



Oral Trimethoprim-sulfamethoxazole - A new frontier in the management of recalcitrant acne vulgaris : A case report.

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Abstract : Acne vulgaris is a common dermatological disease, in recalcitrant cases leads to significant morbidity that is associated with residual scarring and psychological disturbances such as poor self-image, depression, and anxiety, which leads to a negative impact on quality of life.³ Trimethoprim-sulfamethoxazole is used in dermatology to treat various skin conditions and is one of the most prescribed sulfonamide drugs. We reported 3 cases of recalcitrant acne vulgaris successfully managed on oral Trimethoprim-Sulfamethoxazole. Oral Trimethoprim-Sulfamethoxazole reduces use of antibiotics, had longer remission period, cheaper, can be combined with isotretinoin & safe.

Keywords – Recalcitrant Acne Vulgaris, psychological impact, oral trimethoprim-sulfamethoxazole, safe and cheaper modality, longer remission.

INTRODUCTION

Acne vulgaris is a common dermatological disease, often seen in adolescents. It occurs most frequently the face cheeks and to a lesser degree on the nose, forehead and chin.¹ It is characterized by seborrhea, comedones, papules and pustules, less frequently by nodules, deep pustules, or pseudocysts and in some case, is accompanied by scarring.²

Acne leads to significant morbidity that is associated with residual scarring and psychological disturbances such as poor self-image, depression, and anxiety, which leads to a negative impact on quality of life.³ Trimethoprim-sulfamethoxazole is used in dermatology to treat various skin conditions and is one of the most commonly prescribed sulfonamide drugs. Trimethoprim-sulfamethoxazole as monotherapy is an effective treatment option in many diseases but due to drug resistance, a combination therapy, usually of two drugs may be considered.

CASE DETAILS

Case 1

A 20 years male student, complaints of steroid induced nodulocystic acne with multiple papulopustular and nodulocystic acne over face in the last 3-4 years, had received multiple courses of antibiotics, steroids and retinoids in the past 3 years. Clinical response was very poor and with more frequency of recurrence. He was also facing with psychological symptoms like depression, lack of self-esteem and social withdrawal.

In past, patient received oral doxycycline 100 mg, oral tetracycline 500 mg, oral azithromycin 500 mg, intermittently over 3 years. Topical medications like clindamycin gels, retinoids, benzoyl peroxide, glycolic acid, salicylic acid facewashes, but poor clinical response observed.

On local examination, multiple 5-15mm wide nodulocystic lesions over face involving right cheek, chin, perinasal region and eyebrow region were noted. On magnifying lens, there were multiple open & closed comedons on both Checks which are cardinal features of acne vulgaris. Diagnosed as acne grade 4. No evidence of pityriasis sicca on Scalp. On systemic examination, no abnormality detected. All routine & special Investigations such as CBC, LFT, RFT, HbsAg, Tridot, urine examination, serum testosterone and serum cortisol were within normal limits.

Patient received tablet Bactrim-DS (800 mg sulfamethoxazole and 160 mg trimethoprim) B.D. for 8 weeks, topical Persole forte cream (benzoyl peroxide-10%w/w + sulfur-5%w/w) & Salicylic acid facewash. Dietary changes advised. Follow up taken for every 2 weeks by photographic evaluation, Clinical assessment, side effect profiles and blood investigations (CBC, LFT, RFT).

Patient had no side effects throughout the treatment. Patient was not found allergic to cotrimoxazole, no anaphylactic reactions or adverse drug reactions were observed. Patient followed up for 24 weeks with no major adverse effects other than residual scars. Patient maintained on oral Azithromycin as required. Good clinical response was observed.

Follow up charting for acne

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Induration	Grade
Baseline	25	44	Moderate	Moderate	Moderate	4
2 nd week	16	14	Mild	Mild	Mild	4
4 th week	13	6	Mild	Mild	Mild	3
6 th week	11	0	No	No	No	1
8 th week	8	0	No	No	No	0
10 th week	2-3	0	No	No	No	0
12 th week	0	0	No	No	No	0

Research Through Innovation

Side effect profile

Follow up visit time	Skin rash/urticaria	Anaphylactic reaction	Adverse drug reaction	Gastro-intestinal side effects	Headache	Seizures	Blood investigations
2 nd week	No	No	No	No	No	No	WNL
4 th week	No	No	No	No	No	No	WNL
6 th week	No	No	No	No	No	No	WNL
8 th week	No	No	No	No	No	No	WNL
10 th week	No	No	No	No	No	No	WNL
12 th week	No	No	No	No	No	No	WNL

Relapse charting after stoppage of treatment

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Grade
16 th week	0	0	0	0	1
20 th week	2-3	1	0	0	1
24 th week	1-2	0	0	0	1
28 th week	0	0	0	0	0
32 th week	0	0	0	0	0
36 th week	0	0	0	0	0



