



## Medical synopsis: Antioxidant supplementation may support reduction in pelvic pain in endometriosis



Meredith East-Powell<sup>a</sup>, Rebecca Reid<sup>a,b,\*</sup>

<sup>a</sup>Office of Research, Endeavour College of Natural Health, Fortitude Valley, Queensland, Australia

<sup>b</sup>Australian Research Centre in Complementary and Integrative Medicine, University of Technology Sydney, Ultimo, New South Wales, Australia

### ARTICLE INFO

#### Article history:

Received 3 July 2019

Accepted 28 July 2019

Available online 30 July 2019

#### Keywords:

Endometriosis

Nutritional medicine

Antioxidants

Inflammation

### ABSTRACT

**Design:** Randomised, placebo-controlled trial.

**Participants:** Women included in this trial were aged between 19 and 41 years and were recruited from Emory Clinic and Crawford Long Hospital, affiliated to Emory University School of Medicine in Atlanta, Georgia. The inclusion criteria included women with pelvic pain and a history of endometriosis and/or infertility. A total of 59 women were included in the trial.

**Intervention:** The total of 59 women were randomised into one of the two research arms of group A (n = 46) given vitamin E and vitamin C combinations or group B (n = 13) placebo pills. The interventions involved vitamin E 1200 IU (3 capsules of 400 mg each) and vitamin C 1000 mg (2 tablets of 500 mg each) daily for eight weeks prior to surgery.

**Comparator:** A placebo arm of 13 women with endometriosis and/or infertility.

**Settings:** Emory University School of Medicine, Atlanta, Georgia, United States of America.

**Conclusion:** This trial identified that daily antioxidant supplementation with vitamin E and vitamin C for a period of eight weeks showed significance in reducing peritoneal inflammatory markers, which may be responsible for the development of pain in endometriosis. The trial also demonstrated that combination supplementation of vitamin E and vitamin C lowered chronic pelvic pain in women with endometriosis. The findings indicate that supplementation with nutritional medicines that interact with inflammatory processes may be of benefit to women with endometriosis and may be used in conjunction with other treatment regimens from their health care provider.

© 2019 Published by Elsevier Ltd.

**The synopsis is based on the following article:** Antioxidant supplementation reduces endometriosis-related pelvic pain in humans. Santanam N, Kavtaradze N, Murphy A, et al. Translational research: the journal of laboratory and clinical medicine. 2018 161:189–195. doi:<https://doi.org/10.1016/j.trsl.2012.05.001>.

### 1. Commentary

Endometriosis is an estrogen-dependent chronic inflammatory disease, where endometrial-like tissue is located outside the normal location of the uterus [1]. Endometriosis affects approximately 10% of women of reproductive age and the prevalence of women with endometriosis and pelvic pain is estimated to be 30–45% of the infertile population [1,4]. It is estimated that

40%–87% of women with chronic pelvic pain have endometriosis [4]. Common symptoms of endometriosis include three main types of pain: dysmenorrhea, dyspareunia and chronic pelvic pain [2]. Infertility is another common problem associated with endometriosis, along with urinary and bowel symptoms, and lower back pain [2]. Women with endometriosis also report a range of non-physical symptoms such as depression, feelings of isolation and fatigue [2]. Endometriosis does not only have an adverse effect on physical, mental and social wellbeing but it also impacts health-related quality of life [2].

While the aetiology of endometriosis is not yet fully elucidated, it is believed that genetics, epigenetics and immune dysregulation are involved and more recent studies have implicated oxidative stress in its' development [1]. Oxidative stress is defined as an imbalance between reactive oxygen species (ROS) and antioxidants, causing an inflammatory response in the peritoneal cavity [1]. Erythrocytes, macrophages and apoptotic endometrial cells transplant into the peritoneal cavity via retrograde menstruation and can induce oxidative stress, therefore the production of ROS may be implicated in endometriosis [1]. Cells have developed an

\* Corresponding author at: Office of Research, Endeavour College of Natural Health, Level 2, 269 Wickham Street, Fortitude Valley, Queensland, 4006 Australia.

