WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 1, 1543-1558. Research Article ISSN 2277– 7105

ASSESSMENT OF THE EFFICACY AND SAFETY OF SNEC 30 (CURCUMA LONGA) CAPSULES AND SNEC ORAL GEL TOPICAL APPLICATION IN THE TREATMENT OF ORAL SUBMUCOUS FIBROSIS: A PROSPECTIVE, COMPARATIVE, RANDOMIZED STUDY

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Article Received on
15 November 2021,
Revised on 05 Dec. 2021,
Accepted on 26 Dec. 2021
DOI: 10.20959/wjpr20221-22743

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ABSTRACT

Background and Aim: Oral submucous fibrosis (OSMF) is a prevalent potentially malignant disorder associated with betel quid chewing frequently observed in the Indian population. The present study aims to evaluate the efficacy and safety of snec 30 (curcuma longa) capsules and snec oral gel topical application in the treatment of oral Submucous fibrosis in a prospective, comparative, randomized study. **Materials and Methods:** Seventy nine patients were divided randomly into two groups treatment arm A and treatment arm B. After fulfilling the eligibility criteria, subjects were randomly allotted into two groups: thirty nine patients in Treatment Arm A and forty patients in Treatment Arm B. Treatment Arm A subjects received 2 capsules of SNEC30 (curcumin therapy) twice daily with 240 ml water and SNEC ORAL GEL for local application 3 times a day for 12 weeks and Arm B received conventional treatment (prescribed by the investigator). Body weight and height were measured, physical examination was performed, and vital signs including blood pressure and heart rate were

recorded. Laboratory parameters were performed at the time of screening. VAS (Visual analog scale) was used as a measure of burning sensation, mouth opening measurement was done in both groups viz., Treatment group A & Treatment group B. The statistical analysis was done using SPSS Version 22.0 statistical Analysis Software. **Results:** In Group A, the initial burning sensation was 8.4 ± 1.2%, and in Group B, it was 8.76 ± 1.51% (as measured through the visual analog scale). After 3 months, there was complete cessation of burning sensation in treatment arm A. Decrease in burning sensation between the groups was statistically significant ($p > 0.05$). In Group A, mean mouth opening at baseline (1st visit) was 3.35 ± 1.07 cm which improved to 3.77 ± 1.22 cm after 3 months of the treatment period. In Group B, mean mouth opening at baseline (1st visit) observed was 3.92 ± 1.66 cm which improved to 3.17 ± 1.48 cm after 3 months of the treatment period**.** On comparing intergroup, the difference was statistically non significant ($P > 0.05$). However, on comparing intergroup, average percent change in mean mouth opening from 1st visit to subsequent time intervals across the time period was found to be statistically significant ($P < 0.05$). **Conclusion:** SNEC 30 capsule and SNEC gel (Test formulations) showed better results than conventional treatment in improving mouth opening; also test formulations were more effective in decreasing burning sensation in OSMF patients.

KEYWORDS: Curcumin, oral submucous fibrosis, self nano emulsifying curcumin.

INTRODUCTION

Oral Submucous fibrosis (OSMF) is a potentially malignant disease that results in progressive juxta epithelial fibrosis of the oral soft tissues. It is a chronic, insidious, debilitating disease involving oral mucosa, the oropharynx, and rarely, the larynx. OSMF results in an increasing loss of tissue mobility, marked rigidity and an eventual inability to open the mouth. The most commonly involved site is buccal mucosa, followed by palate, retromolar region, faucial pillars and pharynx.

WHO has categorized oral submucosal fibrosis (OSMF) as one of the potentially malignant disorders.[1] In 1996, OSF was defined by Pindborg JJ & Sirsat SM as "An insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/ or associated with vesicle formation, it is always associated with a juxta-epithelial inflammatory reaction followed by a fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.[2-7] The prevalence of OSMF in India has been estimated to range from

0.2–2.3% in males and 1.2–4.6% in females, with a broad age range from 11 to 60 years.[8,9,10] Seedat and Van Wyk have reported about the irreversible nature of the disease, that is, once OSMF induced by the habit of chewing betel nut, the reversal of the disease after cessation of the habit could not occur.[11] Xerostomia, recurrent ulceration, pain in the ear or deafness, nasal intonation of the voice, restriction of the movement of the soft palate, thinning and stiffness of lips and pigmentation of oral mucosa are some of the symptoms of this progressively debilitating condition.

