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The Therapeutic Potential of Ascorbic Acid in Enhancing Health-Related Quality of Life and Modulating Relapse Rates in Multiple Sclerosis Patients: A Clinical Study in West Libya

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ABSTRACT

Multiple sclerosis is a chronic inflammatory autoimmune disease characterized by CNS lesions that can lead to severe physical or cognitive disability as well as neurological defects, and reduce quality of life. This disease is associated with demyelination, neurodegeneration, and increased oxidative stress.

Although the etiology and pathogenesis of multiple sclerosis remain unclear, the present documents illustrate that the cause of this disease is multifactorial and includes genetic predisposition together with environmental factors such as exposure to infectious agents, vitamin deficiencies, and smoking. These agents can trigger a cascade of events in the immune system, which leads to inflammation, neurodegeneration, demyelination, and neuronal dysfunction. Conventional therapies for this disease are based on the use of anti-inflammatory and immunomodulatory drugs, but these treatments are not able to stop the destruction of nerve tissue. This study hypothesizes that treatment with ascorbic acid (vitamin C) supplementation may reduce symptoms and positively influence the outcome of MS, resulting in improved patient quality of life.

The Multiple Sclerosis Quality of Life 29 questionnaire (MSQL-29) was applied for disease progression and to evaluate the multiple sclerosis patient life style. The investigation of the disease status was performed by magnetic resonance imaging (MRI) and biochemical analysis for vitamin C levels in the blood.

Through laboratory tests, it was found that patients with multiple sclerosis have a deficiency in vitamin C, while Magnetic Resonance Imaging (MRI) showed no structural changes in lesion load. Through the Multiple Sclerosis Quality of Life-29 questionnaire (MSQL-29), the study found that vitamin C has given positive results by improving the general health of patients and has reduced the sense of pain and the extent to which pain interferes with the patient's normal work; vitamin C raises the sense of energy while reducing the sense of frustration and depression and improving the enjoyment of life. Thus, improving the quality of life.

Keywords- *Multiple sclerosis; Vitamin C; MS Patient quality of life.*

INTRODUCTION

Multiple sclerosis (MS) is a chronic inflammatory autoimmune disease of the central nervous system and one of the most common neurological diseases in young people. Most people with MS are in the 20-50 age range;[1] the disease tends to affect women more than men, where women are 2-3 times more prevalent than men.[2,3] This disease can cause death, disability, depression, physical impairment, and reduced quality of life. For instance, 50% of those affected require assistance with mobility, and 10% require wheelchairs 15 years after the onset of the disease.[4]

In multiple sclerosis, the myelin sheet of the nerve fibers is destroyed; the immune system attacks the nervous system, leading to demyelination, where the myelin sheath that covers and protects the nerves is destroyed. This leads to impaired communication between nerve cells and leaves multiple areas of scar tissue or sclerosis.[5]

The course of MS is highly varied and unpredictable. Several reports have revealed genetic and environmental factors, as well as inflammation and oxidative stress, as key players in the pathogenesis of MS.[6] Multiple sclerosis is associated with demyelination, neurodegeneration, and increased oxidative stress.[7] High levels of oxidative stress are associated with inflammation and play an important role in the pathogenesis of MS.[8] The exact cause of MS is not clear; both genetic and environmental factors have been implicated in MS etiology.[9] Multiple sclerosis is a progressive disease with no cure so far. Although treatments are available to manage the disease course, they are only partially effective.[10]

Ascorbic acid (Vitamin C) has a role as a scavenger of free radicals.[11] Vitamin C contributes to the synthesis of collagen, which is associated with myelin formation.[12] Moreover, it is essential to promote Schwann cell myelin formation.[13]

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These properties of Vitamin C have raised the hypothesis that this compound could be useful for the prevention and/or treatment of MS,[14] it may show a reduction in the frequency of relapse and disease symptoms.

Aim of this work: The goals of this study are to decrease relapses, provide symptomatic relief, and improve the quality of life of MS patients. The study will be carried out by estimating the effect of vitamin C (a water-soluble vitamin) on MS patients' quality of life for four months.

This study investigates the effect of vitamin C, that have anti-oxidative stress action and may have a remyelination effect, resulting in a decrease in relapse and improvement in multiple sclerosis patient quality of life. This vitamin may have a therapeutic effect on multiple sclerosis.

MATERIALS AND METHODS

This study was carried out in MS patients at Ali Omar Askar Hospital, Tripoli, Libya. The study involved two groups of MS patients; the first group took the prescribed treatment for MS disease by the specialist; the second group received MS treatment and vitamin C [500mg].

Vitamin C is administered once per day for four months. Investigations for each patient were performed by Magnetic Resonance Imaging (MRI), and biochemical analysis for vitamin C level in the blood.

Multiple Sclerosis Quality of Life-29 Questionnaire (MSQL -29)[15] was applied at the beginning of the study, and at the end of the study after four months. The sample size was twenty subjects in the control group and twenty-two in the vitamin C administered group. Patients with relapsing-remitting MS are involved in this study. This questionnaire shows the lifestyle of patients, the degree of disease, and the changes that happen after patients take vitamin C. This questionnaire was used in personal interviews with the patient. Investigation of the disease status was performed by MRI, and biochemical analysis for vitamin C level in the blood.

***Statistical analysis*:** Data analysis was performed using a computer program (SPPS) version 26. Descriptive results were expressed as mean ± standard error of the mean. Comparing parameters was applied using an independent sample t-test. The difference was considered to be significant at $P \leq 0.05$.

