single drug and 45% had combination of steroids, antibiotics and antifungals. On an average 4.01 drugs per encounter were prescribed in our study suggesting polypharmacy. Furthermore, 52% of drugs were prescribed by generic name. In our study 65% of the drugs were prescribed from the National Essential Medicines (NLEM) List, India and 57% of drugs were prescribed from the WHO Essential Medicines List. **Conclusions:** The percentage of drugs prescribed from NLEM and the prescription of drugs by generic names was found to be satisfactory. Present study showed polypharmacy which may lead to wide spectra of problems. Hence, overall prescribing in our set-up requires formulation of guidelines to be used for appropriate and more rational use of medications in acne vulgaris.

KEY-WORDS: Acne vulgaris, dermatology, drug utilization pattern, polypharmacy, Fixed Dose Combinations.

INTRODUCTION

Acne vulgaris is the most common skin condition affecting more than 85% of adolescents across the globe with over 40% having persistent acne into their twenties and some continues into adulthood.^[1] Acne vulgaris is characterized by noninflammatory, open or closed comedones and by inflammatory papules, pustules, and nodules.^[2] It typically affects the areas of skin with the densest population of sebaceous follicles; these areas include the face, the upper part of the chest and the back.

The disease causes significant morbidity and affects patients both physically and psychologically in terms of scarring, depression, anxiety and low self esteem.^[3]

Treatment is challenging in part because the pathophysiology of acne is complex. Acne is a "polymorphic" disorder which exhibits series of widespread and diverse lesions.^[4] Four key factors have been identified in the etiology of acne: increased sebum

production, follicular hyperkeratinization, colonization of the pilosebaceous unit with *Propionibacterium acnes* and the production of inflammation.^[2] Acne needs to be managed aggressively from the outset using a Systemic, local and combination of treatments directed against each of the relevant factors. Treatment aims to either reduce the bacterial population of the pilosebaceous follicles, reduce rate of sebum production or reduce inflammation.^[5]

A prescription by a doctor is a reflection of physician's attitude towards the disease and the role of drug in its treatment. The ultimate outcome of the dermatological prescription analysis is to provide useful information to prescribe rationally. Information available at the time of drug marketing is sufficient to prove drug efficacy but not drug effectiveness.^[6] Drug utilization research provides insight into the efficiency of drug use, i.e. whether a certain drug therapy provides value for money

and the results of such research can be used to help to set priorities for the rational use of drugs.^[7]

There is paucity of drug utilization studies for acne vulgaris, thus this study was conducted to assess the prescribing pattern of the drugs using WHO core indicators and to determine Anatomical therapeutic chemical (ATC) coding and compare Prescribed daily dose (PDD) and Defined daily dose (DDD) for antibiotics.

MATERIALS AND METHODS

The study was a prospective and observational drug utilization study carried out in the Dermatology, Venereology & Leprosy department of a tertiary care teaching hospital, Gujarat, India. The data was collected for 14 months from January 2013 to February 2014. The Institutional Ethics Committee permission was taken to conduct this study (Date of approval 26/11/2012).

Inclusion criteria

- 12 to 40 yrs of age of either sex.

- Patients with total count of lesions in between 2 to 30; inflammatory (papules and pustules) and or non-inflammatory (open or closed comedones) lesions over face.

Exclusion criteria

- Patient lost to follow up during the period of study.
- Subjects regularly using anti-acne medications in last 30 days before study entry.
- Patients with severe form of acne that is acne conglobate, acne fulminans or secondary acne.
- Pregnant women.

In this study total 1164 prescriptions were analyzed. Data was collected from physicians records and documented in predesigned case record form.

RESULTS

Out of total 1164 prescriptions, vitamins were the most commonly prescribed followed by antibiotics as the second most commonly prescribed class of drugs.

Table 1: Distribution of commonly prescribed drugs

Group of drug	Number of prescription(n=1164)
Vitamins	1710(37%)
Antibiotics	1533(33%)
Antifungal	284(6%)
NSAIDs	259(5%)
Antihistaminics	205(4%)
Steroids	59(1%)
Miscellaneous	627(13%)

Among the oral acne medications, vitamin A was the most commonly prescribed and azithromycin was the most frequently prescribed oral antibiotic. Oral

preparations of vitamins and azithromycin were mostly prescribed simultaneously.

