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Comparison of TENS and Astaxanthin monotherapy for myofascial pain dysfunction syndrome

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Abstract:
Myofascial Pain Dysfunction Syndrome (MPDS) is a common chronic temporomandibular disorder characterized by pain, tenderness, and restricted jaw movement, making its management challenging. Hence, 60 patients with MPDS received either TENS or astaxanthin and were followed for one month to assess symptom relief, C-reactive protein (CRP) levels, and quality of life. Both groups showed improvement, but the astaxanthin group demonstrated significantly greater reductions in pain and CRP levels and better improvement in mouth opening, mandibular movements, and SF-36 scores than the TENS group. Thus, we show that astaxanthin is a promising non-invasive therapeutic option for MPDS. Further, we show the potential anti-inflammatory and functional benefits of astaxanthin over a commonly used conservative treatment modality.

Keywords: MPDS, Astaxanthin, Transcutaneous Electrical Nerve Stimulation (TENS), CRP, Quality of life

Background:
Myofascial Pain Dysfunction Syndrome (MPDS) is a prevalent chronic musculoskeletal disorder characterized by pain, tenderness, and restricted jaw function arising from hyperirritable trigger points within the masticatory muscles **[1, 2]**. It constitutes a major subset of temporomandibular disorders (TMDs) and significantly affects patients' daily activities, psychological well-being, and overall quality of life **[3–5].** Despite its high prevalence, the multifactorial ethology of MPDS—which includes parafunctional habits, psychological stress, occlusal discrepancies, and muscle overuse—continues to make its diagnosis and management clinically challenging **[1].** Conservative therapies remain the mainstay of MPDS management. Among these, Transcutaneous Electrical Nerve Stimulation (TENS) is widely utilized for its analgesic and muscle-relaxing effects. TENS modulates pain perception through peripheral and central mechanisms, promoting muscle relaxation and enhancing local circulation. Although TENS has demonstrated efficacy in reducing Myofascial pain, the degree and duration of symptomatic relief vary among individuals **[6, 7].** In recent years, interest has grown in the use of nutraceuticals and antioxidant-based therapies for musculoskeletal pain. Astaxanthin, a potent natural carotenoid with strong anti-inflammatory and antioxidant properties, has shown promise in reducing oxidative stress and muscle inflammation—both of which play key roles in the pathophysiology of MPDS **[8–10].** However, evidence comparing its therapeutic effectiveness with established modalities like TENS remains limited. Given the need for effective, minimally invasive, and patient-friendly treatment options, a comparative evaluation of these two modalities is clinically relevant. Understanding their relative impact on pain reduction, muscle tenderness, functional outcomes, inflammatory markers, and patient-reported quality of life can contribute meaningfully to MPDS management protocols **[11, 12].** Therefore, it is of interest to evaluate the effectiveness of TENS and Astaxanthin monotherapy in the management of Myofascial Pain Dysfunction Syndrome**.**

Materials and Methods:
After obtaining prior permission from institutional ethical committee DIMMS (DU)/IEC/2022/05 the study was conducted on MPDS patients after diagnosis (clinical) in department of oral medicine and radiology. The study was registered in the Clinical Trials Registry- India (CTRI) (CTRI/2023/05/052453). CONSORT diagram for a RCT has been used to illustrate the design of the study **(Figure 1).** An informed consent was obtained from the patients for treatment. Patients was divided into 2 groups I, II respectively Astaxanthin and TENS each group having 30 patients. Evaluations of the treatment outcome was made by-

[1] Intensity of pain,
[2] Palpation of muscles,
[3] Range of Mandibular Motion (ROM),
[4] Quality of life

Only those patients who fulfilled at least 3 out of 5 of the following criteria were included in the present study, unilateral or bilateral pain in preauricular region, tenderness of one or more muscles of mastication on palpation, limitation or deviation of mandible on opening, bruxism, clicking or popping noises in the temporomandibular joint (TMJ). Patients with congenital anomalies of TMJ, history of trauma, and any other diseases causing TMJ pain were excluded from the study. All the included patients were divided into two groups by simple randomization technique after elimination the preliminary cause.