RESULTS

Results of Multiple Sclerosis Patient Quality of life_29 questionnaire (MSQL_29)

Compared to one year ago, how would you rate your health in general now?

The collected information showed a significant improvement in general health in patients administered vitamin C in the second visit compared to the first visit ($P = 0.037$); while the general health was not changed in the control group ($P = 0.910$) compared to the first visit (Table 1-A and 1-B).

Table 1-A: The effect of vitamin C on the general health of MS patients.

Parameter (General health) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	3.2 ± 1.29	3.35 ± 1.461
Second Visit	3.2 ± 1.24	2.45 ± 0.852 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 1– B showed that the number of patients administered vitamin C was much better or somewhat better in general health in the second visit compared to the first visit. The number of patients in the control group showed no change in general health compared to the first visit.

Table 1-B: The number of cases of general health in the first visit and the second visit.

Parameter General) (health	Visit	1-much better	2-somewhat better	about the same 3-	somewhat worse 4-	much worse 5-
Patients (Control)	First visit	1	6	5	3	5
	Second visit	1	6	5	4	4
Vitamin C	First visit	4	3	5	4	6
	Second visit	6	6	5	4	1

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing football

The results showed no change in moderate activity in patients administered vitamin C on the second visit compared to the first visit ($P = 0.128$); also, the moderate activity was not changed in the control group ($P = 0.852$), compared to the first visit (Table 2– A and 2-B).

Table 2-A: The effect of vitamin C on the moderate activities of MS patients.

Parameter (Moderate activity) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First visit	2.1 ± 0.85	1.9 ± 0.85
Second visit	2.0 ± 0.82	2.2 ± 0.70

Table 2 – B showed that the number of patients administered vitamin C was not changed in the second visit compared to the first visit ($P > 0.05$); also, the number of patients in

the control group did not show any changes in moderate activity compared to the first visit ($P > 0.05$).

Table 2-B: The number of patient cases who had moderate activity in the first visit and second visit.

Parameter (Moderate activity)	Visit	1-a limit a lot	2- limited a little	3-not limited at all
Patients (Control)	First visit	6	6	8
	Second visit	6	7	7
Vitamin C	First visit	8	7	7
	Second visit	3	10	9

Lifting or carrying groceries

Patients administered vitamin C in the second visit showed no change in lifting or carrying groceries compared to the first visit ($P = 0.400$); also, the lifting or carrying of groceries by patients was not changed in the control group ($P = 1.00$) compared to the first visit (Table 3-A and 3-B).

Table 3-A: The effect of vitamin C on the lifting or carrying of Groceries for MS patients.

Parameter (Lifting or carrying groceries) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First visit	1.8 ± 0.76	1.8 ± 0.76
Second visit	1.8 ± 0.76	2.0 ± 0.75

Table 3 – B showed that the number of patients administered vitamin C was not changed in lifting or carrying groceries in the second visit compared to the first visit. The number of patients in the control group did not show any changes in lifting or carrying groceries compared to the first visit.

Table 3-B: The number of patient cases in lifting or carrying groceries.

Parameter (Lifting or carrying groceries)	Visit	1-alimit a lot	2- limited a little	3-not limited at all
Patients (Control)	First visit	8	8	4
	Second visit	8	8	4
Vitamin C	First visit	10	8	4
	Second visit	6	10	6

Climbing several flights of stairs

Results showed no change in patients administered vitamin C, in climbing several flights of stairs, in the second visit compared to the first visit ($P = 0.710$); also, the climbing several flights of stairs in the second visit did not change in the control group ($P = 1$) compared to the first visit (Table 4-A and 4-B).

Table 4-A: The effect of vitamin C on climbing several flights of stairs of MS patients.

Parameter (Climbing several flights of stairs) *(Mean ± S.E.)*	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	1.9 ± 0.85	1.9 ± 0.91
Second Visit	1.9 ± 0.85	2.0 ± 0.81

Table 4– B showed that the number of patients administered vitamin C, in climbing several flights of stairs, did not change in the second visit compared to the first visit; also, the number of patients in the control group did not show any changes in climbing several flights of stairs compared to the first visit.

Table 4-B: The number of cases of climbing several flights of stairs

Parameter (Climbing several flights of stairs)	Visit	1-a limit a lot	2- limited a little	3-not limited at all
Patients (Control)	First visit	8	6	6
	Second visit	8	6	6
Vitamin C	First visit	10	5	7
	Second visit	7	8	7

Climbing one flight of stairs

Results showed that there was no change in patients administered vitamin C, climbing one flight of stairs, in the second visit compared to the first visit ($P = 0.151$); also, the climbing one flight of stairs was not changed in the control group of patients ($P = 1$) compared to the first visit (Table 5-A and 5-B).

Table 5-A: The effect of vitamin C on the climbing of one flight of stairs of MS patients.

Parameter (climbing one flight of stairs) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First visit	1.8 ± 0.87	1.8 ± 0.89
Second visit	1.8 ± 0.87	2.1 ± 0.75

Table 5– B showed that the climbing one flight of stairs was a little better in patients administered vitamin C on the second visit compared to the first visit; also, the number of patients in the control group did not show any changes in climbing one flight of stairs compared to the first visit.

