

Effect of Astaxanthin Supplementation on Glycaemic Control in Patients with Type 2 Diabetes Mellitus with Diabetic Neuropathy: An Interventional Study

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Abstract

Background

Type 2 diabetes mellitus (T2DM) is associated with chronic hyperglycaemia and metabolic disturbances that contribute to the development and progression of diabetic neuropathy. Oxidative stress and inflammation are important mechanisms involved in diabetic nerve injury. Astaxanthin, a xanthophyll carotenoid with antioxidant and anti-inflammatory properties, may have a beneficial role in metabolic regulation. However, clinical evidence regarding its effect on glycaemic parameters in patients with T2DM with diabetic neuropathy remains limited. Therefore, the present study investigated the effect of astaxanthin supplementation on glycaemic parameters in patients with T2DM with diabetic neuropathy.

Methods: This interventional before-and-after study included patients with T2DM and diabetic neuropathy who received astaxanthin 8 mg/day orally as an adjunct to their routine diabetes treatment for 3 months. Fasting blood sugar (FBS), postprandial blood sugar (PPBS) and glycated haemoglobin (HbA1c) were assessed before and after supplementation. The pre- and post-supplementation values were compared using a paired t-test.

Results: Fifty-two participants with complete paired observations were included in the analysis. Following 3 months of astaxanthin supplementation, FBS decreased from 158.67 ± 41.92 to 147.65 ± 25.73 mg/dL, although the change was not statistically significant ($p=0.055$). PPBS decreased from 234.40 ± 56.28 to 219.48 ± 37.22 mg/dL ($p=0.035$), while HbA1c decreased from $8.79 \pm 1.79\%$ to $8.09 \pm 1.50\%$ ($p=0.003$).

Conclusion: In patients with T2DM with diabetic neuropathy, 3 months of adjunctive astaxanthin supplementation was associated with significant improvements in PPBS and HbA1c, while the reduction in FBS did not reach statistical significance. These findings suggest a potential beneficial role for astaxanthin in glycaemic management; however, controlled studies with larger sample sizes are required to confirm the findings.

Keywords: Astaxanthin; type 2 diabetes mellitus; diabetic neuropathy; glycaemic control; fasting blood sugar; postprandial blood sugar; HbA1c.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from impaired insulin secretion, insulin resistance, or a combination of both. Prolonged hyperglycaemia contributes to a range of microvascular and metabolic complications, among which diabetic neuropathy is one of the most common. Diabetic neuropathy may present with sensory disturbances, neuropathic pain, altered vibration and pressure perception, and loss of protective sensation, ultimately increasing the risk of foot ulceration and other complications.^{1,2}

The development of diabetic neuropathy is multifactorial and involves chronic hyperglycaemia, dyslipidaemia, oxidative stress, mitochondrial dysfunction, inflammation and impaired neuronal homeostasis. Persistent metabolic abnormalities increase the generation of reactive oxygen species and reactive nitrogen species while impairing endogenous antioxidant defence. This imbalance can promote oxidative damage to neurons, Schwann cells and the peripheral nerve microenvironment.^{3,4} Recent evidence has further emphasized the interaction between oxidative stress, mitochondrial dysfunction and inflammatory signalling in the progression of diabetic neuropathy.⁵

Although good glycaemic control remains an important component of diabetes management, diabetic neuropathy may progress through several interacting metabolic and vascular pathways. Current management therefore includes glycaemic and cardiovascular risk-factor control, prevention of foot complications and treatment of neuropathic symptoms, but effective interventions that directly modify the underlying pathophysiology remain limited.^{1,6} This has generated interest in nutritional and pharmacological approaches that may simultaneously influence metabolic abnormalities, oxidative stress and inflammation.

Astaxanthin is a naturally occurring xanthophyll carotenoid found predominantly in microalgae such as *Haematococcus pluvialis*. Its conjugated polyene structure and polar terminal groups enable interaction with cellular lipid membranes and aqueous environments. Astaxanthin has demonstrated antioxidant, anti-inflammatory and cytoprotective properties and has been investigated for its ability to modulate reactive oxygen species and endogenous antioxidant defence systems.^{7,8}

The potential relevance of astaxanthin to diabetes has been supported by experimental and clinical studies investigating its effects on glucose metabolism, insulin sensitivity, oxidative stress and inflammation. A review of the antidiabetic potential of astaxanthin suggested that its antioxidant and metabolic actions may be relevant to diabetes and its complications.⁹ More recent human evidence has also indicated that astaxanthin can influence oxidative and inflammatory pathways, supporting further investigation of its role as an adjunctive nutritional intervention in metabolic disease.¹⁰

Patients with T2DM who have already developed diabetic neuropathy represent an important population in which an intervention targeting both metabolic and oxidative pathways may be clinically relevant. However, evidence specifically evaluating changes in glycaemic parameters following astaxanthin supplementation in patients with T2DM with diabetic neuropathy remains limited. Therefore, the present study was undertaken to evaluate changes in fasting blood sugar (FBS), postprandial blood sugar (PPBS) and glycated haemoglobin (HbA1c) before and after 3 months of astaxanthin supplementation in patients with T2DM with diabetic neuropathy.