GROUP I: Patients was treated for 8 mg Astaxanthin once a day for a month with one month follows up
GROUP II: was treated with TENS for 10 sessions, 3 sessions per week for 10 minutes with one month follow-up.

During each visit patients was examined for following clinical features **[13, 14]:**

[1] Range of motion (ROM) – a. Interincisal distance - It was recorded in mm by venire calliper from mesio-incisal angle of upper central incisor up to the mesio-incisal line angle of lower incisor on 1st and last day of treatment. b. Lateral excursion movements on 1st and on the last day of treatment
[2] Observation of pain intensity at rest, on movement of jaw – It was assessed by visual analog scale (VAS) on 1st and on the last day of treatment

[3] Palpation of muscle (grading based on scale for grades of tenderness): Grade of tenderness in various muscles at 1st and on the last day of treatment
[4] SF-36 Quality of life Questionnaire **[4]**
[5] Estimation of pre and post evaluation of oxidative stress using serum marker (CRP) **[12]**

TENS therapy technique - Before starting the treatment, patient was explained about the nature of treatment and duration of treatment. Subjects were made to sit down on the chair. TENS electrode was placed over TMJ region or on the trigger point (TrP). TENS intensity was increased gradually according to patient pain threshold. No complications occurred in any of the patients after therapy. Statistical analysis was carried out by using the Kolmogorov–Smirnov test Wilcoxon signed-rank test, Mann–Whitney U test. All statistical analyses were performed using SPSS version 21, with statistical significance set at $p < 0.05$

Results:

The Astaxanthin and TENS groups consisted of 30 patients each **(Table 1).** The mean age in the Astaxanthin group (41.37 years) was notably higher than that in the TENS group (30.57 years). The duration of pain was similar between the groups, with mean durations of 9.83 months (Astaxanthin) and 8.03 months (TENS).Both groups showed comparable minimum and maximum pain durations (2 to 36 months), confirming similar chronicity of MPDS at baseline. Although age differed between the groups, duration of pain was comparable, indicating baseline similarity in chronicity of symptoms. **Figure 2** showed Females predominated in both groups—70% in Astaxanthin and 60% in TENS. Both groups showed similar gender distribution, supporting baseline comparability. Significant improvements were observed in all measured clinical and biochemical parameters: Astaxanthin immunotherapy produced marked clinical and biochemical improvements in all the parameters. All pre-post changes were statistically significant ($p < 0.001$) (**Table 2, 4).** VAS pain scores at rest and during motion decreased dramatically from mean values of 7.07 and 7.70 to 0.13, indicating near-complete pain relief. Jaw function showed significant enhancement, with mouth opening (ROM) increasing from 29.60 mm to 33.27 mm and lateral excursion improving from 5.10 mm to 8.20 mm. Quality of life also improved substantially, as reflected by an increase in SF-36 scores from 55.59 to 73.92. In addition, CRP levels reduced sharply from 6.43 mg/L to 0.51 mg/L, suggesting a strong anti-inflammatory effect. Overall, astaxanthin immunotherapy resulted in significant improvement in pain intensity, mandibular function, inflammatory status, and overall quality of life. All parameters showed significant improvement post-intervention ($p < 0.001$) **(Table 3, 5)**. VAS pain at rest decreased from a mean value of 6.63 to 0.27, while VAS pain during motion reduced from 7.47 to 1.13. Mandibular function improved, with mouth opening (ROM) increasing from 29.90 mm to 32.80 mm and lateral excursion improving from 5.10 mm to 7.73 mm. Quality of life, as measured by SF-36, also showed improvement, increasing from 52.86 to 61.68. Additionally, CRP levels decreased from 6.11 mg/L to 2.79 mg/L, indicating a reduction in inflammatory activity. Both groups showed highly significant reductions in tenderness grades ($p < 0.001$) **(Table 6).** At baseline, all patients had moderate or severe tenderness and Post-treatment evaluation showed that 76.7% of patients in the astaxanthin group and 70% of those in the TENS group achieved a status of "no tenderness **(Table 7)**. On VAS pain during motion was significantly lower in the astaxanthin group ($p = 0.0001$), SF-36 quality-of-life scores were significantly higher ($p = 0.001$), and CRP levels were significantly lower ($p = 0.0001$) compared with the TENS group. Overall, astaxanthin was significantly superior to TENS in reducing inflammatory markers and in improving quality of life and movement-related pain **(Table 8).** Statistically greater improvements were observed in the astaxanthin group for VAS score pain at rest, VAS score pain during motion, range of motion, SF-36 scores, and CRP levels, while improvement in lateral excursion showed a trend toward greater benefit with astaxanthin but did not reach statistical significance.