Table 5-B: The number of cases of climbing one flight of stairs

Parameter (Climbing one flight of stairs)	Visit	1-limited a lot	2-limited a little	3-not limited at all
Patients (Control)	First visit	5	9	6
	Second visit	5	9	6
Vitamin C	First visit	5	11	6
	Second visit	8	5	9

Walking more than a mile

Results of patients walking more than a mile showed no change in patients administered vitamin C in the second visit compared to the first visit (P = 0.850); also, the walking more than a mile by patients was not changed in the control group (P = 1) compared to the first visit (Table 6-A and 6-B).

Table 6-A: The effect of vitamin C on walking more than a mile by MS patients.

Parameter (Walking more than a mile) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	1.8 ± 0.81	1.9 ± 0.78
Second Visit	1.8 ± 0.81	2.0 ± 0.61

Table 6– B shows that the number of patients administered vitamin C and walking more than a mile was not changed in the second visit compared to the first visit. The number of patients in the control group did not show any changes in walking more than a mile compared to the first visit.

Table 6-B: The number of cases of walking more than a mile.

Parameter (Walking more than a mile)	Visit	1-a limit a lot	2- limited a little	3-not limited at all
Patients (Control)	First visit	8	7	5
	Second visit	8	7	5
Vitamin C	First visit	9	6	7
	Second visit	7	8	7

Walking one block

Walking one block by patients administered vitamin C in the second visit was not changed compared to the first visit (P = 0.886); also, walking one block by patients was not changed in the control group (P = 0.849) compared to the first visit (Table 7-A and 7-B).

Table 7-A: The effect of vitamin C on walking one block by MS patients.

Parameter (Walking one block) (Mean ± (.S.E	Patients (Control)	Patients were administered vitamin C
First Visit	0.81 ± 1.8	0.91 ± 2.0
Second Visit	0.83 ± 1.8	0.84 ± 1.9

Walking one block by patients was not changed in patients administered vitamin C in the second visit, compared to the first visit. The number of patients in the control group did not show any changes in walking one block, in the second visit, compared to the first visit (Table 7– B).

Table 7-B: The number of cases of patients who walk one block in the first visit and the second visit

Parameter (Walking one block)	Visit	1-a limit a lot	2-limited a little	3-not limited at all
Patients (Control)	First visit	8	7	5
	Second visit	9	6	5
Vitamin C	First visit	9	5	8
	Second visit	8	7	7

How much bodily pain have you had during the past 4 weeks?

Results showed a significant decrease in patients' bodily pain who were administered vitamin C in the second visit compared to the first visit (P= 0.004); while the bodily pain in the second visit was not changed in the control group (P = 0.844) compared to the first visit (Table 8-A and 8-B).

Table 8-A: The effect of vitamin C on the bodily pain of MS patients.

Parameter (Bodily pain) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	2.8 ± 0.81	3.1 ± 0.96
Second Visit	2.9 ± 0.78	2.2 ± 0.86 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 8– B showed that the number of patients who suffered pain after administration of vitamin C was much better or somewhat better in the second visit, compared to the first visit; the number of patients in the control group did not show any changes in suffering bodily pain in the second visit, compared to the first visit

Table 8-B: The number of cases of bodily pain in the first visit and the second visit.

Parameter (Bodily (pain	Visit	1-none	2-Very mild	3-mild	4-moderate	5-sever	6-very sever
Patients (Control)	First visit	1	5	10	4	0	0
	Second visit	1	4	11	4	0	0
Vitamin C	First visit	1	5	12	1	3	0
	Second visit	2	16	2	1	1	0

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Results showed a significant decrease in pain interfering with patients' normal work who were administered vitamin C on the second visit compared to the first visit (P = 0.052); while the pain interfered with patients' normal work was not changed in the second visit compared to the first visit in the control group (P = 1) compared to the first visit (Table 9-A, and 9-B).

Table 9-A: The effect of vitamin C on the pain interferes with normal work of MS patients.

Parameter (pain interferes with normal work) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	3.2 ± 1.32	3.4 ± 1.14
Second Visit	3.2 ± 1.32	2.7 ± 1.03 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 9– B shows that the number of patients administered vitamin C had a better feeling in pain interference with the patient's normal work on the second visit compared to the first visit. The number of patients in the control group did not show any changes in the pain interfering with the patient's normal work between the first visit and the second visit.

Table 9-B: The number of patient cases who suffered pain that interfered with normal work in the first visit and second visit.

Parameter (Pain interferes with normal work)	Visit	1-not at all	2-a little bit	3-moderately	4-quite a bit	5-extremely
Patients (Control)	First visit	2	4	7	2	5
	Second visit	2	4	7	2	5
Vitamin C	First visit	1	2	11	3	5
	Second visit	2	8	7	4	1

How much of the time during the past 4 weeks have you felt so down in the dumps that nothing could cheer you up?

Results showed no change in feeling so down in patients administered vitamin C in the second visit compared to the first visit (P = 0.227); also, the feeling so down in the dumps was not changed in the control group (P = 0.772) compared the second visit to the first visit (Table 10-A and 10-B).

Table 10-A: The effect of vitamin C on the felt so down by MS patients.

Parameter (Felt so down)	*Patients (Control) (mean ± SE)*	*Patients were administered vitamin C*
First Visit	3.1 ± 1.53	3.3 ± 1.72
Second Visit	3.3 ± 1.72	3.9 ± 1.73

Table 10– B showed that the number of patients administered vitamin C was slightly better in feeling down on the second visit compared to the first visit, although it was insignificant. The number of patients in the control group did not show any changes in feeling down in the dumps on the second visit compared to the first visit.

Table 10-B: The number of cases of patients who felt so down on the first visit and the second visit.

