Reproductive BioMedicine Online (2013) **26**, 323–336

www.sciencedirect.com
www.rbmonline.com

REVIEW

Diet and endometriosis risk: A literature review

Fabio Parazzini [a], Paola Viganò [b,*], Massimo Candiani [c], Luigi Fedele [a]

[a] *Dipartimento Materno-Infantile, Fondazione IRCCS Ca'Granda, Ospedale Maggiore Policlinico, Università degli Studi of Milano, Italy;* [b] *Obstetrics and Gynecology Unit, San Raffaele Scientific Institute, Milano, Italy;* [c] *University Vita-Salute, San Raffaele Scientific Institute, Milano, Italy*

[*] Corresponding author. *E-mail address:* vigano.paola@hsr.it (P Viganò).

Dr Parazzini Fabio is a clinical scientist of obstetrics and gynaecology at the University of Milan, Italy in the Department of Obstetrics and Gynecology of the 'Luigi Mangiagalli' Institute. His research focuses on the identification of epidemiological determinants in different areas of obstetrics and gynaecology. He is author and co-author of over 500 peer-reviewed scientific articles and has contributed numerous book chapters.

Abstract A connection between dietary factors and endometriosis onset has become a topic of interest mostly due to the observation that physiological and pathological processes of the disease can be influenced by diet. This paper systematically reviews prior publications dealing with this aspect in order to identify potentially modifiable risk factors. Comprehensive searches in the electronic databases MEDLINE, EMBASE and Science Citation Index Expanded were conducted to identify published studies evaluating the association between food intake (nutrients and food groups) and endometriosis. Eleven studies were identified: 10 case–control and one cohort study. Information on diet was collected using food frequency questionnaires in seven studies, while in one study the questionnaire focused on caffeine and alcohol intake. Women with endometriosis seem to consume fewer vegetables and omega-3 polyunsaturated fatty acids and more red meat, coffee and *trans* fats but these findings could not be consistently replicated. Most data have also been discussed herein in light of the available experimental and animal model results. At present, evidence supporting a significant association between diet and endometriosis is equivocal. Further studies are needed to clarify the role of diet on endometriosis risk and progression.

KEYWORDS: coffee, endometriosis, fat, nutrition, vegetables, vitamin

Introduction

Endometriosis is a hormone-dependent, chronic inflammatory gynaecological condition that causes pelvic pain symptoms impacting on the physical, mental and social wellbeing of reproductive-age women (Bianconi et al., 2007). Despite the high prevalence, which has been estimated to be between 6–10% (Parazzini et al., 1994) and the recognized economic burden associated with the disease (Simoens et al., 2012), its aetiology remains elusive. Various pathogenetic factors – menstrual, genetic, environmental, lifestyle – have been claimed to be implicated in the disease establishment and development (Viganò et al., 2004, 2012).

The role of nutrition in determining the establishment and progression of endometriosis has recently become a topic of interest, mostly due to the observation that some

1472-6483/$ - see front matter
http://dx.doi.org/10.1016/j.rbmo.2012.12.011

of the physiological and pathological processes associated with the disease, such as inflammation, oestrogen activity, menstrual cyclicity, organochlorine burden and prostaglandin metabolism, can be influenced by diet (Missmer et al., 2010). The oestrogen dependency of the disease is particularly relevant in this context. In other conditions in which hormones exert a specific role, such as breast (Colditz, 1998; Moorman and Terry, 2004; Chajès et al., 2008; Bravi et al., 2009) and endometrial carcinogenesis (Parazzini et al., 1991; Bidoli et al., 2010), scientific research has demonstrated that diet and fat excess may strongly affect the incidence. Specific habitual dietary patterns appear to have a moderate influence on some inflammatory markers shown to be increased in endometriosis (Galland, 2010). Further, organochlorines — including: (i) polychlorobiphenyls (PCBs), ubiquitary microcontaminants that tend to bioaccumulate in lipid content particularly into meat, liver and dairy products (La Rocca and Mantovani, 2006); and (ii) pesticides/insecticides that can be ingested via consumption of contaminated fruits and vegetables (Grassi et al., 2010) — have been proposed as risk factors for endometriosis since the early 1990s (Gerhard and Runnebaum, 1992). On these bases, the literature on the role of diet on endometriosis risk are herein systematically reviewed, assessing both nutrients and food groups, in order to identify potential modifiable risk factors of the disease.