Table 1: Age and duration of pain among patients in Astazanthin group and TENS group

Parameters	Groups	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	Astazanthin	30	19.00	60.00	41.37	12.25
	TENS	30	19.00	54.00	30.57	10.55
Duration of pain	Astazanthin	30	2.00	36.00	9.83	7.35
	TENS	30	2.00	36.00	8.03	7.59

Table 2: Pre- and post-intervention values of pain, ROM, lateral excursion movement, SF-36, and CRP in the Astazanthin group

Parameters	Time point	N	Minimum	Maximum	Mean	Std. Deviation
VAS pain at rest	Pre	30	4.00	9.00	7.07	1.20
	Post	30	.00	2.00	0.13	0.43
VAS pain at motion	Pre	30	5.00	9.00	7.70	1.12
	Post	30	.00	2.00	0.13	0.43
ROM	Pre	30	22.00	36.00	29.60	4.08
	Post	30	25.00	40.00	33.27	3.98
Lateral excursion movement	Pre	30	4.00	7.00	5.10	0.84
	Post	30	6.00	10.00	8.20	1.06
SF-36	Pre	30	28.30	75.80	55.59	11.84
	Post	30	64.40	89.60	73.92	6.62
CRP	Pre	30	5.10	9.11	6.43	1.15
	Post	30	.10	2.23	0.51	0.45

Table 3: Pre- and post-intervention values of pain, ROM, lateral excursion movement, SF-36, and CRP in the TENS group

Parameters	Time point	N	Minimum	Maximum	Mean	Std. Deviation
VAS pain at rest	Pre	30	4.00	9.00	6.63	1.10
	Post	30	.00	2.00	0.27	0.52
VAS pain at motion	Pre	30	5.00	9.00	7.47	1.14
	Post	30	.00	7.00	1.13	1.46
ROM	Pre	30	22.00	36.00	29.90	4.31
	Post	30	25.00	38.00	32.80	3.91
Lateral excursion movement	Pre	30	4.00	7.00	5.10	0.84
	Post	30	6.00	10.00	7.73	0.94
SF-36	Pre	30	25.18	87.80	52.86	19.51
	Post	30	27.18	91.40	61.68	18.42
CRP	Pre	30	3.76	8.56	6.11	1.01
	Post	30	.23	5.53	2.79	1.99

Table 4: Difference between the pre and post values in Astaxanthin group for pain, ROM, lateral excursion movement, SF-36, and CRP

Parameters	Time point	N	Mean	Std. Deviation	Mean difference	Z	Significance (p)
VAS pain at rest	Pre	30	7.07	1.20	6.93	-4.826	**0.0001***
	Post	30	0.13	0.43			
VAS pain at motion	Pre	30	7.70	1.12	7.57	-4.840	**0.0001***
	Post	30	0.13	0.43			
ROM	Pre	30	29.60	4.08	3.67	-4.818	**0.0001***
	Post	30	33.27	3.98			
Lateral excursion movement	Pre	30	5.10	0.84	3.10	-4.837	**0.0001***
	Post	30	8.20	1.06			
SF-36#	Pre	30	55.59	11.84	18.33	-10.046	**0.0001***
	Post	30	73.92	6.62			
CRP	Pre	30	6.43	1.15	5.92	-4.783	**0.0001***
	Post	30	0.51	0.45			