Parameter (Felt so down)	Visit	1-all of time	2-most of the time	3-good bit the time	4-some of time	5- a little time	6-none of the time
Patients (Control)	First visit	3	6	1	6	3	1
	Second visit	3	6	1	5	2	3
Vitamin C	First visit	3	7	2	5	2	4
	Second visit	3	2	3	4	5	5

How much of the time during the past 4 weeks have you felt calm and peaceful?

Patients administered vitamin C showed an insignificant increase in feeling calm and peaceful in the second visit compared to the first visit ($P = 0.065$); also, the feeling of calm and peaceful was not changed in the control group in the second visit compared to the first visit ($P = 0.772$) (Table 11-A and 11-B).

Table 11-A: The effect of vitamin C on feeling calm and peaceful in MS patients.

Parameter (Felt calm and peaceful) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	3.3 ± 1.18	3.0 ± 1.21
Second Visit	3.4 ± 1.23	2.3 ± 0.95

Table 11– B showed that the number of patients administered vitamin C was slightly better in feeling calm and peaceful, insignificantly, in the second visit compared to the first visit. The number of patients in the control group did not show any changes in the feeling of calm and peace in the second visit compared to the first visit.

Table 11-B: The number of patient cases who felt calm and peaceful in the first and second visits.

Parameter (Felt calm and peaceful)	Visit	1-all of the time	2-most of the time	3-some of the time	4-a little time	5-none of time
Patients (Control)	First visit	1	4	6	5	4
	Second visit	1	6	5	4	4
Vitamin C	First visit	3	4	11	0	4
	Second visit	3	11	6	1	1

How much of the time during the past 4 weeks did you have a lot of energy?

The results of having a lot of energy showed a significant decrease in patients administered vitamin C ($P = 0.005$) in the second visit compared to the first visit, this means that the patients are having a lot of energy during the past 4 weeks; while the patients in the control group did not have a lot of energy and was not changed in the second visit compared to the first visit ($P= 0.873$) (Table 12-A and 12-B).

Table 12-A: The effect of vitamin C on the amount of energy of MS patients.

Parameter (Having (a lot of energy (mean ± SE)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	0.99 ± 3.0	0.97 ± 3.0
Second Visit	0.97 ± 3.0	* 0.56 ± 2.3

*, Significantly different from the first visit at $P \leq 0.05$

Table 12– B shows that the number of patients administered vitamin C was better in the second visit compared to the first visit in having a lot of energy; the number of patients in the control group did not feel of having a lot of energy in the second visit compared to the first visit.

Table 12-B: The number of patient cases of having a lot of energy after the first and second visits

Parameter (Having a lot of energy)	Visit	1-all of the time	2-most of the time	3-some of the time	4-a little time	5-none of the time
Patients (Control)	First visit	0	6	10	1	3
	Second visit	0	6	11	0	3
Vitamin C	First visit	2	3	10	7	0
	Second visit	1	13	8	0	0

How much of the time during the past 4 weeks did you feel worn out?

Results of feeling worn out by patients showed no changes in patients administered vitamin C (P = 0.288), or in the control group of patients (P = 0.905) in the second visit compared to the first visit (Table 13-A and 13-B).

Table 13-A: The effect of vitamin C on feeling worn out in MS patients

Parameter (Feel worn out) (Mean ± SE)	*Patients (Control)*	*Patients received vitamin C*
First Visit	2.9 ± 1.33	2.7 ± 1.41
Second Visit	2.8 ± 1.30	3.2 ± 1.11

Table 13–B showed that the number of patients feeling worn out who were administered vitamin C was slightly insignificantly better in the second visit compared to the first visit; the number of patients in the control group did not show any changes in feeling worn out in the second visit compared to the first visit.

Table 13-B: The number of cases of feeling worn out in the first visit and second visits.

Parameter (Feel worn out)	Visit	1-all of the time	2-most of the time	3-some of the time	4-a little time	5-none of time
Patients (Control)	First visit	4	3	7	3	3
	Second visit	4	3	8	2	3
Vitamin C	First visit	6	3	6	5	2
	Second visit	2	3	7	8	2

How much of the time during the past 4 weeks have you been a happy person?

Results showed an insignificant decrease in patients administered vitamin C (P = 0.063) in the second visit compared to the first visit. This means that patients feel happy compared to the first visit; while the patients' feeling in the second visit was not changed in the control group (P = 1) compared to the first visit (Table 14-A and 14-B).

Table 14-A: The effect of vitamin C on the feeling of MS patients.

Parameter (Feel happy person) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	3.5 ± 0.88	3.4 ± 0.99
Second Visit	3.5 ± 0.88	2.8 ± 0.99

Table 14– B shows that the number of patients administered vitamin C was feeling happy persons somewhat better on the second visit compared to the first visit. The number of patients in the control group did not show any changes in the feeling in the second visit compared to the first visit.

Table 14-B: The number of cases of feeling happy in the first visit and second visit.

Parameter (Feel happy person)	Visit	1-all of time	2-most of time	3-some of time	4-a little time	5-none of time
Patients (Control)	First visit	0	2	8	7	3
	Second visit	0	2	8	7	3
Vitamin C	First visit	0	4	8	7	3
	Second visit	0	10	7	3	2

How much of the time during the past 4 weeks did you feel tired?

Results of feeling tired show an insignificant slight decrease in patients administered vitamin C (P = 0.130) in the second visit compared to the first visit; while the patients feeling tired were not changed in the control group (P = 1) in the second visit compared to the first visit (Table 15– A and 15-B).