Materials and methods

The electronic databases MEDLINE (1966 to 2011), EMBASE (1985 to 2011) and Science Citation Index Expanded (1945 to 2011) were searched using the Medical Subject Heading (MeSH) terms 'diet', 'nutrition', 'vitamin', 'fat', 'vegetables', 'coffee', 'caffeine', 'meat', 'fish', 'dairy' or 'fruit' combined with 'endometriosis'. All pertinent reports were retrieved and the relative reference lists were systematically searched in order to identify any potential additional studies that could be included. Only those that were published as full-length articles and in English were considered.

Data were extracted independently by two investigators (FP and PV) who also performed an initial screening of the title and abstract of all articles to exclude citations deemed irrelevant to both observers. If multiple published reports from the same study were available, only the one with the most detailed information was included. Review articles were considered only if original data were also reported. Abstracts of scientific meetings were not included. For each study, the following information was extracted: first author's last name; year of publication; country of origin; number of subjects and cases; design of the study; and category amounts of nutrient intake. Information regarding the potential role of the considered nutrients has been presented according to the mode in which findings were presented in the original papers. Given the paucity of the information reported so far, results deriving from the intake of specific food items have sometimes been described and discussed together with those reporting the main nutrients they contained (i.e. red meat and saturated fats). A pooled estimation was not considered since clinical (study populations), methodological (frequency categorization of exposure) and statistical (adjustment for confounding factors) heterogeneity is present across studies. Therefore, in order to avoid misleading conclusions, the results of this systematic review are presented using a more qualitative approach.

Results

Figure 1 shows the flow diagram of the literature search results. The database search identified 256 abstracts, 17 of which reported findings on dietary factors associated with endometriosis risk; these articles were retrieved for detailed assessment. After searching for further articles in the reference lists, another four papers were found. After the exclusion of ten articles for various reasons (**Figure 1**) a total of 11 studies were identified on the association between dietary components and endometriosis (Grodstein et al., 1993; Berube et al., 1998; Britton et al., 2000; Parazzini et al., 2004; Heilier et al., 2007; Tsuchiya et al., 2007; Matalliotakis et al., 2008; Mier-Cabrera et al., 2009; Missmer et al., 2010; Trabert et al., 2011; Savaris and do Amaral, 2011). Their main methodological characteristics are presented in **Table 1**.

Most studies were case—control studies. One cohort study was identified (Missmer et al., 2010). A total of six studies were conducted in North America (Grodstein et al., 1993; Berube et al., 1998; Britton et al., 2000; Matalliotakis et al., 2008; Missmer et al., 2010; Trabert et al., 2011), two in Europe (Parazzini et al., 2004; Heilier et al., 2007), one in Japan (Tsuchiya et al., 2007), one in Mexico (Mier-Cabrera et al., 2009) and one in Brazil (Savaris and do Amaral, 2011).

Information on diet intake was collected using food frequency questionnaires in seven studies, while in one study the questionnaire focused on caffeine and alcohol intake. Simple 'no' or 'yes' questions were used in one study to evaluate coffee intake (Matalliotakis et al., 2008).

General limits of reviewed papers

Some methodological considerations should be underlined before presenting the results of this review. It should be considered that the identified studies are characterized by marked differences in exposure categorizations, analytic approaches, disease phenotypes, nutrients considered and general methodological design (**Table 1**). All these aspects should be considered in interpreting the inconsistent results deriving from the various studies.

Study design

First of all, the presented results are based on case—control studies. Only one cohort prospective study was identified (Missmer et al., 2010). Retrospective collection of diet items is difficult, particularly in long-lasting diseases. Women with endometriosis usually experience a 6—10-year delay between the onset of symptoms and definitive diagnosis and the disease can be progressive (Bianconi et al., 2007). They might have changed their dietary habits at the symptom onset or their diet might have had an effect on pain experience underlying the disease and requiring a diagnosis.