2. Materials and Methods

2.1 Study design and participants

This interventional study was conducted among patients with diabetic neuropathy at Mahatma Gandhi Medical College and Research Institute (MGMCRI), Puducherry, India.

Participants were recruited according to the predefined eligibility criteria of the study protocol. Patients aged 30–60 years with established T2DM with mild diabetic neuropathy were considered eligible. Diabetic neuropathy was assessed using clinical evaluation and biothesiometer-based assessment. Participants fulfilling the study criteria were enrolled after obtaining written informed consent. The present manuscript represents a focused analysis of glycaemic parameters in participants who received astaxanthin supplementation.

2.2 Ethical approval

The study was conducted after obtaining approval from the Institutional Human Ethics Committee of Mahatma Gandhi Medical College and Research Institute, Puducherry.

2.3 Intervention

Participants received astaxanthin 8 mg/day for 3 months as an adjunct to their routine treatment. Participants continued their prescribed antidiabetic medications and other routine medications throughout the intervention period according to their treating physician's recommendations. Astaxanthin was administered in addition to, and not as a replacement for, standard diabetes treatment.

2.4 Assessment of glycaemic parameters

Glycaemic status was assessed using FBS, PPBS and HbA1c. FBS was measured following an overnight fast and expressed in mg/dL. PPBS was assessed according to the study protocol following food intake and expressed in mg/dL. HbA1c was measured using the laboratory's standardized method and expressed as a percentage. Blood samples were collected at baseline before initiation of astaxanthin supplementation and again following completion of the 3-month intervention.

2.5 Statistical analysis

Data were analysed using appropriate statistical software. Continuous variables were expressed as mean $\pm$ standard deviation. Since the analysis involved paired observations from the same

participants before and after supplementation, the paired t-test was used to assess changes in FBS, PPBS and HbA1c. A two-sided p value <0.05 was considered statistically significant.

3. Results

A total of 52 participants with complete paired observations were included in the final analysis. Following 3 months of astaxanthin supplementation, FBS decreased from 158.67 ± 41.92 mg/dL before supplementation to 147.65 ± 25.73 mg/dL after supplementation; however, the change was not statistically significant ($p=0.055$). PPBS decreased from 234.40 ± 56.28 mg/dL to 219.48 ± 37.22 mg/dL, and this reduction was statistically significant ($p=0.035$). HbA1c decreased from $8.79 \pm 1.79\%$ before supplementation to $8.09 \pm 1.50\%$ after supplementation, with a statistically significant difference ($p=0.003$). Thus, among patients with T2DM with diabetic neuropathy, significant improvement was observed in PPBS and HbA1c following 3 months of astaxanthin supplementation, while the change in FBS did not reach statistical significance.

Table 1. Comparison of glycaemic parameters before and after 3 months of astaxanthin supplementation

Parameter	Before supplementation Mean $\pm$ SD	After supplementation Mean $\pm$ SD	Mean change (After – Before)	Paired 't' test	p - value	95% CI of mean difference
FBS (mg/dL)	158.67 ± 41.92	147.65 ± 25.73	-11.02	1.961	0.055	-22.30 - 0.26
PPBS (mg/dL)	234.40 ± 56.28	219.48 ± 37.22	-14.92	2.168	0.035	-28.74 - -1.10
HbA1c (%)	8.79 ± 1.79	8.09 ± 1.50	-0.70	3.146	0.003	-1.14 - -0.25

CI, confidence interval; SD, standard deviation. A p -value <0.05 was considered statistically significant.

The overall pattern demonstrated a reduction across all three glycaemic measures following the intervention. The reduction was greatest in relative terms for HbA1c, while the absolute reductions in FBS and PPBS reflected improvements in fasting and postprandial glucose concentrations, respectively. Statistical significance was observed for PPBS and HbA1c, indicating that these changes were unlikely to be explained by sampling variation alone under the assumptions of the paired analysis.

4. Discussion

In the present study, 3 months of astaxanthin supplementation as an adjunct to routine diabetes treatment was associated with improvement in glycaemic control among patients with T2DM with diabetic neuropathy. The improvement was more evident for PPBS and HbA1c, whereas the reduction in FBS did not reach statistical significance. As all participants had diabetic neuropathy,

these findings represent changes following supplementation rather than comparisons between patients with and without neuropathy.