E-mail addresses: [meredith@qendo.org.au](mailto:meredith@qendo.org.au) (M. East-Powell), [rebecca.reid@endeavour.edu.au](mailto:rebecca.reid@endeavour.edu.au) (R. Reid).

antioxidant system to limit and deactivate ROS production and to repair damage to cells enzymes such superoxide dismutase, glutathione peroxidase and catalase, as well as nutritional medicine compounds including vitamin E and vitamin C may play a role in repair mechanisms [1].

Oxidative stress may occur due to inadequate antioxidant protection or an excess of ROS production, therefore antioxidant interventions may offer an additional treatment for endometriosis [1]. Antioxidant treatment, may refer to the use of clinical nutritional medicines such as vitamin E and vitamin C that show activity in reducing or inhibiting inflammatory markers such as interleukin-1, interleukin-6 and monocyte-chemotactic protein-1 which may be responsible for the release of molecules that induce pain [4]. Vitamin E also exerts an anti-inflammatory effect by inhibiting the release of prostaglandin E2 from arachidonic acid via a reduction in cyclooxygenase activity [5]. Hernández Guerrero et al (2006) identified an inverse association between antioxidant intake and endometriosis pathology and Mier-Cabrera et al (2009) showed an improvement in antioxidant markers in women with endometriosis through the intake of a high antioxidant diet, which involved consuming a variety of vegetables, fruit and seeds that provided a daily intake of 1050 µg of vitamin A, 500 mg of vitamin C and 20 mg of vitamin E [6,7]. Combining antioxidant nutrients such as vitamin E and C with conventional medicine and other complementary treatments, may assist in lowering inflammation and reducing pain in patients with endometriosis.

## 2. Clinical significance

This study demonstrates vitamin E and vitamin C may be effective in reducing peritoneal inflammatory markers and lowering chronic pelvic pain in women with endometriosis. Combining vitamin E and vitamin C in-conjunction with other treatment approaches through standard and complementary care may assist in reducing inflammation and chronic pain in women with endometriosis.

## Author statement

All authors have made contributions to this manuscript. MEP conducted the trial overview and drafted the commentary. RR contributed to the commentary and a critical review of the medical synopsis.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. This manuscript has not received any funding.

## Declaration of Competing Interest

The authors do not have any conflicts of interests to declare.

## References

- [1] G. Scutiero, P. Iannone, G. Bernardi, G. Bonaccorsi, S. Spadaro, C.A. Volta, P. Greco, L. Nappi, Oxidative stress and endometriosis: a systematic review of the literature, *Oxid. Med. Cell. Longev.* 7265238 (2017), doi:<http://dx.doi.org/10.1155/2017/7265238>.
- [2] N. Bourdel, P. Chauvet, V. Billone, G. Douridas, A. Fauconnier, L. Gerbaud, M. Canis, Systematic review of quality of life measures in patients with endometriosis, *PLoS One* 14 (1) (2019)e0208464, doi:<http://dx.doi.org/10.1371/journal.pone.0208464>.
- [4] N. Santanam, N. Kavtaradze, A. Murphy, C. Dominguez, S. Parthasarathy, Antioxidant supplementation reduces endometriosis-related pelvic pain in humans, *Transl. Res.: J. Lab. Clin. Med.* 161 (3) (2012) 189–195, doi:<http://dx.doi.org/10.1155/2013/859619>.
- [5] S. Vilvapriya, S. Vinodhini, Vitamin E in the treatment of primary dysmenorrhoea, *Int. J. Reprod. Contracept. Obstet. Gynecol.* 7 (6) (2018), doi:<http://dx.doi.org/10.18203/2320-1770.ijrcog20182331>.
- [6] C.A. Hernández Guerrero, L. Bujalil, Montenegro, J. de la Jara Díaz, J. Mier Cabrera, P. Bouchán Valencia, Endometriosis and deficient intake of antioxidants molecules related to peripheral and peritoneal oxidative stress, *Ginecol. Obstet. Mex.* 74 (1) (2006) 20–28.
- [7] J. Mier-Cabrera, T. Aburto-Soto, S. Burrola-Méndez, L. Jiménez-Zamudio, M.C. Tolentino, E. Casanueva, C. Hernández-Guerrero, Women with endometriosis improved their peripheral antioxidant markers after the application of a high antioxidant diet, *Reprod. Biol. Endocrinol.* 7 (2009) 54, doi:<http://dx.doi.org/10.1186/1477-7827-7-54>.