The fundamental clinical highlights incorporate trismus, mucosal torment on devouring spicy foods diminished interincisal distance, stomatopyrosis (burning mouth syndrome), reduced tongue development, substantial fibrotic bands in buccal mucosa, staining and desquamation of oral mucosa. During early OSMF, there is dysgeusia, blisters in the palate and oral mucosa. In later stages, There is whitening of the mucosa, fixation of soft palate, shortening of uvula, persevering or repetitive glossitis/stomatitis.

In clinical practice, there are various treatment options for OSMF, ranging from clinical and surgical interventions, exercise based intervention, and habit control. Regularly a combination of procedures is utilized. Individuals with OSMF distinctively complain of two issues: decreased mouth opening, burning sensation and intolerance to spicy foods that are the backbone of the Asian eating routine, leaving an individual disadvantaged both physically and mentally. In view of the clinical highlights, the aims of treatment are to reverse these signs and symptoms, stop sickness, and to minimize the risk for malignant transformation.

There is an array of reported medical interventions including dietary supplementation mainly for proteins, vitamins, anti-oxidants, anti-inflammatory agents or immunomodulatory drugs (principally corticosteroids) and proteolytic agents (such as hyaluronidase and placental extracts), and anti-cytokines. Such agents may be administered orally, topically or via submucosal injection.[12] Physical therapy may be used as a single modality or combined with other interventions. Surgical interventions are generally reserved for more advanced cases of OSMF. These treatment modalities have not been proven completely effective in treating OSMF.

Curcumin(CUR), is a yellow coloured turmeric spice (Curcuma longa) that belongs to the ginger family (Zingiberaceae). Besides its identity as colouring additive and preservative in foods, turmeric is used as an antibacterial agent and to balance blood sugar levels in human

subjects. It has been used in many other common illnesses including stomach upset, stomach ulcers, dysentery, jaundice, arthritis, wounds, acnes, and skin/eye infections.[13] Curcumin has been shown to have wide range of pharmacological activities including anti-inflammatory[14], anti-cancer[15], anti-oxidant[16,17] wound healing[18] and anti-microbial effects.[19,20] Curcumin, 1, 7-bis (4-hydroxy-3-methoxyphenol)-1, 6-heptadiene-3, 5-dione, is the primary active substance isolated from Curcuma Longa L. rhizome. It is widely available, inexpensive and has almost no side effects; it has been long used as a spice and pigment in food processing industry. Curcumin has some important biological properties such as anti-inflammatory, antioxidant and anti-cancer activity. Recently, many studies have reported curcumin's role in the prevention and reduction of fibrosis caused by harmful factors.[21,22]

The treatment of OSF especially medicinal remains an enigma. Corticosteroids have been found to be the medicine of choice by professionals. Turmeric (Curcuma longa) is a medicinal plant extensively used in Ayurveda, Unani and Siddha medicine as a home remedy for various diseases. A large number of studies have revealed that Curcumin has wide therapeutic actions such as anti-inflammatory, antioxidant and anticancer properties. Use of Curcumin has been studied as a treatment option for OSMF.

A study by Chainani-Wu et al.[23] conducted to determine the efficacy of curcumin in the treatment of OSMF and compare this to one of the available standard non invasive drug treatment as topical application of corticosteroid such as clobetasol propionate (0.05%). The present study aims to evaluate the efficacy and safety of snec30 (curcuma longa) capsules and snec oral gel topical application in the treatment of oral Submucous fibrosis in a prospective, comparative, randomized study. Therefore, this study aims to assess the effectiveness of SNEC 30 (Curcuma Longa) Capsule and SNEC Oral Gel topical application with Conventional treatment or standard treatment group in the treatment of Oral Submucosal Fibrosis (OSF) and also assess the side effects and acceptability of the study regimen.

METHODOLOGY

The study protocol was approved by KGMC Institute Ethics Committee 86th ECM II A/P 24 and written informed consent was obtained from all the participants. The Clinical trial was registered in CTRI/2018/02/011939 [Registered on: 16/02/2018]. A was an open label, prospective, comparative and randomized controlled study was conducted among 109 subjects and randomly screened 80 subjects. Study duration of clinical part was approximately 12 weeks from the initiation of study. The estimated duration of study was

about 6-8 Months, enrolment duration was 3 months and duration of protocol therapy was around 12 weeks. The screening procedure was done within one month prior to the assignment of treatment. Subjects were selected in keeping with the inclusion and exclusion criteria. Inclusion criteria required the patient or his legally accepted representative to give informed consent, age of the patient included was to be between 18-65 years and patient should be clinically diagnosed with OSMF (diagnosis was done on the basis of reduction in interincisal distance on maximum mouth opening and palpable fibrous bands involving oral mucosa). Patient willing to discontinue the use of tobacco in any form or areca nut from 1-month prior to the commencement of the treatment were included in the study. All patients included were healthy according to clinical examination (including vital signs) and laboratory tests. Patients who were suffering from liver diseases, kidney diseases or any inflammatory disease, or were on treatment using herbal agents or multivitamins and minerals for past 3 months and patients not willing to give informed consent were excluded from the study.