Table 2: Frequency and percentage of different oral acne medications

No. of drug	No. of encounters(n=1164)
<i>Single drug (36%)</i>	
Vitamin A	227(20%)
Azithromycin	78(7%)
Doxycycline	60(5%)
Vitamin C	49(4%)
<i>Two drugs (53%)</i>	
Vit A + Azithromycin	270(23%)
Vit A + Vit C	207(18%)
Doxycycline + Vit C	38(3%)
Vit C + Azithromycin	42(4%)
Doxycycline + Vit A	28(2%)
Others	35(3%)
<i>Three drugs (10.6%)</i>	
Vit A + Vit C + Azithromycin	110(9%)
Vit A + Vit C + Doxycycline	14(1%)
Vit A + Azithromycin + Metronidazole	2(0.2%)
Vit C + Doxycycline + Azithromycin	2(0.2%)
Others	2(0.2%)

Among the topical acne medications, Clindamycin was most commonly prescribed.

Table 3: Frequency and percentage of different topical acne medications

No. of drug	No. of encounters(n=1139)
<i>Single (55%)</i>	
Clindamycin	320(28%)
Benzoyl Peroxide	141(12%)
Tretionin	117(10%)
Others	52(5%)
<i>Two drugs (45%)</i>	
Clindamycin + Benzoyl Peroxide	281(25%)
Clindamycin + Tretionin	146(13%)
Others	77(7%)
<i>Three drugs (0.5%)</i>	
Benzoyl Peroxide + Salicylic acid + Clindamycin	2(0.2%)
Clindamycin + Tretionin + Glycolic acid	2(0.2%)
Benzoyl Peroxide + Clindamycin + Glucolic acid	1(0.1%)

For comorbid conditions, antifungal drugs fluconazole orally and terbinafine topically were commonly prescribed. For symptomatic relief ibuprofen orally and Calamine topically were most commonly prescribed.

WHO core drug prescribing indicators were determined.

Table 4: WHO core drug prescribing Indicators

Indicator	Value
Average number of drugs per encounter	4.01
Percentage of drugs prescribed by generic name	52%
Percentage of encounters with an antibiotic prescribed	75.26%
Percentage of drugs prescribed from essential drug list	65%

ATC code and PDD and DDD of antibiotics prescribed during study period were determined. The present study was carried out to evaluate the drug utilization pattern of

patients with acne vulgaris in a tertiary care teaching hospital.

Table 5: ATC, PDD and DDD of antibiotics

Drug	ATC code	PDD(mg)	DDD(mg)	Compare PDD and DDD	Use
Azithromycin	J01FA10	500	300	PDD>DDD	Overuse
Doxycycline	J01AA02	100	100	PDD=DDD	Optimum
Amoxicillin	J01CA04	500	1000	DDD>PDD	Underuse
Cefixime	J01DD08	100	400	DDD>PDD	Underuse
Cefadroxil	J01DB05	250	2000	DDD>PDD	Underuse
Erythromycin	J01FA01	500	1000	DDD>PDD	Underuse
Ampicillin	J01CA01	500	2000	DDD>PDD	Underuse

Antibiotic consumption was determined by calculating DDD/1000registered patients/ day of each antibiotic individually by the formula:

$$\text{DDD/1000registered patients/day} = \frac{\text{Amount of drug sold in a year(mg)} \times 10000}{\text{DDD (mg)} \times 365 \times \text{Total number of patients}}$$

Table 6: Antibiotic consumption

Antibiotic	DDD/1000registered patients/day
Azithromycin	32.89
Doxycycline	25.59
Amoxicillin	0.09
Cefixime	0.03
Cefadroxil	0.01
Erythromycin	0.03
Ampicillin	0.04

As shown in Table 6, this implies that of the total treated patients 3.2% of them were treated with 300mg of azithromycin and 2.6% of patients were treated with 100mg of doxycycline.

DISCUSSION

Drug utilization studies have the potential to make objective evaluation and analysis of health professionals' work and provide them with feedback to stimulate thinking about their practice. This will help to determine and employ rational use of drugs among population. Present study analyzes the utilization pattern of acne medications in patients attending out-patient department in dermatology.