*#t value presented as the data was normally distributed; *Significance at p<0.05*

Table 5: Difference between the pre and post values in TENS group for pain, ROM, lateral excursion movement, and CRP

Parameters	Time point	N	Mean	Std. Deviation	Mean difference	Z	Significance (p)
VAS pain at rest	Pre	30	6.63	1.10	6.37	-4.852	**0.0001***
	Post	30	0.27	0.52			
VAS pain at motion	Pre	30	7.47	1.14	6.33	-4.749	**0.0001***
	Post	30	1.13	1.46			
ROM	Pre	30	29.90	4.31	2.90	-4.836	**0.0001***
	Post	30	32.80	3.91			
Lateral excursion movement	Pre	30	5.10	0.84	2.63	-4.852	**0.0001***
	Post	30	7.73	0.94			
SF-36#	Pre	30	52.86	19.51	8.82	-4.217	**0.0001***
	Post	30	61.68	18.42			
CRP	Pre	30	6.11	1.01	3.32	-4.782	**0.0001***
	Post	30	2.79	1.99			

*#t value presented as the data was normally distributed; *Significance at p<0.05*

Table 6: Comparison of pre–post changes and between-group differences in grade of tenderness in the Astaxanthin and TENS Groups

Groups	Grade of tenderness	Pre (frequency)	Pre (percentage)	Post (frequency)	Post (percentage)	Z	Significance (p)
Astaxanthin group	No tenderness	0	0.0	23	76.7	-4.972	**0.0001***
	Mild tenderness	0	0.0	7	23.3		
	Moderate tenderness	17	56.7	0	0.0		
	Severe tenderness	13	43.3	0	0.0		
TENS group	No tenderness	0	0.0	21	70.0	-5.063	**0.0001***
	Mild tenderness	0	0.0	9	30.0		
	Moderate tenderness	20	66.7	0	0.0		
	Severe tenderness	10	33.3	0	0.0		
U		405.00		420.00			
Significance (p)		0.430		0.563			

**Significance at p<0.05*

Table 7: Difference between Astaxanthin and TENS group at pre and post intervention for pain, ROM, lateral excursion movement, and CRP

Parameters	Groups	N	Mean	Std. Deviation	Mean difference	U	Significance (p)
Pre VAS pain at rest	Astaxanthin	30	7.07	1.20	.43333	344.500	.106
	TENS	30	6.63	1.10			
Post VAS pain at rest	Astaxanthin	30	0.13	0.43	-.13333	392.000	.185
	TENS	30	0.27	0.52			
Pre VAS pain at motion	Astaxanthin	30	7.70	1.12	.23333	393.000	.384
	TENS	30	7.47	1.14			
Post VAS pain at motion	Astaxanthin	30	0.13	0.43	-1.00000	219.000	**0.0001***
	TENS	30	1.13	1.46			

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Pre ROM	Astaxanthin	30	29.60	4.08	-.30000	431.000	.777
	TENS	30	29.90	4.31			
Post ROM	Astaxanthin	30	33.27	3.98	.46667	420.500	.661
	TENS	30	32.80	3.91			
Pre lateral excursion movement	Astaxanthin	30	5.10	0.84	.00000	450.000	1.000
	TENS	30	5.10	0.84			
Post lateral excursion movement	Astaxanthin	30	8.20	1.06	.46667	332.500	.068
	TENS	30	7.73	0.94			
Pre SF-36#	Astaxanthin	30	55.59	11.84	2.74	0.657	0.514
	TENS	30	52.86	19.51			
Post SF-36#	Astaxanthin	30	73.92	6.62	12.25	3.427	**0.001***
	TENS	30	61.68	18.42			
Pre CRP	Astaxanthin	30	6.43	1.15	.32267	388.500	.363
	TENS	30	6.11	1.01			
Post CRP	Astaxanthin	30	0.51	0.45	-2.28133	111.000	**0.0001***
	TENS	30	2.79	1.99			