The study was divided into two groups;
Treatment Arm A: SNEC 30 (Curcumin Therapy) Capsule and SNEC Oral gel
Treatment Arm B: Conventional or Standard Treatment (As per Investigator discretion)
Arm A received 2 capsules of SNEC30 (curcumin therapy) twice daily with 240 ml water and SNEC ORAL GEL local application 3 times a day for 12 weeks.
Arm B received conventional treatment (prescribed by the investigator).

Socio-demographic data, history, data prior to taking medications, anthropometric measurements like weight, height, physical examination, vital signs including blood pressure and heart rate were recorded and laboratory parameters were performed at the time of screening. Our aim was to measure the efficacy the treatment has been measured by including the patient's response to Visual Analog Scale that is based on the subjective perception of burning sensation from no sensation (rated as 0) to maximum burning sensation (rated as 10) on consuming normal food as well as on consuming spicy food. Scoring of mouth opening was done according to the score allotment by SK Katharia et al (1992)[24] based on the mouth opening between upper and lower central incisors with score 0 denoting that mouth opening is normal (41 mm or more) and score 10 denoting that mouth opening is severely restricted (0 mm to 04 mm). VAS scale for burning sensation, mouth opening measurement was done in both groups viz., Reference & Test Group.

RESULTS

Efficacy Evaluation

The study consists of two groups. i.e. Reference group (n=40) and Test group (n= 39). Both the groups have almost same number of study subjects. Results are presented in tables:

Table 1: Demographic and physiological characteristics of reference and test group.

Variable name	Groups	N	Mean	Std. Deviation	P-value	95% Confidence Interval of the Difference	
						Lower	Upper
Age	**Reference**	38	36.58	14.665	.282	-9.238	2.729
	Test	36	39.83	10.737			
Weight	**Reference**	40	59.90	11.026	.571	-7.488	4.159
	Test	39	61.56	14.747			
Height	**Reference**	40	5.0933	1.24374	.928	-.59413	.65088
	Test	39	5.0649	1.52412			
SBP	**Reference**	40	123.6500	9.66768	.834	-3.55738	4.39584
	Test	39	123.2308	7.97846			
DBP	**Reference**	40	81.1250	7.51132	.556	-4.49437	2.43668
	Test	39	82.1538	7.95560			
Heart Rate	**Reference**	40	74.4000	4.10628	.768	-1.41068	1.90299
	Test	39	74.1538	3.22440			
RR	**Reference**	40	17.4000	2.44740	.357	-11.09333	4.04718
	Test	39	20.9231	23.92025			
BT	**Reference**	40	36.7750	.53048	.303	-4.76391	1.50339
	Test	38	38.4053	9.93944			

Table 2: Comparison of pre and post treatment in reference group II using paired T test.

Paired Samples Test	Paired Differences				
	Mean	Std.	95% Confidence Interval		p-value
			LL	UL	
Iron V1 - Iron V2	17.90000	54.21978	.55967	35.24033	.043
B12 (V1) - B12 (V2)	19.20000	191.84665	-42.15554	80.55554	.530
MO (V1) - MO (V2)	-.42500	.54948	-.60073	-.249[27]	.000
VAS (s)/V1 - VAS (s)/ V2	-.20000	1.87014	-.79810	.39810	.503
VAS (n)/V1 - VAS (n)/2	-1.40000	2.67754	-2.25632	-.54368	.002
Hb/V1 - Hb/V2	-.48000	2.59726	-1.31064	.35064	.250
RBC/V1 - RBC/V2	-.10900	.75067	-.34908	.13108	.364
WBC/V1 - WBC/V2	-.33125	1.92767	-.94775	.28525	.284
N/V1 - N/V2	-.41750	11.26287	-4.01954	3.18454	.816
L/V1 - L/V2	.11750	10.30130	-3.17702	3.41202	.943
E/V1 - E/V2	-1.44500	5.41072	-3.17543	.28543	.099
M/V1 - M/V2	.47000	1.79117	-.10285	1.04285	.105
B/V1 - B/V2	-.19250	1.39750	-.63944	.25444	.389
s.Ca/V1 - s.Ca/V2	1.47000	3.44592	.33735	2.60265	.012
Plt/V1 - Plt/V2	-17.47500	76.52082	-41.94754	6.99754	.157
ESR/ V1 - ESR/ V2	-3.25000	24.66363	-11.13781	4.63781	.410