Fig.1 – Case 1- Baseline images (A, B, C) - A. Front profile, B. Right profile, C. Left profile; After 2 weeks (D, E) – D. Right profile, E. Left profile



Fig. 2 – Case 1 - Front profiles A. Before treatment, B. After 8 weeks of treatment

Case 2

A 19 years male student, complaints of steroid abuse nodulocystic acne with multiple papulopustular and nodulocystic acne over face for 7 years, he had history of steroid use on his own after which he had got treatment from dermatologist, who treated him with minocycline & isotretinoin for 5 months. After 20 days of remission lesions appeared all over face suggestive of poor clinical response to the treatment. He also started affecting psychologically with symptoms like social withdrawal & depression. Then also he received oral minocycline 100 mg, oral isotretinoin 10 mg, oral azithromycin 500 mg, topical steroids, nadifloxacin cream, salicylic acid facewashes, intermittently over 3 years, but poor clinical response observed.

On local examination. Multiple papulopustular & nodulocystic lesions which apparently coalescing & giving appearance of diffuse erythematous plaques involving both cheeks, chin, forehead sparing perinasal region. On systemic examination, no abnormality detected. All routine & special Investigations such as CBC, LFT, RFT, HbsAg, Tridot, urine examination, serum testosterone and serum cortisol were within normal limits.

Patient received tablet Bactrim-DS (800 mg sulfamethoxazole and 160 mg trimethoprim) B.D. for 8 weeks, topical Persole forte cream (benzoyl peroxide-10%w/w + sulfur-5% w/w) & salicylic acid facewash. Dietary changes advised. Follow up every 2 weeks by photographic evaluation, Clinical assessment, side effect profiles and blood investigations (CBC, LFT, RFT).

Patient had no side effects throughout the treatment. Patient was not found allergic to cotrimoxazole, no anaphylactic reactions or adverse drug reactions observed. Patient followed up for 24 weeks with no major adverse effects other than residual scars. Patient maintained on oral Azithromycin as required. Good clinical response was observed.

Follow up charting for acne

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Induration	Grade
Baseline	60	100	Severe	Severe	Severe	I
2 nd week	45	63	Moderate	Moderate	Moderate	I
4 th week	20	12	Mild	Mild	Mild	I
6 th week	8-10	5-6	Mild	No	No	0
8 th week	2-3	0	No	No	No	0
10 th week	0	0	No	No	No	0
12 th week	0	0	No	No	No	0

Side effect profile

Follow up visit time	Skin rash/urticaria	Anaphylactic reaction	Adverse drug reaction	Gastro-intestinal side effects	Headache	Seizures	Blood investigations
2 nd week	No	No	No	No	No	No	WNL
4 th week	No	No	No	No	No	No	WNL
6 th week	No	No	No	No	No	No	WNL
8 th week	No	No	No	No	No	No	WNL
10 th week	No	No	No	No	No	No	WNL
12 th week	No	No	No	No	No	No	WNL

Relapse charting after stoppage of treatment

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Grade
16 th week	0	0	0	0	1
20 th week	2-3	1	0	0	1
24 th week	1-2	0	0	0	1
28 th week	0	0	0	0	0
32 th week	0	0	0	0	0
36 th week	0	0	0	0	0



Fig. 3 – Case 2- Baseline images (A, B) - A.Front profile, B.Right profile; After 4 weeks (C, D, E) - A.Front profile, B.Right profile, C.Left profile

Case 3

A 21 years male student complaints of acne vulgaris with nodulocystic acne over face & trunk since 1 year & received multiple courses of treatment but no clinical improvement observed. On local examination. Multiple papulopustular & nodulocystic acne over face & trunk involving forehead, both cheeks, chin, upper chest, upper back, & shoulders with secondary changes like crusts, scab formations & scars. On magnifying lens, there were multiple open & closed comedons over both cheeks, no evidence of pityriasis sicca on Scalp, on systemic examination, no abnormality detected. All routine & special investigations such as CBC, LFT, RFT, HbsAg, Tridot, urine examination, serum testosterone and serum cortisol were within normal limits.

Patient received tablet Bactrim-DS (800 mg sulfamethoxazole and 160 mg trimethoprim) B.D. for 8 weeks, topical Persole forte cream (benzoyl peroxide-10%w/w + sulfur-5%w/w) & salicylic acid facewash. Dietary changes advised. Follow up every 2 weeks by photographic evaluation, Clinical assessment, side effect profiles and blood investigations (CBC, LFT, RFT).

Patient had no side effects throughout the treatment. Patient was not found allergic to cotrimoxazole, no anaphylactic reactions or adverse drug reactions observed. Patient followed up for 24 weeks with no major adverse effects other than residual scars. Patient maintained on oral Azithromycin as required. Good clinical response was observed.