These findings are supported by previous clinical studies. Sokri-Mashhadi et al. reported that 8 mg/day of astaxanthin for 8 weeks significantly reduced fructosamine, although the reduction in plasma glucose was marginal.¹¹ Similarly, Urakaze et al. demonstrated that 12 weeks of astaxanthin supplementation improved 120-minute glucose during an oral glucose tolerance test and HbA1c, together with improved insulin sensitivity.¹² Although their study populations differed from the present study, the improvement in post-challenge and longer-term glycaemic measures is consistent with the present findings.

A recent meta-analysis by Molani-Gol et al., including nine randomized controlled trials involving 403 participants with prediabetes or T2DM, also reported significant reductions in fasting blood glucose and HbA1c with astaxanthin supplementation.¹³ The non-significant change in FBS in the present study may reflect differences in sample size, baseline glycaemic status, intervention duration, concomitant treatment and study design. A systematic review and meta-analysis by Shokri-Mashhadi et al. similarly reported improvements in glycaemic parameters with carotenoid supplementation, although the authors emphasized limitations in the certainty of evidence.¹⁴

The metabolic effects of astaxanthin may be related to its antioxidant, anti-inflammatory and metabolic actions. Sokri-Mashhadi et al. reported reductions in malondialdehyde and interleukin-6 following 8 mg/day astaxanthin supplementation, while Roustaei Rad et al. demonstrated changes in antioxidant defence and Nrf2 expression.^{15,16} Taghiyar et al. further reported that 10 mg/day astaxanthin for 12 weeks modified the serum fatty-acid profile and increased SIRT1 expression and AMPK activity in patients with T2DM, suggesting involvement of pathways related to energy and lipid metabolism.¹⁷

More recent clinical evidence from Sharifi-Rigi et al. also indicates effects on inflammation-related microRNAs and metabolic parameters, supporting a potential role for cellular inflammatory signalling.¹⁸ Ciaraldi et al. observed non-significant trends toward improved insulin-stimulated glucose disposal, fasting insulin and HOMA2-IR after 24 weeks of supplementation in adults with prediabetes and dyslipidaemia, suggesting a possible influence on insulin action.¹⁹

Additional evidence from Basereh et al. supports effects of astaxanthin on oxidative stress and inflammatory responses in individuals with T2DM.²⁰ Experimental findings by Sakayanathan et al. further suggest that an astaxanthin-S-allyl cysteine ester may attenuate oxidative and endoplasmic reticulum stress and preserve insulin secretion under glucolipotoxic conditions.²¹ However, these experimental findings cannot be directly extrapolated to patients, and oxidative-stress, inflammatory and molecular pathways were not assessed in the present study. Therefore, they provide biological plausibility rather than direct evidence for the mechanisms underlying the observed glycaemic changes.

The present findings should nevertheless be interpreted cautiously. Astaxanthin was administered in addition to routine diabetes treatment; therefore, the observed changes cannot be attributed

exclusively to astaxanthin. Dietary intake, medication adherence and other changes in diabetes management may also have contributed to glycaemic changes. Furthermore, although all participants had diabetic neuropathy, neuropathy-specific outcomes were not reassessed after supplementation. Thus, the present study demonstrates changes in glycaemic parameters and should not be interpreted as evidence of improvement in diabetic neuropathy itself.

Overall, the findings add to the emerging clinical evidence suggesting a potential role for astaxanthin as an adjunct to conventional treatment in T2DM with diabetic neuropathy. Larger controlled studies with longer follow-up and simultaneous assessment of glycaemic, oxidative-stress and neuropathy-related outcomes are needed to determine the clinical significance of these effects.

5. Strengths

A major strength of the study is that the same participants were assessed before and after astaxanthin supplementation, allowing evaluation of within-participant changes in glycaemic parameters. The study also focused specifically on patients with T2DM with diabetic neuropathy, an understudied clinical population, and used a defined astaxanthin dose and supplementation period.

6. Limitations

The study had a relatively small sample size and lacked a parallel placebo or untreated control group. Astaxanthin was given alongside routine diabetes treatment, and therefore the observed changes cannot be attributed solely to supplementation. In addition, the study did not include direct assessment of oxidative-stress biomarkers or neuropathy-specific outcomes after supplementation.

7. Conclusion

Three months of adjunctive astaxanthin supplementation was associated with significant improvements in PPBS and HbA1c, but not FBS, in patients with T2DM with diabetic neuropathy. Larger controlled studies are needed to confirm these findings.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the ethical principles governing research involving human participants and received approval from the Institutional Human Ethics Committee of Mahatma Gandhi Medical College and Research Institute (MGMCRI), Puducherry, India. Written informed consent was obtained from all participants before enrolment in the study.

Conflict of interest: The authors declare that there is no conflict of interest.

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