Table 15-A: The effect of vitamin C on the feeling tired in MS patients.

(Parameter (Feel tired (.Mean ± S.E)	Patients (Control)	Patients were administered vitamin C
First Visit	1.14 ± 2.5	1.10 2.4±
Second Visit	1.14 ± 2.5	1.04 ± 2.9

Table 15– B showed the number of patients receiving vitamin C feeling less tired in the second visit compared to the first visit, whereas patients in the control group did not show any changes in feeling tired in the second visit compared to the first visit.

Table 15-B: The number of cases of feeling tired in the first visit and second visit.

Parameter (Feel tired)	Visit	1-all of the time	2-most of time	3-some of time	4-a little time	5-none of time
Patients (Control)	First visit	6	2	8	4	0
	Second visit	6	2	8	4	0
Vitamin C	First visit	6	4	8	4	0
	Second visit	2	6	5	9	0

During the past 4 weeks, how much of the time have your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

Results of social activity by patients showed no change in patients administered vitamin C ($P = 0.205$) in the second visit compared to the first visit; even the patients' social activity was not changed in the control group ($P = 1$) in the second visit compared to the first visit (Table 16– A and 16-B).

Table 16-A: The effect of vitamin C on social activity of MS patients.

Parameter (social (activity (.Mean ± S.E)	Patients (Control)	Patients were administered vitamin C
First Visit	1.37 ± 2.2	1.65 2.7±
Second Visit	1.37 ± 2.2	1.32 ± 3.3

Table 16– B showed that the number of patients administered vitamin C was slightly better in the second visit compared to the first visit in social activity, insignificantly. The number of patients in the control group did not show any changes in social activity in the second visit compared to the first visit.

Table 16-B: The number of cases of patients social activity in the first visit and second visit.

Parameter (Social activity)	Visit	1-all of time	2-most of time	3-some of time	4-a little time	5-non of time
Patients (Control)	First visit	9	3	3	4	1
	Second visit	9	3	3	4	1
Vitamin C	First visit	9	2	2	4	5
	Second visit	2	5	4	6	5

How TRUE or FALSE is the following statement for you: I am as healthy as anybody I know?

Results of the patients' health, as others were not changed, were compared in patients administered vitamin C ($P = 0.288$) in the second visit compared to the first visit; also, the patients' health compared with others was not changed in the second visit in the control group ($P = 1$) compared to the first visit (Table 17– A and 17-B).

Table 17-A: The effect of vitamin C on health compared with other MS patients.

Parameter (Health compared with others) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	3.2 ± 0.91	3.3 ± 0.93
Second Visit	3.2 ± 0.91	3.0 ± 0.89

Table 17– B shows that the number of patients administered vitamin C was slightly better in the second visit compared to the first visit in health. The number of patients in the control group did not show any changes in health in the second visit compared to the first visit.

Table 17-B: The number of patient cases who feel as healthy as anybody

Parameter (Health compared with others)	Visit	1-definitely true	2-mostly true	3-mostly false	4-definitely false
Patients (Control)	First visit	0	6	3	11
	Second visit	0	6	3	11
Vitamin C	First visit	1	3	6	12
	Second visit	1	5	8	8

How much of the time during the past 4 weeks were you discouraged by your health problems?

Results of feeling discouraged by health problems show an insignificant, slightly better change in patients who received vitamin C (P = 0.118) in the second visit compared to the first visit; even patients feeling discouraged by health problems were not changed in the control group (P = 1) in the second visit compared to the first visit (Table 18-A and 18-B).

Table 18-A: The effect of vitamin C on the feel discourage by The health problem of MS patients.

Parameter (Discourage by health problem) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	2.4 ± 1.50	2.8± 1.59
Second Visit	2.4 ± 1.50	3.4 ± 1.40

Table 18– B showed that the number of patients who felt discouraged by health problems who were administered vitamin C was slightly better on the second visit compared to the first visit; while the number of patients in the control group did not show any changes in feeling discouraged by health problems in the second visit compared to the first visit.

Table 18-B: *The number of patient cases who feel discouraged by health problems*

Parameter (Feel discouraged by health problems)	Visit	1-all of time	2-most of the time	3-good bit the time	4-some of the time	5- a little time	6-none of the time
Patients (Control)	First visit	8	3	4	2	3	0
	Second visit	8	3	4	2	3	0
Vitamin C	First visit	8	3	3	5	2	1
	Second visit	2	5	3	7	4	1

How much of the time during the past 4 weeks were you frustrated and depressed about your health?

Results showed a somewhat significant decrease in feeling frustrated by health in patients administered vitamin C (P = 0.053) in the second visit compared to the first visit; while the patients' feeling frustrated by health was not changed in the control group (P = 1) in the second visit compared to the first visit (Table 19-A and 19-B).

Table 19-A: The effect of vitamin C on the feeling of frustration in MS patients.

Parameter (Feel frustrated by health) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	3.3 ± 1.56	2.9 ± 1.37
Second Visit	3.3 ± 1.56	3.7 ± 1.31 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 19– B shows that the number of patients who felt frustrated by their health who administered vitamin C was much better on the second visit compared to the first visit, while the number of patients in the control group did not show any changes in the feeling frustrated by health compared to the first visit.

Table 19-B: The number of patient cases feel frustrated by health on the first and second visit.

