



Manuscript ID

ZUMJ-2003-1768 (R1)

DOI

10.21608/zumj.2020.25329.1768

ORIGINAL ARTICLE

Role of Antioxidants (Vitamin E and Vitamin C) Supplementation for Management of Chronic Pelvic Pain Related to Endometriosis

Mahmoud A. Al-Naggar *,Ibtesam Saeed, Ahmed T. Abdelfattah

Department of Obstetrics and Gynecology ,Faculty of Medicine – AL-Azhar University ,Egypt.

***Corresponding author:**

Mahmoud A. Al-Naggar ,
Faculty of medicine AL-
Azhar university ,Egypt.

Email:

drelnaggar24@gmail.com

Submit Date 2020-05-06

Revise Date 2020-05-27

Accept Date 2020-06-19

ABSTRACT

Background: Endometriosis is a common gynecological disorder affecting around 10% of reproductive aged women. Endometriosis is found in 25% to 40% of women with infertility and 40-87% of women with chronic pelvic pain (CPP) have endometriosis. This work aimed to evaluate the role of antioxidants supplementation in the management of CPP related endometriosis.

Methods: A randomized controlled clinical trial was conducted on gynecological outpatient clinic at Al-Hussein Hospital 60 women, aged 19–41 years with body mass index [BMI] between 18- 24.9 Kg/m² with pelvic pain and history of endometriosis and/or infertility. All women were consented to be on trial for 2 months before surgical intervention.

Results: There was non-significant difference between the studied groups as regard age, gravidity, parity, or fertility, anthropometric measures (weight, height, BMI), complaint distribution (Pelvic pain and no subfertility, subfertility and no Pelvic pain, pelvic pain and subfertility, no pelvic pain and no subfertility). Our results showed that there was non-significant difference between the studied groups as regard baseline clinical data, hormonal contraception in past 3 months or reasons for hormonal contraception and months since surgical diagnosis of endometriosis in between the studied groups. Our results showed that there is significant difference between the two studied groups as regard every day pain as 30% in antioxidant group showed decreased pain compared to 0% in placebo group, dysmenorrhea as 26.6% in antioxidant group showed decreased pain compared to 0% in placebo group and dyspareunia as 16.6% in antioxidant group showed decreased pain compared to 0% in placebo group.

Conclusions: Our results showed that there was non-significant difference between the studied groups as regard age, gravidity, parity, or fertility, anthropometric measures.complaint distribution (Pelvic pain and no subfertility, subfertility and no Pelvic pain, pelvic pain and subfertility, no pelvic pain and no subfertility).

Keywords: Antioxidants; Vitamin E and vitamin C supplementation; Management; Chronic pelvic pain; Endometriosis



INTRODUCTION

Endometriosis is a chronic gynecological disease that affects around 10% of women of reproductive age[1]. Endometriosis occurs in 25%–40% of infertile women [2] and 40–87% of individuals with chronic pelvic discomfort are endometriosis[3]. The pathophysiology and speculative role of endometriosis, i.e. abortion and pelvic pain, is not well understood. Sampson's theory shows the retrograde menstruation triggered by the presence of endometrial cells in the peritoneal cavity[4]. The mobilization and activation of mononuclear phagocytes, will result in endometrial cell growth and maintenance, can be a warning[5]. People with endometriosis shown to have an increase of oxidative stress in the

peritoneal cavity[3]. A well-known vitamin E and vitamin C placebo-induced research is being performed in women who have pelvic pain and endometriosis to assess if antioxidant supplementation may enhance symptoms of endometriosis[9,10,12].

Peroxidized lipids and lipoproteins have been documented to be implicated in endometriosis. In fact, pseudo-prostaglandin-like lipid oxidation molecules may be implicated in endometriosis pain[3]. Vitamin E is a lipid-soluble, chain-breaking antioxidant that prevents lipid peroxidation spread via radical vitamin E growth. Adding vitamin C along with vitamin E will enable vitamin C to restore vitamin radicals to the stable form of vitamin E[6]. The dose

administered was selected according to a cardiovascular study[7].This work aimed to evaluate the role of antioxidants supplementation in the management of CPP related endometriosis.