S.Creatinine/V1 - S.Creatinine/V2	.03375	.17336	-.02169	.08919	.226
BUN/ V1 - BUN/V2	.23575	4.11245	-1.07948	1.55098	.719
S.Uric acid/ V1 - S.Uric acid/ V2	.15250	.80511	-.10499	.40999	.238
SGOT/ V1 - SGOT/ V2	6.21500	22.78375	-1.07160	13.50160	.092
SGPT/ V1 - SGPT/ V2	.06225	14.47801	-4.56804	4.69254	.978

Paired t-test was applied to measure the mean difference between the pre and post quantitative variables. As the table indicates, it was found that in the Reference group (n=40) study subjects pre values of Iron, MO, VAS (n), S.Ca were found to be statistically significant with p-value < 0.05 with the post value of the variables. Meanwhile, it was also found that Vitamin B12, VAS (s), Hb level, WBCs, RBCs, N,L,E,M, Platelet, Serum creatinine, BUN, Uric acid SGOT and SGPT were statistically insignificant while testing mean difference between pre and post values of the variables.

Table 3: Comparison of pre and post treatment in test group I using paired T test.

Paired Samples Test	Paired Differences				
	Mean	Std.	95% Confidence Interval		p-value
			LL	UL	
Iron V1 - Iron V2	13.35897	38.96860	.72681	25.99113	.039
B12 (V1) - B12 (V2)	4.20513	218.33378	-66.57050	74.98075	.905
MO (V1) - MO (V2)	.74359	.75107	.50012	.98706	.000
VAS (s)/V1 - VAS (s)/ V2	8.71795	1.50348	8.23058	9.20532	.000
VAS (n)/V1 - VAS (n)/2	7.56410	2.01043	6.91240	8.21581	.000
Hb/V1 - Hb/V2	.37436	2.44236	-.41736	1.16608	.345
RBC/V1 - RBC/V2	-.21333	1.95607	-.84742	.42075	.500
WBC/V1 - WBC/V2	-.35308	2.01654	-1.00677	.30061	.281
N/V1 - N/V2	1.05359	15.51048	-3.97433	6.08151	.674
L/V1 - L/V2	-.53282	10.04736	-3.78980	2.72416	.742
E/V1 - E/V2	-.21590	4.97305	-1.82797	1.39618	.788
M/V1 - M/V2	-.44154	2.07999	-1.11579	.23272	.193
B/V1 - B/V2	.03667	.10261	.00341	.06993	.032
s.Ca/V1 - s.Ca/V2	2.04974	3.97893	.75992	3.33956	.003
Plt/V1 - Plt/V2	-9.33333	51.67221	-26.08353	7.41686	.266
ESR/ V1 - ESR/ V2	2.60513	16.83158	-2.85104	8.06130	.340
S.Creatinine/V1 - S.Creatinine/V2	.01974	.10368	-.01387	.05335	.242
BUN/ V1 - BUN/V2	.16744	2.12189	-.52040	.85527	.625
S.Uric acid/ V1 - S.Uric acid/ V2	.04359	1.41473	-.41501	.50219	.848
SGOT/ V1 - SGOT/ V2	-11.82205	69.62778	-34.39277	10.74866	.296
SGPT/ V1 - SGPT/ V2	-13.98462	67.40367	-35.83436	7.86513	.203

The above table illustrates that when paired t-test was applied to measure the mean difference between the pre and post quantitative variables. It was found that in the overall study subjects (n=39) pre values of Iron, Mouth opening, VAS (s), VAS (n), B_{12}, S.Ca were found to be

statistically significant with p-value < 0.05 with the post value of the variables. Meanwhile, it was also found that Vitamin B12, Hb level, WBCs, RBCs, N,L,E,M, Platelet, Serum creatinine, BUN, Uric acid SGOT and SGPT were statistically insignificant while testing mean difference between pre and post values of the variables.