In present study drugs from multiple classes were prescribed, among which Vitamins were commonly prescribed. This could be because of vitamins proposed role in acne and to limit antibiotic usage for acne since indiscriminate use of antibiotics increase bacterial resistance.^[8] In our study, most commonly used oral drug was Vitamin A. Oral vitamin A is available in two forms: retinol and isotretinoin. Retinol had no proven role in treatment of acne. Retinol was prescribed in majority of cases 50,000 IU per day for duration upto 2 months. Extensive vitamin A (retinol) usage could be due to physician's choice in accordance to the patient's characteristics as well as availability of the drug. In our study, azithromycin and clindamycin were the most commonly prescribed oral and topical antibiotics respectively. Similar results were seen in study conducted by Kumar S et al.^[9]

Majority of the patients in the present study received more than one oral drug simultaneously for acne. Oral preparations of vitamins and azithromycin were mostly prescribed simultaneously. This was in accordance with review study by Dawson LA et al^[10] which states that combined regimens of these drugs would result in complementary mechanisms and improved treatment outcomes.

In present study for acne, most common topical preparations prescribed simultaneously were benzoyl peroxide, clindamycin and salicylic acid. Several double blind randomized controlled trials have found that addition of benzoyl peroxide with antibiotics improve treatment outcomes.^[10] Salicylic acid has been shown to be more effective in reducing non-inflammatory and inflammatory acne lesions in a randomized controlled trial.^[11] Salicylic acid has been used for many years for the treatment of acne, although few well-designed trials of its safety and efficacy exist. It often is used when patients cannot tolerate a topical retinoid because of skin irritation.^[8]

In our study, fluconazole was most commonly prescribed oral drug for co-morbid conditions for Pityriasis and Tinea infection. Similar result was also seen with another study conducted by Kumar S et al.^[9] Topical treatment is

the first choice for patient with Pityriasis infection and single oral dose of fluconazole is often preferred in resistant cases, recurrence and non-compliance to topical therapy.^[2] Fluconazole is drug of choice for Tinea infection. This justifies the use of fluconazole in our study. Topical preparation of terbinafine was most commonly prescribed for pityriasis infection, which is a co-morbid condition in our study.

On an average 4.01 drugs per encounter were prescribed in our study suggesting polypharmacy. Polypharmacy may lead to wide spectra of problems like increase incidence of drug interactions, side effects, economic burden to the patients and resources wastage. Percentage of drugs prescribed by generic name measures the tendency to prescribe by generic name, in our study 52% of drugs were prescribed by generic name. Of the total no. of encounters antibiotic were constituting 75.26% of prescriptions. This accounts for the wider usage of antibiotics in treatment of acne.

In our study 65% of the drugs were prescribed from the National Essential Medicines List (2011),^[12] 57% drugs were prescribed from the WHO Essential Medicines List (2013).^[13] Most of the orally prescribed drugs were included in Essential list but many of the topical ones prescribed during study period were not mentioned in either of the two lists which includes Clindamycin, Benzoyl Peroxide, Salicylic acid, Terbinafine, Tretinoin, Alpha hydroxyl quinone, Glycolic acid, Nadifloxacin and Fusidic acid.

Anatomical therapeutic chemical (ATC) coding, Prescribed daily dose (PDD) and Defined daily dose (DDD) were determined for antibiotics used over the entire study period. The main purpose of the ATC classification is as a tool for presenting drug utilization statistics and it is recommended by WHO for use in international comparisons.^[14] DDD should ideally be presented as numbers of DDD per 1000 inhabitants per day. In the present study however calculation of DDD/1000 registered patients/day was done.^[15] As data in the present study was obtained from a medical aid, total number of inhabitants could not be used in calculation as only a sample of doctors who were serving only a portion of the total number of inhabitants of the area was chosen, thus DDD/1000 registered patients/day was determined.