Parameter (Feel frustrated)	Visit	1-all of the time	2-most of the time	3-good bit the time	4-some of the time	5- a little time	6-none of the time
Patients (Control)	First visit	4	2	3	6	4	1
	Second visit	4	2	3	6	4	1
Vitamin C	First visit	3	7	2	6	3	1
	Second visit	0	6	3	5	7	1

How much of the time during the past 4 weeks did you feel weighed down by your health problems?

Results of feeling weighed down by health problems show no change in patients administered vitamin C (P = 0.345), also in the control group (P = 1), in the second visit compared to the first visit (Table 20-A and 20-B).

Table 20-A: The effect of vitamin C on feeling weighed by the health problems of MS patients.

Parameter (feel weighed by health problem) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	2.5 ± 1.10	2.6 ± 1.27
Second Visit	2.5 ± 1.10	2.9 ± 1.13

Table 20– B showed the number of patients feeling weighed down by health problems who were administered

vitamin C. Also, the patients of the control groups did not show any change in the second visit compared to the first visit.

Table 20-B: The number of patient cases who feel weighed down by health problems of two groups of patients.

Parameter (Feel weighed down)	Visit	1-all of time	2-most of time	3-some of time	4-a little time	5-none of time
Patients (Control)	First visit	3	9	4	3	1
	Second visit	3	9	4	3	1
Vitamin C	First visit	4	9	4	3	2
	Second visit	3	3	4	10	2

How much of the time during the past 4 weeks have you had difficulty concentrating and thinking?

Results of the difficulty in concentrating and thinking show no change in patients administered vitamin C (P = 0.232), also in the control group (P = 1), in the second visit compared to the first visit (Table 21-A and 21-B).

Table 21-A: The effect of vitamin C on the difficulty concentrating and thinking of MS patients.

Parameter (difficulty concentrating and thinking) (Mean ± S.E.)	*Patients (Control)*	*Patients were administered vitamin C*
First Visit	3.3 ± 1.45	2.6 ± 1.39
Second Visit	3.3 ± 1.45	3.0 ± 1.23

Table 21– B shows the number of patients who have difficulty concentrating and thinking who received vitamin C compared to the control group. Both treatments did not show any changes in the second visit compared to the first visit.

Table 21-B: The number of patient cases with difficulty concentrating and thinking in two groups of patients.

Parameter (Difficulty concentrating and thinking)	Visit	1-all of time	2-most of the time	3-some of the time	4-a little time	5-none of the time
Patients (Control)	First visit	4	1	5	5	5
	Second visit	4	1	5	5	5
Vitamin C	First visit	8	1	7	3	3
	Second visit	2	6	5	6	3

How much of the time during the past 4 weeks did you have trouble keeping your attention on an activity for long?

Results of having trouble keeping attention on an activity for long show insignificant slightly decrease in patients received vitamin C (P = 0.267) in the second visit compared to the first visit; In the control group of patients, trouble keeping attention on an activity for long was not changed in the control group (P = 1) in the second visit compared to the first visit (Table 22-A and 22-B).

Table 22-A: The effect of vitamin C on having trouble keeping attention on activity for long of MS patients.

Parameter (Have trouble keeping attention) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	2.6 ± 1.39	2.7 ± 1.66
Second Visit	2.6 ± 1.39	3.2 ± 1.57

Table 22– B shows the number of patients who have trouble keeping attention on an activity for long, who were administered vitamin C, slightly better results in the second visit compared to the first visit. The number of patients in the control group did not show any changes in having trouble keeping attention on an activity for long in the second visit, compared to the first visit.

Table 22-B: The number of patient cases having trouble keeping attention on an activity for long.

Parameter (Trouble keeping attention)	Visit	1-all of time	2-most of the time	3-good bit the time	4-some of the time	5- a little time	6-none of time
Patients (Control)	First visit	6	5	1	7	1	0
	Second visit	6	5	1	7	1	0
Vitamin C	First visit	7	6	1	4	3	1
	Second visit	2	9	1	3	6	1

How much of the time during the past 4 weeks have you had trouble with your memory?

Results showed that trouble with memory was not changed when patients received vitamin C (P = 0.345) in the second visit compared to the first visit; also, patients in the control group (P = 1) did not show any change in trouble with memory compared to the first visit (Table 23-A and 23-B).

Table 23-A: The effect of vitamin C on having trouble with memory in MS patients.

Parameter (have trouble with memory) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	2.8 ± 1.47	2.8 ± 1.60
Second Visit	2.8 ± 1.47	3.2 ± 1.57

Table 23– B showed the number of patients having trouble with memory in patients in the control group or vitamin C did not show any changes in having trouble with memory in the second visit compared to the first visit.

Table 23-B: The number of patient's cases having trouble in memory

Parameter (Have trouble with memory)	Visit	1-all of time	2-most of time	3-some of time	4-a little time	5-none of time
Patients (Control)	First visit	6	2	5	4	3
	Second visit	6	2	5	4	3
Vitamin C	First visit	6	5	3	2	1
	Second visit	2	4	7	3	6

During the past 4 weeks, how much of a problem was the lack of sexual interest?

Lack of sexual interest was not changed in patients administered vitamin C (P = 0.345) in the second visit compared to the first visit; also, patients' lack of sexual interest was not changed in the control group (P = 1) in the second visit compared to the first visit (Table 24-A and 24-B).

Table 24-A: The effect of vitamin C on the lack of sexual activity of MS patients

Parameter (lack of sexual interest) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	1.6 ± 1.04	1.4 ± 0.88
Second Visit	1.6 ± 1.04	1.5 ± 0.96

Table 24– B showed that the number of patients who lack sexual interest who were administered vitamin C had no change in the second visit compared to the first visit; also, the number of patients in the control group, in the second visit, did not show any changes in the lack of sexual interest compared to the first visit.