Table 4: Relationship of anthropometric and physiological parameters with outcome variables (Mouth opening and Vas score) in pre and post treatment using Pearson coefficient of correlation in reference group.

Correlations		MO (V1)	MO (V2)	VAS (s)/V1	VAS (s)/ V2	VAS (n)/V1	VAS (n)/2
Age	**(r)**	-0.22	-.419**	0.01	-.357*	.338*	-0.14
	p-value	0.19	0.01	0.96	0.03	0.04	0.39
Wt	**(r)**	-0.1	-0.07	0.06	-.322*	0.16	-0.15
	p-value	0.53	0.65	0.69	0.04	0.34	0.36
Ht	**(r)**	0.07	0.05	0.24	0.05	0.15	0.15
	p-value	0.67	0.77	0.14	0.76	0.35	0.34
SBP	**(r)**	-0.1	-0.14	0.07	-0.18	0.07	-0.04
	p-value	0.54	0.37	0.65	0.25	0.69	0.82
DBP	**(r)**	-0.12	-0.19	-0.09	-0.25	-0.01	-0.08
	p-value	0.45	0.24	0.58	0.12	0.96	0.64
HR	**(r)**	-0.04	-0.04	-0.03	-0.2	-0.28	-0.07
	p-value	0.79	0.79	0.87	0.22	0.08	0.67
RR	**(r)**	0.08	0.01	-0.07	-0.18	-0.17	0.01
	p-value	0.62	0.98	0.66	0.26	0.29	0.96
BT	**(r)**	-0.17	-.315*	-0.1	-0.17	-0.12	-0.01
	p-value	0.29	0.05	0.52	0.3	0.45	0.94

Table 5: Relationship of Biochemical parameters with outcome variables (Mouth opening and Vas score) in pre and post treatment using Pearson coefficient of correlation in reference group.

Correlations		MO (V1)	MO (V2)	VAS (s)/V1	VAS (s)/ V2	VAS (n)/V1	VAS (n)/2
Iron V1	**(r)**	0	-0.05	0.11	0.22	0.25	0.22
	p-value	0.99	0.77	0.51	0.16	0.12	0.18
Iron V2	**(r)**	-0.05	-0.05	-0.31	-0.01	0.01	-0.09
	p-value	0.78	0.76	0.05	0.97	0.95	0.6
B12 (V1)	**(r)**	0.18	0.22	-0.02	0.06	-0.03	0.02
	p-value	0.26	0.17	0.88	0.69	0.83	0.92
B12 (V2)	**(r)**	0.1	0.16	0.15	0.16	0.08	-0.14
	p-value	0.55	0.31	0.35	0.33	0.61	0.4
S.Ca/V1	**(r)**	0.18	0.26	0.14	0.12	-0.04	-0.05
	p-value	0.28	0.11	0.38	0.46	0.81	0.78
S.Ca/V2	**(r)**	0.29	0.19	0.07	-0.06	-0.03	0.02
	p-value	0.08	0.25	0.66	0.73	0.86	0.92

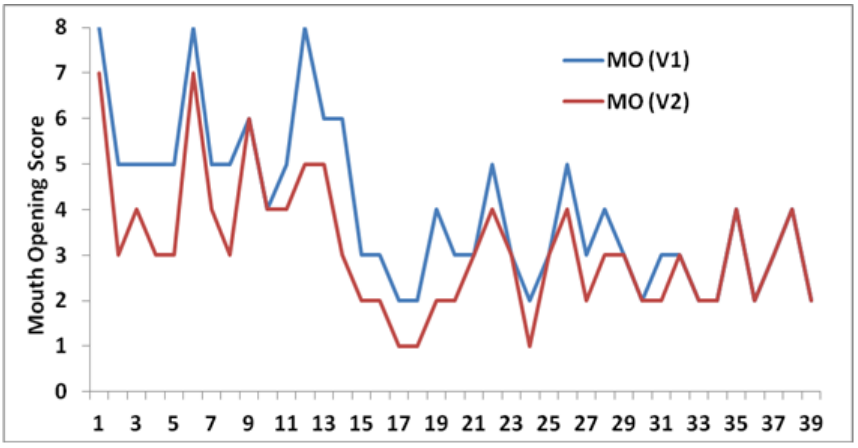

Figure 1: Showing mouth opening of pre and post treatment in treatment group. MO Represents Mouth Opening, V1: Pre treatment, V2: Post treatment.