METHODS

Double blinded randomized control trial is performed. Sixty women aged between 19 and 40 years with pelvic discomfort and a diagnosis of endometriosis and/or infertility at Al-Hussein University Hospital were recruited from Gynecology ambulatory clinic at Al-Hussein Hospital. A written informed consent was obtained from all participants, the study was approved by the research ethical committee of Al-Hussein Hospital. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Both women were required to be screened 2 months before surgery. Participants were allocated randomly to two groups: Group A (n=30)-given vitamin E (1200 IU-3 400 mg capsules) and Vitamin C (1000 mg-2 tablet of 500 mg each) or group B (n= 30)-placebo tablets. Both tablets were similar in shape, smell, and taste. The duration of the study was 8 weeks treatment before surgical removal of the endometriosis. No other treatment was administered at least one week before the start of the trial and during the antioxidant’s supplementation. Patient characteristics included in this study are the following the age categories ranged from 19 to 41. Their body mass index (BMI) ranged from 18 to 24.9Kg/m². The patients should be diagnosed with pelvic pain accompanied with endometriosis and or history of infertility. On the contrary, the exclusion criteria were to exclude patients with BMI: > 25 or < 18 Kg / m² in patients aged over 41 years or under < 19 years. Additionally, patients who are exposed to extra antioxidants a week before or during the therapy. Furthermore, patients who are treated with corticosteroids, statins, aspirin, and oral contraceptives as these medications could influence carbohydrate and lipid metabolism. Moreover, patients diagnosed with autoimmune and pregnant female. The visual analog scale was used to evaluate patient’s preoperative quality of life and pain evaluation to evaluate endometriosis associated symptoms including dysmenorrhea, non-menstrual pelvic discomfort, dyspareunia and dyschesia at the

end of eight weeks. Due to an arbitrary degree of "zero, mild, moderate and extreme" discomfort, discomfort was experienced before, after (bi-weekly) and after diagnosis and examination.

Statistical analysis

Analysis of data was done using Statistical Program for Social Science version 20 (SPSS Inc., Chicago, IL, USA). Quantitative variables were described in the form of mean and standard deviation. Qualitative variables were described as number and percent. In order to compare parametric quantitative variables between two groups, Student t test was performed. Qualitative variables were compared using chi-square (X²) test or Fisher’s exact test when frequencies were below five. Pearson correlation coefficients were used to assess the association between two normally distributed variables. When a variable was not normally distributed, Man Whitney test for comparing two non-Parametric variables. Kruskal wallis test for comparing more than two non-Parametric variables. Spearman’s correlation P value < 0.05 is considered significant coefficients were used to assess the association between two variables which are not normally distributed.

RESULTS

Table (1), this table showed that there was non-significant difference between the studied groups as regard gravidity, parity, fertility or BMI.

Table (2), this table showed that there is no significant difference between the studied groups as regard Complaint distribution.

Table (3), this table showed that there is significant difference between the two studied groups as regard every day pain, as 30% in antioxidant group showed decreased pain compared to 0% in placebo group

Table (4), this table showed that there is significant difference between the two studied groups as regard dysmenorrhea, as 26.6% in antioxidant group showed decreased pain compared to 0% in placebo group.

Table (5), this table showed that there is significant difference between the two studied groups as regard dyspareunia, as 16.6 % in antioxidant group showed decreased pain compared to 0% in placebo group.

Table(1): Demographic data in between the studied groups:

Variable	Antioxidant (n=30)	Placebo (n=30)	t-test MW	P value
Age: (Years):				
Mean ± SD	32.5±4.5	31.4±5.2	1.41	0.324
Range	(20-40)	(20-38)		
Gravidity:				

Variable	Antioxidant		Placebo		t-test	P value
Median range	1 (0-3)		1 (0-2)		321.0	0.491
Parity:						
Median Range	1 (0-2)		0 (0-2)		325.0	0.544
Age groups	No.	%	No.	%	χ^2	P value
≤30	20	66.7	19	63.3	0.911	0.923
>30	10	33.3	11	36.7		
Fertility status						
Fertile	13	43.3	15	50.0	0.923	0.891
Infertile	17	56.7	15	50.0		

Table (2): Complaint distribution in between the studied groups:

Variable	Antioxidant (n=30)		Placebo (n=30)		χ^2	P value
	No.	%	No.	%		
Complaint:						
Pelvic pain and no subfertility	10	33.3	11	36.7	1.23	0.564
Subfertility and no Pelvic pain	2	6.7	1	3.3		
Pelvic pain and subfertility	15	50.0	14	46.7		
No pelvic pain, no subfertility	3	10.0	4	13.3		

Table (3): Effect of antioxidant supplementation on “everyday pain”:

Variable	Antioxidant (n=30)		Placebo (n=30)		χ^2	P value
	No.	%	No.	%		
Everyday pain:						
Decreased pain	9	30.0	0	0.0	15.79	0.001 (S)
No change	13	43.3	25	83.3		
Increased pain	3	10.0	0	0.0		
No pain at baseline	5	16.7	5	16.7		