*#t value presented as data was normally distributed; *Significance at p<0.05*

Table 8: Difference in the mean change between Astaxanthin and TENS group for pain, ROM, lateral excursion movement, and CRP

Parameters	Groups	N	Change in mean (pre-post)	Std. Deviation	Mean difference	U	Significance (p)
VAS pain at rest	Astaxanthin	30	6.93	1.20	0.57	309.500	**0.031***
	TENS	30	6.37	0.93			
VAS pain at motion	Astaxanthin	30	7.57	1.04	1.23	222.500	**0.001***
	TENS	30	6.33	1.63			
ROM	Astaxanthin	30	3.67	1.54	0.77	322.000	**0.049***
	TENS	30	2.90	1.06			
Lateral excursion movement	Astaxanthin	30	3.10	0.92	0.47	328.500	0.058
	TENS	30	2.63	0.93			
SF-36	Astaxanthin	30	18.33	9.99	8.66	198.000	**0.0001***
	TENS	30	9.67	10.73			
CRP	Astaxanthin	30	5.92	1.20	2.60	137.500	**0.0001***
	TENS	30	3.32	2.09			

**Significance at p<0.05*

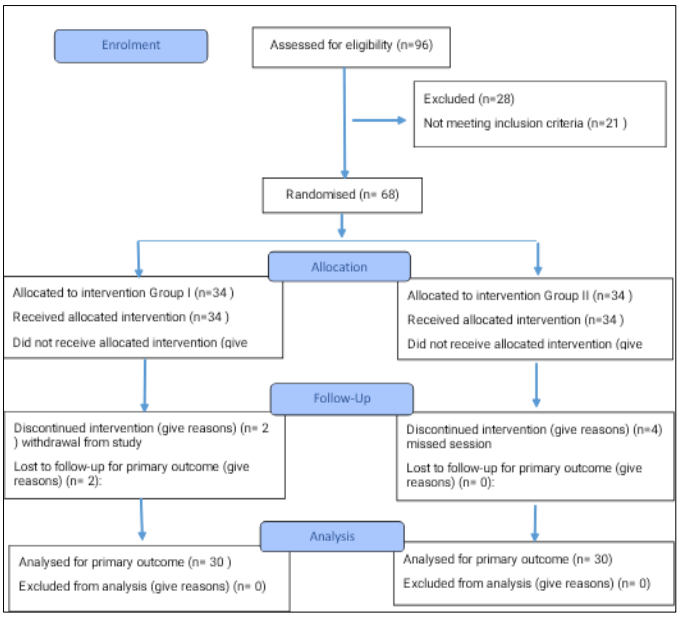

Figure 1: Flow diagram of the progress through the phases of a randomised trial of two groups (that is, enrolment, intervention allocation, follow-up, and data analysis

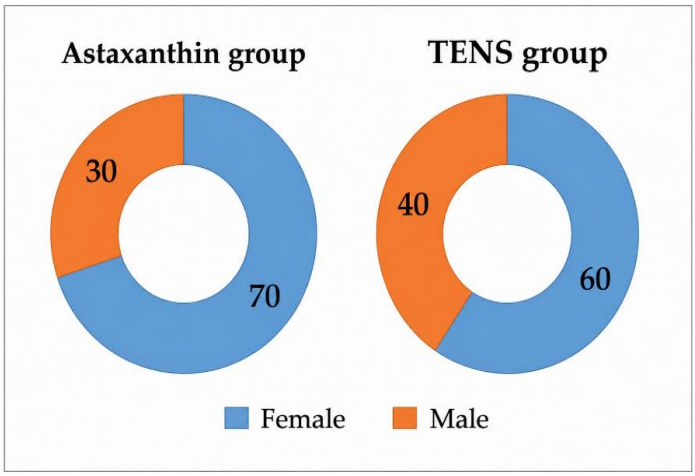

Figure 2: Pie chart representing distribution of patients with respect to gender in Astaxanthin and TENS group