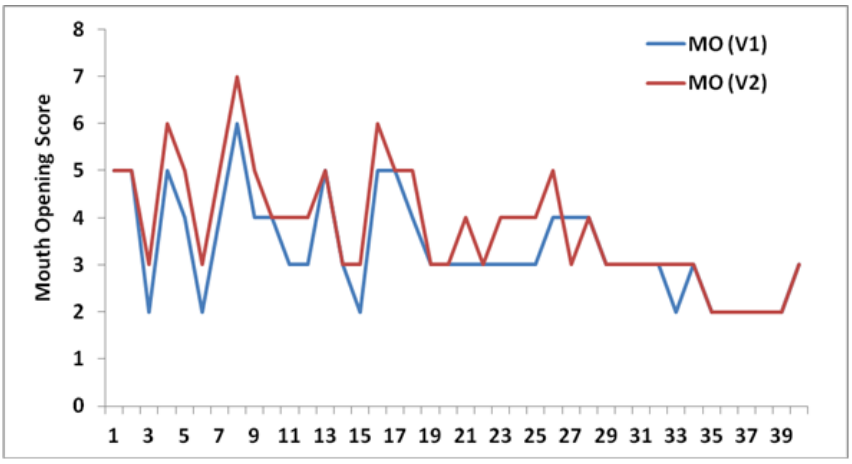

Figure 2: Showing mouth opening of pre and post treatment in reference group. MO Represents Mouth Opening, V1: Pre treatment, V2: Post treatment.

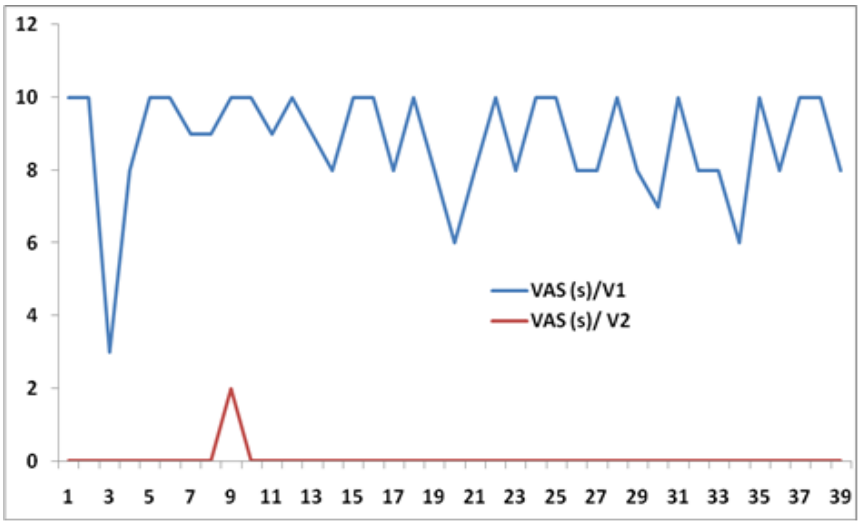

Figure 3: Showing VAS (S) score of pre and post treatment in treatment group. VAS: Visual Analog Score, V1: Pre treatment, V2: Post treatment.

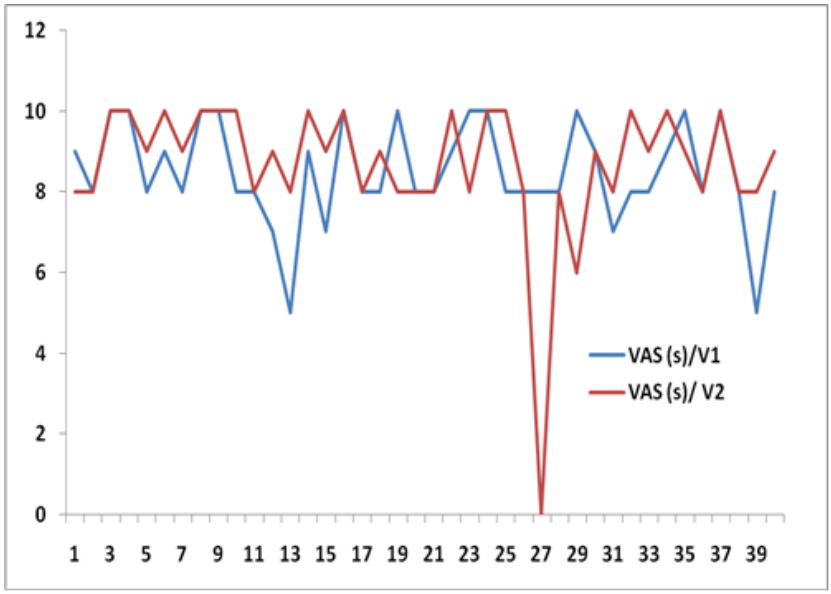

Figure 4: Showing VAS (S) score of pre and post treatment in reference group. VAS: Visual Analog Score, V1: Pre treatment, V2: Post treatment.