Table 24-B: The number of patient cases with a lack of sexual interest

Parameter (Lack of sexual activity)	Visit	1-not a problem	2- a little problem	3-somewhat of a problem	4-very much problem
Patients (Control)	First visit	13	3	2	2
	Second visit	13	3	2	2
Vitamin C	First visit	17	1	2	2
	Second visit	17	1	4	0

During the past 4 weeks, how much did pain interfere with your enjoyment of life?

Results showed that patients who received vitamin C enjoyed life much better (P = 0.020) on the second visit compared to the first visit; also, patients' enjoyment of life was not changed in the control group (P = 0.798) in the second visit compared to the first visit (Table 25-A and 25-B).

Table 25-A: The effect of vitamin C on the enjoyment of life of MS patients.

Parameter (Enjoyment of life) (Mean ± S.E.)	Patients (Control)	Patients were administered vitamin C
First Visit	3.2 ± 1.19	3.7 ± 1.35
Second Visit	3.1 ± 1.25	2.8 ± 0.99 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 25– B showed that the number of patients administered vitamin C was much better in the second visit compared to the first visit; while the number of patients in the control group did not show any changes in the enjoyment of life in the second visit compared to the first visit.

Table 25-B: Number of patient cases enjoying life.

Parameter (Enjoyment of life)	Visit	1-not at all	2- slightly	3-moderately	4-quite a bit	5-extremely
Patients (Control)	First visit	3	0	10	4	3
	Second visit	1	1	11	4	3
Vitamin C	First visit	1	2	11	3	4
	Second visit	1	6	10	2	3

Overall, how would you rate your own quality of life?

Results show the quality of life was improved in patients administered vitamin C (P = 0.018) in the second visit compared to the first visit; while the quality of life, in the second visit, was not improved in patients of the control group (P = 0.318), compared to the first visit (Table 26-A and 26-B).

Table 26-A*:* The effect of vitamin C on the quality of life of MS patients**.**

Parameter (Rate quality of life) (Mean ± S.E.)	Patients (Control)	Patients administered vitamin C
First Visit	4.9 ± 1.23	5.7± 1.46
Second Visit	5.3 ± 1.26	6.8 ± 1.25 *

*, Significantly different from the first visit at $P \leq 0.05$

Table 26– B showed that the number of patients administered vitamin C was much better in the second visit compared to the first visit. The number of patients in the control group did not show any changes in the rate of quality of life compared to the first visit.

Table 26-B: The number of patient cases with the rate of quality of life

(Parameter (Rate quality of life	Visit	1 (The worst quality of life)	2	3	4	5	6	7	8	9	(The best quality of life) 10
Patients (Control)	First visit	0	1	2	2	8	6	1	0	0	0
	Second visit	0	0	3	0	8	5	4	0	0	0
Vitamin C	First visit	0	0	3	0	6	7	2	4	0	0
	Second visit	0	0	0	1	2	5	8	4	2	0

DISCUSSION

Most Patients with MS suffer from vitamin C deficiency. Administration of vitamin C improves a patient's general health, reduces bodily pain, reduces pain interference with normal work, increases the feeling of energy, decreases feelings of frustration and depression, and increases enjoyment of life and quality of life.

Patients with MS suffer from vitamin C deficiency. Multiple sclerosis is a chronic inflammatory disease of the CNS associated with demyelination, neurodegeneration, and increased oxidative stress.[7] High levels of oxidative stress are associated with inflammation and play an important role in the pathogenesis of multiple sclerosis.[8] Vitamin C, as an antioxidant, is considered to be an important neuroprotective agent.[16] The blood of MS patients shows signs of significant oxidative stress manifested by low levels of some of the antioxidants.[17] There is significant evidence that the pathogenesis of several neurological diseases, including MS, may involve the generation of reactive oxygen species (ROS) and/or reactive nitrogen species (RNS) associated with mitochondrial dysfunction.[18] Vitamin C, as an antioxidant, has a protective role in neurons (inhibition of apoptosis) and is involved in nerve regeneration.[19,20] Oligodendrocytes, a type of glial cells that produce the myelin sheath, are susceptible to oxidative stress due to lower levels of antioxidant enzymes and free radical scavengers, and high levels of polyunsaturated fatty acids and iron. Oxidative stress could also inhibit the expression of myelin genes in human primary oligodendrocytes through H_2O_2.[21]

Vitamin C has a role in the synthesis of collagen, which is essential for the formation of myelin in Schwann cells, and that have raised the hypothesis that this compound could be useful for the prevention and/or treatment of multiple sclerosis.[14] Vitamin C in this study showed improvement of some symptoms of MS.