Doxycycline had PDD=DDD and was prescribed 100mg once daily for 21 days, thus optimally used during the study. Azithromycin in the present study was overused. DDD/1000registered patients/day for azithromycin was 32.89 DDD/1000registered patients/day this shows that out of every 100 patients azithromycin 300mg was prescribed in 3 prescriptions. In our study, azithromycin was prescribed as 500mg once daily for 3 days and this cycle is repeated every 10th day for 4-7 times with total 6000mg to 10,500mg of azithromycin for each patient. Whereas, standard dose for azithromycin for acne is 500

mg given on 1st day and then 250 mg per day given from 2nd day upto 5th day^[16] i.e total 1500mg for each patient. Thus, overuse of azithromycin is seen in our study. Antibiotics used for co-morbid conditions were ampicillin, amoxycillin, cefixime, and cefadroxil.

Optimizing the management of acne vulgaris corresponds with improved outcomes, reduced scarring and a positive influence on the profound psychosocial disability that frequently accompanies this debilitating skin condition. Many effective, cost-effective therapies are widely available, but significant improvement or clearance can only be achieved if these agents are employed with a logical approach.

CONCLUSION

The present study revealed lacunas in the prescribing practices, which is evidenced by the frequency of administration and duration of therapy in many prescriptions. This can be addressed through proper sensitization and formulation of guidelines to be used for more rationale use of medications in acne vulgaris.

REFERENCES

1. Rathi SK. Acne Vulgaris treatment: The Current Scenario. *Indian J Dermatol.* 2011 Jan; 56(1): 7-13.
2. Burns T, Breathnach S, Cox Neil, Griffiths C. *Rook's Textbook of Dermatology.* 8th ed. Chapter 42, Disorders of the Sebaceous glands. Singapore. Blackwell Publishing Ltd. 2010; 42:17-0.68.
3. Bhambari S, Rosso JQ, Bhambari A. Pathogenesis of acne vulgaris: recent advances. *J. Drugs Dermatol.* 2009 July; 1-6.
4. Kligman AM. An overview of acne. *J Invest Dermatol.* 1974; 62(3): 268-87.
5. Gen LT, Tutakne MA, Vaishampayan CC. *IAVDL Textbook of Dermatology.* 3rd ed. Chapter 29, Acne, Rosea and Perioral dermatitis. Mumbai: Bhalani Publication House; 2008; 837-64.
6. Strom BL. Methodologic Challenges to studying patient safety and Comparative effectiveness. *Med care.* 2007 Nov 10; 10(2): S13-15.
7. *Introduction to Drug Utilization Research* Oslo: World Health Organization; 2003. Chapter 1, What is drug Utilization research and why is it needed?: p.8-12.
8. Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC et al. Guidelines of care for acne vulgaris management. *J Am Acad Dermatol.* 2007 Feb 6; 56: 651-63.
9. Kumar S, Dutta S, Beg MA, Mehta AK, Anjoom MM, Sindhu S. Drug utilization pattern in acne vulgaris in skin outpatients department of a tertiary care teaching hospital at dehradun, Uttarakhand. *Int J Med Public Health.* 2014; 3(7): 855-59.
10. Dawson AL, Dellavalle RP. Clinical review: Acne vulgaris. *BMJ.* 2013 May; 346: 1-7.
11. Kligman AM. An Overview of Acne. *J Invest Dermatol.* 1974; 62(3): 268-87.
12. National list of Essential Medicines of India. [Online].2011 [cited 2014 Aug 22]; Available from: URL: <http://pharmaceuticals.gov.in/nlem.pdf>
13. WHO Model List of Essential Medicines.[Online]. 2013 [Cited 2014 Aug 21]; Available from: URL: http://apps.who.int/iris/bitstream/10665/93142/1/EM_L_18_eng.pdf?ua=1
14. *Introduction to Drug Utilization Research* Oslo: World Health Organization; 2003. Chapter 5, Drug Classification System: p33-35.
15. Truter I, Wiseman IC, Kotze TJVW. The defined daily dose as a measure of drug consumption in South Africa. *S Afr Med J.* 1996 June; 86(6): 675-80.
16. Mac Dougall C, Chambers HF. Protein Synthesis inhibitors and Miscellaneous antibacterial agents. In: Authors, Brunton LL, Chabner BA, Knollmann BC. *Goodmann and Gilman's The Pharmacological Basis of Therapeutics.* 12th ed. China. Mc Graw Hill; 2010.p.1521-40.