Or

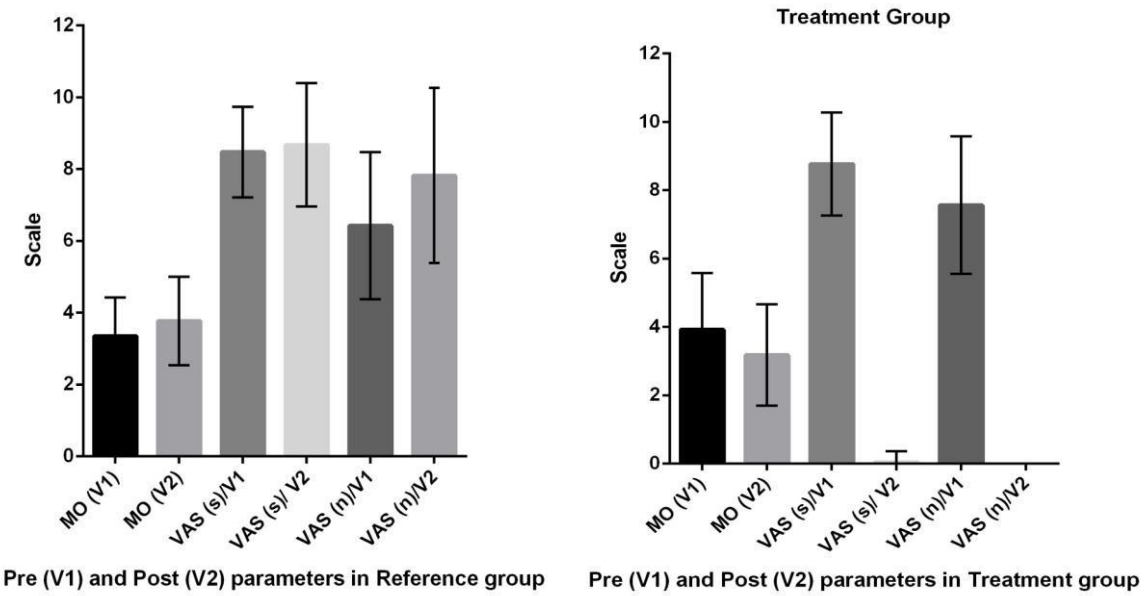

Figure 5: Represents pre and post parameters viz., Mo: Mouth opening and VAS: Visual Analog Scale in reference and treatment group.

DISCUSSION

It is well known that many plants remedies, herbal extracts, synthetic drugs etc have been introduced and tried for the treatment of OSMF which promote wound healing, and also have anti inflammatory, immunomodulatory, and antioxidant properties. Curcumin, the chief component of Curcuma longa was responsible for the majority of turmeric's therapeutic

effects. Turmeric has also been widely used for its antioxidant, analgesic, and anti-inflammatory properties.[25] Curcumin's potent antioxidant and free-radical quenching properties play an important role in the inhibitory effects of the compound on the initial stages of carcinogenesis.[26]

Curcumin exhibits low oral bioavailability in rodents and may undergo intestinal metabolism and absorbed curcumin undergoes rapid first‑pass metabolism and excretion in the bile. It is estimated that about 40%–85% of curcumin remains unaltered after ingestion in the gastrointestinal tract where it is absorbed by the intestinal mucosa. Therefore, as the bioavailability of curcumin is low, its effect also reduces in the oral mucosa.[1] The results of the present study highlights that curcumin formulations are effective in reducing the burning sensation and also have ability to increase some amount of mouth opening in patients with early stages of OSMF.

