Arch Gynecol Obstet (2013) 288:961–963
DOI 10.1007/s00404-013-2844-6

LETTER TO THE EDITOR

Are ABO and Rh blood groups new genetic risk factors for endometriosis?

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Received: 25 October 2012 / Accepted: 3 April 2013 / Published online: 18 April 2013

Introduction

Endometriosis is a complex gynecologic disorder with a particular genetic roots and 5–7 % recurrent risk for first-degree relatives of patients and occurs in about 5–10 % of women in reproductive age and up to 50 % of women with infertility. Several studies have revealed that endometriosis arises from an interaction between genetics and environmental factors [1, 2]. Up to now, association between different malignancies with ABO and Rh antigens (which are located on the membrane of human cells especially blood cells) have documented in the literature while explanation for these associations is still unknown although an important hypothesis is that these antigens facilitate cellular mobility in tumors [3].

ABO and Rh genes are located on 9q34 and 1p36 chromosome, respectively, and have been assumed as genetic risk factors for tumor or tumor-like disease. It is worthy to mention that endometriosis shows some malignancy behaviors such as local invasion and genetic changes [4].

An American study of 231 women with endometriosis showed a significant increased risk of endometriosis among individuals with blood group A, while blood group O was less predominant. The overall risk of having blood type A and endometriosis was 2.89 (95 % CI, 1.85–4.52) while a decreased number in blood type O in the patients was reported [5].

In the second case–control study in Turkey, ABO and Rh blood groups distribution of 307 patients—whose endometriosis were confirmed by laparoscopy and pathology—compared with control group. An increased incidence of endometriosis among the patients with Rh^+ in comparison with control group (84 vs. 76 %, respectively; *P* 0.03) was reported, while no significant difference was found for ABO blood types (*P* 0.09) [6].

In the last case–control study in Republic of Korea by Duck-An and Think-You Kim, a significant distribution of blood type A and O in patients with endometriosis was revealed. Although they expected their results in Korea be similar to the Demir's result in Turkey—they are both Asian countries—interestingly, their findings were similar to the American one [7].

Recently, we criticized all above published articles by a letter to editor. We also clarified that these controversial findings may be because of a common mistake in their project design, i.e., the method of control group selection [8].

Motivated by evidence that ABO and Rh distribution in the patients of United States, Turkey and South Korea were controversial, we designed a case–control study in Southern population of Iran (Fars province) with new project design for the first time in an effort for further clarification of how endometriosis and ABO–Rh blood groups might be associated.

Methods

The project was approved by Human Research Committee at the Shiraz University of Medical Sciences. In addition,

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the donor database of Shiraz Blood Transfusion Organization was used as controls. The Blood Bank Organization collects blood mainly in southwestern of Iran and includes all individual's data that have made a blood donation over the past approximately 30 years.

Of 539 eligible patients with endometriosis in the registry, information of 470 was available in the Hospital Service's database for ABO and Rh blood groups. Furthermore, medical records of 470 patients who have been diagnosed as endometriosis by laparoscopy and pathology analysis and have been referred to Zeinab Hospital and Dr. Rostami Infertility Center, Shiraz, Iran were also chosen as cases.

Finally, proportions of ABO and Rh blood types in both cases and controls were compared using Chi square in Medcalc software.

Results

No significant differences were revealed between patients and control groups (ABO blood groups $P > 0.05$, Rh blood type $P > 0.05$, 95 % CI) (Table 1).

Discussion

While previous studies in the American and the South Korea population had shown a significant association between ABO and Rh blood type and risk of endometriosis, our results demonstrated no significant differences between endometriosis patients and control groups [5, 7].

In addition, our population is next to Turkey (an Asian country), and as we expected our results were similar to Demir et al.'s [6] results, even though Rh^+ were high in Turkish patients in comparison with their control.

The most possible reason for variation between our results and other studies is our new project design. In other words, all participants of us were from a defined geographical area, Southern population of Iran, while the origin of control population in other studies differed from the origin of their cases. Considering that every population or country consists of different subpopulations, so that the frequency of ABO and Rh blood groups among these sub groups may show quite a bit discrepancy, therefore the association between main blood types and the risk of endometriosis can vary in different populations [8].

We also challenged preceding results in a letter to editor by demonstrating a common mistake in all, i.e., project design or the selection of control group. Furthermore, we strongly recommended that to determine any possible relationship between main blood types and endometriosis, control group should be selected from the same population, i.e., a specific geographical area, not from the total population. So, a strength of the present study is its design, because case's information was compared with data of Southern population of Iran instead of total population's data [8].

The precise biological explanations for the association of main blood types and a certain disease are unknown, even though a recent Genome Wide Association Study showed that particular SNPs on ABO locus were related with the inflammatory cytokines tumor necrosis factor and intercellular adhesion molecule. A possible explanation is ABO and Rh antigens may have an indirect role in pathogenesis of diseases. Particularly, it is promising that ABO and Rh genes are in linkage disequilibrium with other important genes [3].

In conclusion, facts from different studies verified that the association between endometriosis and main blood groups (ABO and Rh type) is controversial and further investigations in different populations are suggested to make straightforward this controversial area.

Table 1 Distribution of ABO and Rh types among endometriosis and control group (CI = 95 %)

Blood type	Blood donors (control) *n* (%)	Endometriosis patients (case) *n* (%)
A	27.98	25.78
B	24.94	27.07
AB	5.57	4.03
O	41.51	43.12
Rh positive	86.95	84.47
Rh negative	13.05	15.43
Total	100.00	

Conflict of interest None.

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