Discussion:

Quality of life is substantially compromised in patients affected with MPDS, a multifactorial musculoskeletal disorder of the masticatory apparatus, clinically manifesting as or facial pain, trigger-point hyperalgesia, and progressive impairment of mandibular kinematics. As conservative therapeutic strategies constitute the primary modality of intervention, current management protocols encompass pharmacological regimens, physiotherapeutic rehabilitation, and electrotherapeutic applications. Concurrently, nutraceutical supplementation has

garnered considerable scientific interest owing to its proposed analgesic, anti-inflammatory, and ant oxidative properties in musculoskeletal pain paradigms. Accordingly, the present investigation was designed to systematically evaluate the clinical efficacy of Astaxanthin immunotherapy and Transcutaneous Electrical Nerve Stimulation (TENS) with respect to pain intensity attenuation, restoration of mandibular function, modulation of inflammatory mediators, and improvement of health-related quality-of-life indices among patients presenting with MPDS. All sixty patients reported with pain as the universally reported symptom i.e. 100% prevalence, ranging from 2 months to 36 months **[11, 13-15].** As reported in the available scientific literature, the findings of the present study are consistent with established data, wherein the peak age of occurrence of MPDS was identified within the third and fourth decades of life with more female predilection **[13-15].** In the Group I patients, Astaxanthin immunotherapy was the basic modality of treatment considering the superior analgesic response attributed to its potent antioxidant and anti-inflammatory activity, which reduces mitochondrial oxidative stress, inhibits pro-inflammatory cytokines (IL-1β, TNF-α), and enhances micro vascular perfusion in muscle tissue. These mechanisms directly target the pathophysiology of MPDS, where inflammation and oxidative stress play crucial roles. Documented data in the current study reports decrease in pain at the end of 60th day, which was statistically significant. The efficacy of Astaxanthin therapy in reducing pain in MPDS observed in the present study is similar to the observations made by previously reported scientific literature **[16-24]**. Also, Astaxanthin demonstrated a slightly higher mean increase in ROM and leaning toward greater improvement in lateral excursion. The functional gains in the Astaxanthin group may be explained by reduced muscle stiffness, improved mitochondrial energy metabolism, and decreased oxidative muscle fatigue. Additionally, CRP levels reduced sharply from 6.43 mg/L to 0.51 mg/L, suggesting a strong anti-inflammatory effect. The efficacy of Astaxanthin therapy in reducing pain in MPDS observed in the present study is similar to the observations made by other original research work. Shakouri *et al.* 20202 **[11, 12]** reported that reactive oxygen and nitrogen species contribute to nociceptor sensitization, muscle dysfunction, and myopathy in MPS. Their findings showed that higher his-CRP and lower total antioxidant capacity were associated with greater pain intensity and duration, suggesting a role of systemic inflammation in MPS. Experimental and clinical studies further support the pro-nociceptive role of inflammatory cytokines, with CRP correlating with pain and poorer quality-of-life scores in patients with MPS. Overall effect of Astaxanthin therapy enhanced the Quality of life, by an increase in SF-36 scores from 55.59 to 73.92. TENS (Group II) an established treatment modality used in MPDS provided significant pain relief, consistent with literature indicating that it modulates pain through gate control theory, activation of endogenous opioids, and improved muscle relaxation. However, its mechanism is primarily symptomatic and neuromodulator, possibly explaining its comparatively lesser effect on deep Myofascial inflammation. In TENS the decrease in pain at the end of 60th day was observed, which was statistically significant and similar to the finding of Abe *et al.* **[15]**, Mishra *et al.