The serum levels of Vitamin C were evaluated in 24 patients with multiple sclerosis and 24 healthy sex□ and age□matched individuals as controls. It was observed that the levels of Vitamin C were decreased in the serum of patients with multiple sclerosis during an attack, an effect associated with increased oxidative burden, as reflected by increased lipid peroxidation product.[22]

Administration of vitamin C by MS patients increases general health, where there is significantly better general health on the second visit compared to the first visit in the vitamin C-administered group. Vitamin C is one of the important and essential vitamins for human health; it is needed for many physiological functions in human biology and is essential for collagen, carnitine, and neurotransmitter biosynthesis. Many health benefits have been attributed to vitamin C, such as antioxidant, anti-atherogenic, anti-carcinogenic, and immunomodulator effects.[23]

Vitamin C plays an important role in the maintenance of collagen, which represents about one-third of the total body protein. It constitutes the principal protein of skin, bones, teeth, cartilage, tendons, blood vessels, heart valves, intervertebral discs, cornea, and eye lens; also, it participates in the synthesis of myelin sheath in the central and peripheral nervous system. An increase in collagen synthesis due to vitamin C would increase membrane mechanical integrity and cohesion.[24] Vitamin C enhances the immune system by elevating the production

of infection-fighting white blood cells and endogenous interferon levels.[25] The interferon family of cytokines is secreted by many immune and non-immune cell types, including macrophages, lymphocytes, fibroblasts, and endothelial cells.[26]

Administration of vitamin C by MS patients decreases the bodily pain feeling, and less pain interferes with normal work. Recent epidemiological evidence has indicated an association between suboptimal vitamin C status and spinal pain. Furthermore, accumulating evidence indicates that vitamin C administration can exhibit analgesic properties in some clinical conditions.[27,28] Several recent clinical studies have shown that vitamin C administration to patients with chronic regional pain syndrome decreases their symptoms.[29,30] Several mechanisms have been proposed for vitamin C's analgesic properties through a novel analgesic mechanism for vitamin C; as a cofactor for the biosynthesis of amidated opioid peptide; it is well established that vitamin C participates in the amidation of peptides, through acting as a cofactor for peptidyl-glycine α-amidating monooxygenase, the only enzyme known to amidate the carboxy-terminal residue of neuropeptides and peptide hormones.[31]

The impact of vitamin C on pain relief is explained by various mechanisms. First, vitamin C has anti-inflammatory effects by stimulating cAMP production, which in turn elevates the production of steroids in the ACTH. Secondly, vitamin C works to help decrease blood calcium levels and enhance calcium uptake in bone. As a result, bone pain is relieved.[25]

Administration of vitamin C by MS patients increases feelings of energy. Vitamin C is essential for the synthesis of muscle carnitine (β-hydroxy butyric acid); it acts as a co-factor for hydroxylation involved in carnitine synthesis.[24] Carnitine is required for the transport and transfer of fatty acids into mitochondria, where it can be used for energy production.[32] It was discovered that vitamin C also supports the body's energy generation; the mechanism of ergogenic activity of vitamin C is probably due to vitamin C's oxidation-reduction potential, capable of providing necessary electrons to the electron transport system in the mitochondria for increased energy production.[25]

Administration of vitamin C by MS patients decreases the feeling of frustration and depression. Vitamin C has a significant role in modulating neurotransmitter synthesis and release in the brain. The functions of vitamin C in the brain include acting as a cofactor for dopamine beta-hydroxylase in the conversion of dopamine to noradrenaline, involvement in the modulation of both dopaminergic and glutamatergic neurotransmission, and regulation of catecholamine and acetylcholine release from synaptic vesicles.[33] In people with depression, there may be a decrease in the amount of these neurotransmitters available, which can cause symptoms like loss of interest or pleasure in activities, changes in appetite or sleep, and feelings of anxiety.[34] Research has shown that depression is associated with changes in the structure and function of the brain; these changes can lead to a decrease in the activity of certain neurotransmitters, such as serotonin and norepinephrine, which can result in symptoms such as low mood, lack of pleasure, and disturbed sleep.[35] Neurotransmitters in the brain, such as serotonin, norepinephrine, and dopamine, can lead to changes in a person's mood, energy, and overall mental state.[34] These neurotransmitters are monoamines; more specifically, norepinephrine is believed to have a particular effect on anxiety and attention; depression occurs when there is too little norepinephrine in certain brain circuits. Serotonin especially affects obsessions and compulsions, while dopamine is involved in pleasure, motivation, and engagement. Serotonin is thought to be a major neurotransmitter that can even regulate other neurotransmitters.[36,37]

Reduced dopamine levels can contribute to depression in some people. Dopamine creates positive feelings associated with reward or reinforcement that motivate individuals to continue with a task or activity.[38] Dopamine plays an important role in regulating the drive to seek out rewards, as well as the ability to obtain a sense of pleasure. Low dopamine levels may in part explain why many depressed patients or people don't derive the same sense of pleasure from activities or people that they did before becoming depressed.[39,40]

Vitamin C also has antioxidant properties in the brain, limiting the damage caused by ischemia-reperfusion injury and protecting against glutamate excitotoxicity.[14] Many studies have shown that vitamin C deficiency is associated with an increase in depression and cognitive impairment.[33,41]

Administration of vitamin C by MS patients increases the enjoyment of life and also the quality of life. In this study, patients reported significantly better change in MSQOL-29 questionnaire for physical, emotional, and cognitive function after administration of vitamin C. Patients suffered less bodily pain and less pain interfered with normal activity; also, they reported significantly better change in general health, feeling a lot of energy, and reduced frustration after administration of vitamin C. All this consequently leads to improvement in the rate of quality of life and enjoyment of life. In terminal MS patients, the quality of life is as important as the cure. The use of vitamin C is considered a safe and effective therapy to improve the quality of life of multiple sclerosis patients.

CONCLUSION

In conclusion, vitamin C shows improvement in some MS symptoms, where it has a positive impact on general health, pain relief, energy generation, less feeling frustrated, enjoyment of life, and quality of life. The use of vitamin C is considered safe and effective in improving the quality of life of multiple sclerosis patients.

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