Table (4): Effect of antioxidant supplementation on dysmenorrhea:

Variable	Antioxidant (n=30)		Placebo (n=30)		χ^2	P value
	No.	%	No.	%		
dysmenorrhea:						
Decreased pain	8	26.6	0	0.0	14.1	0.002 (S)
No change	14	46.7	25	83.3		
Increased pain	3	10.0	0	0.0		
No pain at baseline	5	16.7	5	16.7		

Table (5): Effect of antioxidant supplementation on dyspareunia:

Variable	Antioxidant (n=30)		Placebo (n=30)		χ^2	P value
	No.	%	No.	%		
dysmenorrhea:						
Decreased pain	5	16.6	0	0.0	9.52	0.023 (S)
No change	17	56.7	25	83.3		
Increased pain	3	10.0	0	0.0		
No pain at baseline	5	16.7	5	16.7		

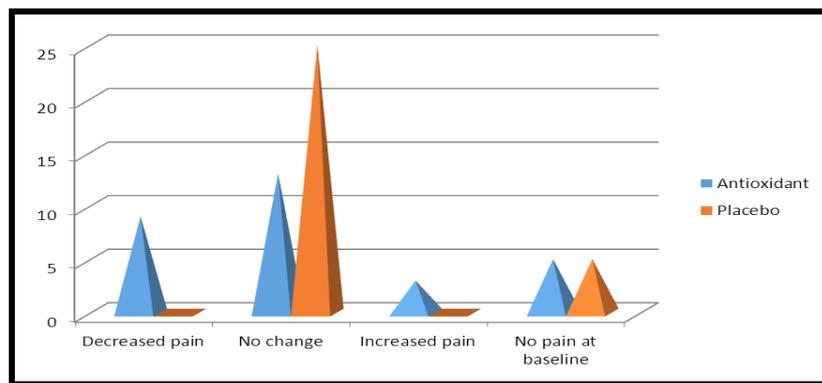


Fig. (1): Effect of antioxidant supplementation on “everyday pain”.

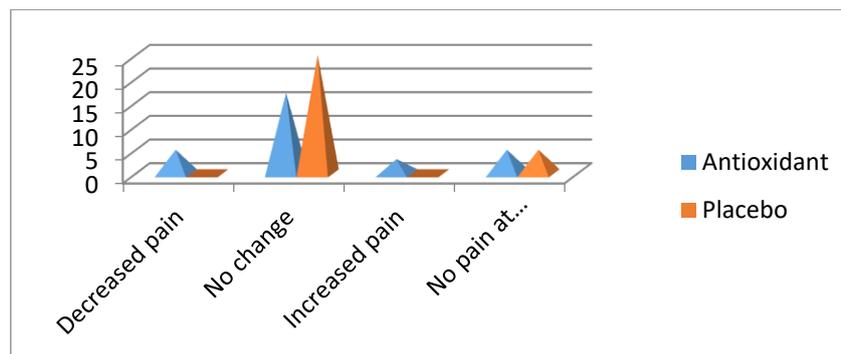


Fig. (2): Effect of antioxidant supplementation on dyspareunia compared to placebo group.

DISCUSSION

Endometriosis is considered one of the conditions that can affect the patients’ quality of life and their fertility. Endometriosis affects 70 million females worldwide [8]. Endometriosis is suggested to be due to oxidative stress in the pelvic area. The aim of this study to evaluate the efficacy of antioxidants administration on the patients’ chronic pelvic pain associated with endometriosis. This was achieved by this double blinded randomized control study. The study findings revealed that the gap among the study groups was insignificant regarding the following characteristics: age, gravity, parity or fertility, BMI, distribution of complaint (pelvic pain and no subfertility; sub-fertile pain and no pelvic pain; pelvic pain and subfertility; no pelvic pain and no subfertility). The tests showed that there was a negligible disparity between clinical average, hormonal contraception over the past three months, or hormonal contraception purposes, and months after the surgical diagnosis of endometriosis between studied classes. This study showed that there is significant difference between the two studied groups as regard to every day pain showed 30% reduction in antioxidant group compared to 0% reduction in placebo group. Dysmenorrhea exhibited 26.6% reduction in antioxidant group compared to 0% reduction in placebo group. Dyspareunia showed 16.6 % reduction in