* 2024. **[28]** Where authors were found significant pain and tenderness reduction in MPDS with significant improvement in QOL. There is statistically significant reduction in CRP is also noticed by other Authors. At baseline, both groups were comparable in terms of duration of pain, gender distribution, frequency, timing, and type of pain, supporting appropriate randomization and group homogeneity. Tenderness grades were also comparable, with most patients exhibiting moderate to severe tenderness, indicating significant initial muscle involvement. Both Astaxanthin and TENS resulted in statistically significant reductions in VAS pain scores at rest and motion **[11, 12 and 15].** However, the magnitude of improvement was markedly greater in the Astaxanthin group, which showed near-complete elimination of pain (mean post-intervention VAS ≈ 0.13), while the TENS group demonstrated residual pain, particularly during mandibular movement (mean VAS = 1.13). Both treatment modalities led to statistically significant improvements in mouth opening and lateral excursion. The recovery rate was faster in the mean muscle pain, general pain reported by patients, pain in the masseter and pterygoid muscles and pain and limitation in lateral movements in both laser with medication and TENS groups **[15].** Astaxanthin demonstrated a slightly higher mean increase in ROM compared to TENS (mean change: 3.67 mm vs. 2.90 mm), and a trend toward greater improvement in lateral excursion. Both groups showed significant reductions in muscle tenderness, with a high proportion of patients achieving "no tenderness" post-treatment (76.7% in Astaxanthin vs. 70% in TENS). The absence of a significant between-group difference suggests that both interventions effectively alleviate trigger-point sensitivity. This finding aligns with previous evidence that both anti-inflammatory agents and electrical stimulation techniques can disrupt myofascial trigger-point activity. Astaxanthin produced significantly higher improvements in SF-36 scores compared to TENS **[11, 12, 25–28].** The greater improvement in the Astaxanthin group likely reflects reduced pain, better jaw function, and improved psychological well-being. Since MPDS affects sleep, daily activities, emotional health, and social functioning, this improvement suggests that Astaxanthin addresses overall patient well-being beyond pain relief alone. A key finding of this study was the notable reduction in serum CRP levels in the Astaxanthin group, declining from 6.43 to 0.51 mg/L, compared to a smaller decrease in the TENS group, from 6.11 to 2.79 mg/L. This greater anti-inflammatory effect of Astaxanthin is attributed to its ability to inhibit NF-κB inflammatory signaling, reduce oxidative stress, and protect muscle tissue from free radical damage. TENS, in contrast, works by reducing nerve sensitivity and improving blood flow, which relieves local muscle pain but does not significantly reduce systemic inflammation, explaining its modest effect on CRP. Between-group analysis confirmed that Astaxanthin was superior in reducing pain during movement, improving quality of life scores, and lowering CRP levels. However, both treatments showed similar outcomes in reducing trigger-point

tenderness, suggesting that each modality is equally effective in resolving localized muscle sensitivity through different mechanisms **[18].** This study directly compared two treatment modalities with different mechanisms of action. Both clinical symptoms and a biochemical marker (CRP) were assessed, providing a well-rounded evaluation of treatment outcomes. However, the short treatment period limits conclusions about long-term effectiveness. Differences in age between groups may have affected subjective pain reporting. Since only immunotherapy was examined, the results cannot be extended to combination treatment approaches. Future studies with larger sample sizes and longer follow-up periods are needed to confirm these findings. Investigating the combined use of Astaxanthin and TENS may reveal potential additive or synergistic benefits in managing MPDS.

Conclusion:

Both TENS and Astaxanthin significantly improved clinical symptoms of MPDS. However, Astaxanthin demonstrated superior effectiveness, especially in reducing inflammation, improving quality of life, and alleviating movement-related pain. These findings highlight Astaxanthin potential as a promising, non-invasive, and effective therapeutic option in the management of Myofascial Pain Dysfunction Syndrome.

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