Follow up charting for acne

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Induration	Grade
Baseline	163	250	Severe	Severe	Severe	4
2 nd week	70	170	Severe	Severe	Severe	4
4 th week	56	65	Severe	Severe	Severe	4
6 th week	23	30	Moderate	Moderate	Moderate	4
8 th week	12-15	10	Mild	Mild	Mild	3
10 th week	5-6	0	0	0	0	0
12 th week	0	0	0	0	0	0

Side effect profile

Follow up visit time	Skin rash/urticaria	Anaphylactic reaction	Adverse drug reaction	Gastro-intestinal side effects	Headache	Seizures	Blood investigations
2 nd week	No	No	No	No	No	No	WNL
4 th week	No	No	No	No	No	No	WNL
6 th week	No	No	No	No	No	No	WNL
8 th week	No	No	No	No	No	No	WNL
10 th week	No	No	No	No	No	No	WNL
12 th week	No	No	No	No	No	No	WNL

Relapse charting after stoppage of treatment

Follow up visit time	No. of lesions	Inflammation	Erythema	Swelling	Grade
16 th week	0	0	0	0	0
20 th week	2-3	0	0	0	1
24 th week	0	1	0	0	0
28 th week	0	0	0	0	0
32 th week	0	0	0	0	0
36 th week	0	0	0	0	0



Fig. 4 – Case 3 - Baseline images (A, B, C) - A. Right profile, B. Left profile, C. Upper back;

After 6 weeks of treatment (D, E, F) - Baseline images - D. Right profile, E. Left profile, F. Upper back

Discussion

Acne develops due to blockage of follicles, hyperkeratinization and keratin plug formation and sebum (microcomedo). With increased androgen production, sebaceous glands are enlarged and sebum production is increased. The microcomedo may enlarge to form an open comedons (blackhead) or closed comedons(whiteheads). Comedones occur as a result of clogging of sebaceous glands with sebum, naturally occurring oil and dead skin cells.^{4,5}

Predisposing factors for acne vulgaris include genetic predisposition (family history of severe acne), obesity, oily/seborrheic skin, higher skin surface pH, emotional stress, repetitive mechanical trauma, exposure to excess sunlight, premenstruation, mechanical occlusion (e.g. headbands, shoulder pads, surgical masks, N95 respirators), topical application of greasy products or occlusive preparations, medications (e.g. anabolic steroids, hydantoin, benzodiazepines, ramipril, adalimumab, cyclosporin, isoniazid, lithium, iodides), congenital adrenal hyperplasia, adrenal tumors, polycystic ovarian syndrome and body dysmorphic disorders.^{6,7}

The treatment of acne is challenging and often chronic, with high rates of failure and numerous choices. A good therapeutic relationship with the patient is important to establish as well as setting realistic treatment goals.⁸ Commonly used topical treatments

include benzoyl peroxide, antibiotics, sulphur and sodium sulfacetamide, azelaic acid and retinoids. Systemic treatment is frequently used and includes the use of systemic antibiotics, oral contraceptives, antiandrogens, and retinoids.^{9,10}

Conventional treatments target the pathogenic factors and include a variety of topical and oral medications such as antimicrobials, anti-inflammatory agents, hormones and retinoids.¹⁰ Oral antibiotic medications are commonly prescribed as second line therapy for patients with mild-to-moderate acne that is not adequately controlled with topical agents alone and are a mainstay of acne treatment in patients with moderate-to-severe inflammatory acne.¹¹

Importantly, acne treatment recommendations suggest that prolonged antibiotic therapy should be used in combination with other agents, such as topical retinoids and benzoyl peroxide, the latter used to both augment efficacy and reduce the potential for emergence of less sensitive strains of P acnes.^{12,13}

Trimethoprim sulfamethoxazole (TMP/SMX) can be used to treat patients with acne vulgaris that is recalcitrant to macrolide and tetracycline. Sulfamethoxazole is bacteriostatic by blocking bacterial synthesis of folic acid, which is necessary for cell division. Trimethoprim is a folic acid analogue that inhibits the enzyme dihydrofolate reductase. The 2 agents work together to block nucleotide and amino acid synthesis in the bacteria.¹⁴ Jen I¹⁵ conducted a double-blind study showed that TMP/SMX was as effective as treatment with oxytetracycline. The side effects of TMP/SMX include gastrointestinal upset, photosensitivity, and drug eruptions, the most severe of which is Stevens-Johnson syndrome/toxic epidermal necrolysis.¹⁶

Availability of new treatment options to complement the existing armamentarium should help to achieve the successful therapy of greater numbers of acne patients, ensure improved tolerability and fulfil patient expectations. Successful management of acne needs careful selection of anti-acne agents according to clinical presentation and individual patient needs.

CONCLUSION

Acne vulgaris is among the most frequent chronic skin disorders. Acne vulgaris had great psychological impact & it affects quality of life. Oral Trimethoprim-Sulfamethoxazole treatment is necessary for at least 8 weeks for a good clinical response. It also reduces use of antibiotics, had longer remission period, cheaper, can be combined with isotretinoin & safe. Still further studies are required to confirm above findings.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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