antioxidant group compared to 0% in placebo group. The advantages of this study include that it is a randomized control study, thus eliminating different types of bias such as selection bias and decrease the effect of confounding factors that could affect the outcomes results which were eliminated by the exclusion criteria. Another study by East-Powell and Reid [9] was conducted on similar patient group characteristics where they administered similar dose of the antioxidants for the same duration. Their results were like this study where there was significant reduction in the chronic pelvic pain. The only limitation of the that study the patient groups were not balanced as the number of the intervention (n=46) and the placebo (n=13) group, unlike this study we had same number of patients in each group. Durak et al. [10] offer some insight. In a rat model, experimentally induces endometriotic cysts were treated with differing doses of vitamin C (0.5mg, 1.25mg, and 2.5mg) to determine if vitamin C supplementation would alter the volume and weights of these lesions. The cysts from group treated with 2.5mg of vitamin C were significantly reduced in weight and volume. Furthermore, Kavtaradze et al. [11] like our study they had significant decrease in the pelvic pain and discomfort. Finally, Santanam et al. [3] Corresponded to this study and it revealed that

the administration in women with endometriosis and peritoneal fluid inflammatory factors of antioxidants decreases persistent pelvic pain. Dysmenorrhea decreased by 37 percent and dyspareunia declined by 24 percent compared to placebo group.

CONCLUSIONS

Pain control is a priority in endometriosis clinical research. This is due to its significant effect on patient's quality of life. This suggested strategy was selected due to the association of the oxidative stress in the potential cavity in patients who are diagnosed with endometriosis. This study showed that there is significant difference between the two studied groups as regard to every day pain showed 30% reduction in antioxidant group compared to 0% reduction in placebo group. Dysmenorrhea exhibited 26.6% reduction in antioxidant group compared to 0% reduction in placebo group. Dyspareunia showed 16.6 % reduction in antioxidant group compared to 0% in placebo group.

Declaration of interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Funding information: None declared

Acknowledgments: I would like to express my sincere gratitude to Dr Sara Rabie for her great support, encouragement, help, kindness, and advice throughout this work. I am deeply grateful to all staff members of AL-HUSSEIN university Hospital for their help.

REFERENCES

1. de Ziegler D, Borghese B, Chapron C. Endometriosis and infertility: pathophysiology and management. *Lancet*, 2010; 376: 730–8.
2. Allaire C. Endometriosis and infertility: a review. *J Reprod Med.*, 2006; 51: 164–8.
3. Santanam N, Kavtaradze N, Murphy A, Dominguez C, Parthasarathy S. Antioxidant supplementation reduces endometriosis related pelvic pain in humans. *Transl Res.*, 2014; 161(3): 189–95.
4. Sampson J. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obstet Gynecol.*, 1927; 14: 422–69.
5. Cao X, Yang D, Song M, Murphy A, Parthasarathy S. The presence of endometrial cells in the peritoneal cavity enhances monocyte recruitment and induces inflammatory cytokines in mice: Implications for endometriosis. *Fertil Steril.*, 2004; 82(3): 999–1007.
6. Altan Z, Denis D, Kagan D, Grund E, Palmer S, Nataraja S. A long-acting tumor necrosis factor alpha-binding protein demonstrates activity in both in vitro and in vivo models of endometriosis. *J Pharmacol Exp Ther.*, 2010; 334: 460–6.
7. Hathcock J, Azzi A, Blumberg J, Bray T, Dickinson A, Frei B. Vitamins E and C are safe across a broad range of intakes. *Am J Clin Nutr.*, 2005; 81: 736–45.
8. Fader AN, Arriba LN, Frasure HE, von Gruenigen VE. Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survivorship. *Gynecol Oncol.*, 2009; 114: 121–7.
9. East-Powell M, Reid R. Antioxidant supplementation may support reduction in pelvic pain in endometriosis. *Adv Integr Med.*, 2019; 6(4): 181–2.
10. Annika S, Sajal G. The role of antioxidant supplementation in endometriosis therapy. *J Gynecol Women's Health*, 2017; 3(1): 555601.
11. Durak Y, Kokcu A, Kefeli M, Bildircin D, Çelik H. Effect of vitamin C on the growth of experimentally induced endometriotic cysts. *J Obstet Gynaecol Res.*, 2019; 39(7): 1253–8.
12. Kavtaradze N, Celia E, John A, Sampath P, Ana A. Vitamin E and C supplementation reduces endometriosis related pelvic pain. *Fertil. Steril.*, 2003; 80(3): 221–2.

To Cite:

Alnaggar, M., abdelfattah, A., Saeed, I. Role of Antioxidants (Vitamin E and Vitamin C) Supplementation for Management of Chronic Pelvic Pain Related to Endometriosis. *Zagazig University Medical Journal*, 2022; (1269-1273): -. doi: 10.21608/zumj.2020.25329.1768