Majority of the patients in both Test Group (71.8%) and Reference Group (70%) were <30 years; this was similar to the age range reported by Kumar *et al*.[27] (70.69%), Maher *et al*.[28] and Borle *et al.*[29] Among 79 patients, 72.2% were males and 22.8% were female patients, similar male predominance was reported by Pindborg[30] (81 out of 118 were male 2.2:1), Ahmad *et al*. (male to female ratio was 2.7:1),[31] and Hazarey *et al*. (male to female ratio was 4.9:1).[32]

Hastak *et al*.[33] in the study found that turmeric oil treated patients show highest efficacy with 35% of patients showing marked improvement (>5 mm). While patients treated by turmeric oleoresin and turmeric extracts showed maximum results with moderate (3–5 mm) and mild improvement (2 mm) of increase in mouth opening respectively. Das *et al*.[34] in the study reported statistically significant and equal increase in the mouth opening of patients in Groups I (curcumin capsules) and II (turmeric oil) after 1 month and 3 months of treatment and also after the follow-up period. The mean increase was 0.87 cm in both the groups which was significant when compared with the other groups. Rai *et al*.[35] in their study reported that in patients with submucous fibrosis, mouth opening recovered significantly (P <0.05) after 6 months of the treatment.

In addition, findings were reported in the study by Hazarey *et al*.[32] that burning sensation reduced effectively in patients taking curcumin when compared with application of tenovate

ointment. Results also showed that curcumin group showed 5.93 (±2.37) mm increase in mouth opening when compared to the control group 2.66 (±1.76) mm.

Similarly in the present study, in Treatment Arm A, the initial burning sensation was 8.4 ± 1.2%, and in Treatment Arm B, it was 8.76 ± 1.51% (visual analog scale). After 3 months, there was complete cessation of burning sensation in treatment arm A. Burning sensation between the groups was statistically significant (P > 0.05). In Treatment Arm A, mean mouth opening at observes at baseline (1st visit) was 3.35 ± 1.07 cm which improved to 3.77 ± 1.22 cm after 3 months of the treatment period. In Treatment Arm B, mean mouth opening at baseline (1st visit) observed was 3.92 ± 1.66 cm which improved to 3.17 ± 1.48 cm after 3 months of the treatment period. On comparing intergroup, the difference was statistically non significant (P > 0.05) Table 2, 3. However, on comparing intergroup, average percent change in mean mouth opening from 1st visit to subsequent time intervals across the time period was found to be statistically significant (P < 0.05).

Based above on the above results, it was concluded that test formulation i.e Snec 30 capsule and Snec gel manufactured by Arbro Pharmaceuticals Private Limited, India is better than conventional treatment used for OSMF. In the reference group (Conventional treatment) subjects (n=40) it was found that pre values of Iron, MO, VAS (n), S.Ca were statistically significant with p-value < 0.05 (paired t test) with the post value of the variables. Meanwhile, it was also found that Vitamin B12, VAS (s), Hb level, WBCs, RBCs, N, L, E,M, Platelet, Serum creatinine, BUN, Uric acid SGOT and SGPT were statistically insignificant while testing mean difference between pre and post values of the variables. Similarly in the test group (n=39) we found that Pre values of Iron, Mouth open, VAS (s), VAS (n), B, S.Ca are found to be statistically significant with p-value < 0.05 (paired t test) with the post value of the variables. Meanwhile, it was also found that Vitamin B12, Hb level, WBCs, RBCs, N, L,E,M, Platelet, Serum creatinine, BUN, Uric acid SGOT and SGPT are statistically insignificant (p>0.05) while testing mean difference between pre and post values of the variables.

The time courses for the no change in hemoglobin, iron, and Erythrocyte sedimentation rate (ESR) and vitamin B12 levels) in both groups were assessed as a secondary end point of the study and found similar between Test and reference products. SNEC 30 capsule was well tolerated during the conduct of the study. There was no adverse event reported during the trial in type 2 diabetes patients as per the investigator's assessment.

CONCLUSION

SNEC 30 capsule and SNEC gel (Test formulations) showed better results than conventional treatment in improving mouth opening; also test formulations were more effective in decreasing burning sensation in OSMF patients. It can be hereby concluded that this safe and effective combination can be used to relieve the suffering of patients of OSMF.

Author Contributions

Narsingh Verma

1. Inception, headings and material to be referenced for the paper
2. Design of the study
3. Matter to be written under the various sections of the review

Smriti Rastogi

1. Thorough review of the various non pharmacological methods mentioned in the paper
2. Designed both the tables to be added to the review
3. Matter to be written under the various sections of the review

Vandana Awasthi

1. Valuable suggestions for the paper
2. Errors in language, studies etc. were earmarked
3. Proofreading the entire document
4. Role of curcumin in the treatment modality

Author disclosure statements: None.

Conflicts of Interest: None.

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