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Original Article

Serum arylesterase and paraoxonase activities in patients with ovarian tumors

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ABSTRACT

Objective: High levels of toxic reactive oxygen species have been found in many types of cancer cells. Serum arylesterase (ARE) and paraoxonase (PON) are esterase enzymes that have strong antioxidant characteristics. The main purpose of our study was to evaluate the activity of ARE and PON in the sera of patients with ovarian cancer and benign ovarian tumors.

Materials and methods: This study included 30 patients with ovarian cancer, 42 patients with benign ovarian tumors, and 19 healthy age- and sex-matched individuals. ARE and PON activities were measured using spectrophotometry.

Results: Serum ARE activity was significantly different among the three studied groups ($p < 0.0001$). However, posthoc tests revealed that ARE activity was lower in the benign ovarian tumor group (median, 1.53 U/mL; range, 0.43–2.47 U/mL) than in the other groups. There were no differences in ARE activity between patients with ovarian cancer (1.89 U/mL; range, 1.01–2.56 U/mL) and healthy individuals (2.05 U/mL; range, 0.79–2.44 U/mL). We found no differences in PON activity or the PON:ARE activity ratio between the studied groups. Tumor size in the benign ovarian tumor group was positively correlated with ARE activity (R Spearman = 0.46, $p = 0.003$) and negatively correlated with PON activity (R Spearman = −0.50, $p = 0.001$). The ARE and PON activities were not influenced by histological type, ovarian cancer grade, or disease advancement.

Conclusion: ARE activity is higher in patients with ovarian cancer than in patients with benign ovarian tumors; however, the serum activity of ARE is similar between patients with cancer and healthy individuals.

Introduction

Epithelial ovarian cancer is the most lethal gynecologic malignancy and the fifth leading cause of cancer-related death among women in the USA. The lifetime risk of developing ovarian cancer is estimated to be 1.3%, while the 5-year survival rate is approximately 44.6%. The survival rate is strictly related to disease stage at the time of diagnosis. If ovarian cancer is confined to the primary site, the 5-year relative survival is near 92.3%. Unfortunately, only about 15% of ovarian cancer cases are diagnosed before the disease has spread [1]. This is mainly due to the lack of early specific symptoms and screening tests.

Oxidative stress is an imbalance between toxic reactive species [reactive oxygen species (ROS) and reactive nitrogen species (RNS)] and antioxidative defense mechanisms [2], and carcinogenesis is correlated with excessive oxidative stress [3]. Antioxidants and antioxidant enzymes play the main roles in the antioxidative defense mechanism. Arylesterase (ARE) and paraoxonase (PON), different activities of the same enzyme, are serum esterases with strong antioxidant characteristics [4]. Physiologically, PON circulates in the serum in association with high-density lipoprotein and protects low-density lipoproteins against oxidation [5]. Both PON and ARE interact and play a role in the plasma antioxidant system. Disturbances in their activity have been shown to be implicated in several morbidities, especially cerebrovascular diseases [6]. ARE

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and PON activities were recently investigated in cancer patients [7,8].

The main aim of this study was to determine the serum ARE and PON activities in patients diagnosed with ovarian cancer and patients with benign ovarian tumors. Enzyme activities in both groups were compared with the esterase activities of healthy controls. ARE and PON activities were evaluated according to various disease characteristics.

Materials and methods

Serum samples were collected from 72 patients treated in the Division of Gynecological Surgery, Poznan University of Medical Sciences, Poznan, Poland in 2009–2012 and from 19 healthy women. Gynecological and ultrasonographic examinations were conducted 1–3 days prior to surgical treatment during the first 10 days of each participant's menstrual cycle. The studied patients were divided into the following three groups: (1) those with malignant ovarian tumors ($n = 30$); (2) those with benign ovarian tumors ($n = 42$); and (3) healthy women ($n = 19$). The histological types of the tumors analyzed are presented in Table 1. All patients and healthy volunteers were age-matched. Moreover, there were no differences in the patients' body mass index (BMI) and menopausal status. The characteristics of the patients and healthy controls are shown in Table 2.

According to the International Federation of Gynecology and Obstetrics (FIGO) classification, there were five patients with Stage I disease, six patients with Stage II disease, 13 patients with Stage III disease, and six patients with Stage IV disease. The majority of patients (16 women) were diagnosed with histological Grade 3, seven had patients had Grade 2, and six patients had Grade 1 ovarian cancer. Serum samples were obtained within 3 days prior to the operation. PON and ARE activities in the sera were estimated by spectrophotometric method with the use of paraoxon and phenyl acetate as substrates, respectively, according to previously described methods [3,9].

The ARE and PON activities as well as the PON:ARE activity ratios in the patients' sera were compared among the three studied groups. Serum esterase activities were correlated with the histological type of the tumors, tumor volume (estimated using preoperative ultrasonographic examination), patient age, and patient BMI. ARE and PON activities were correlated with the FIGO stage of the disease and tumor histological grade in the group of patients with ovarian cancer.

The study received approval from the local ethics committee.

Results

Serum ARE activities were significantly different among the 3 studied groups ($p < 0.0001$). Median ARE activity assessed in the sera of patients with ovarian cancer was 1.89 U/mL (range, 1.01–2.56 U/mL). For comparison, median ARE activity in the sera of patients with benign ovarian tumors and the healthy controls were 1.53 U/mL (range, 0.43–2.47 U/mL) and 2.05 U/mL (range, 0.79–2.44 U/mL), respectively. *Posthoc* testing revealed statistically significant differences in ARE activities between the ovarian cancer and benign ovarian tumor groups ($p < 0.01$) as well as between the benign ovarian tumor and healthy control groups ($p < 0.001$). However, there were no differences between the malignant ovarian tumor and healthy groups ($p > 0.05$).

There were no differences in PON activity among the studied groups ($p = 0.38$). Median serum PON activity in the ovarian cancer group was 50.31 U/mL (range, 8.4–268.3 U/mL), while the median PON activities in the benign ovarian tumor and healthy control groups were 71.6 U/mL (range, 0–430.1 U/mL) and 77.6 U/mL (range, 15.1–307.7 U/mL), respectively. Similarly, there was no statistically significant difference in the PON:ARE activity ratio among the studied groups ($p = 0.24$). Median PON:ARE activity ratios in the ovarian cancer, benign ovarian tumor, and healthy control groups were 30.1 (range, 3.28–183.5), 55.00 (range, 8.51–1000.2), and 43.53 (range, 6.51–389.49), respectively. The esterase activity measurements are shown in Table 3.

We evaluated the activities of esterases in relation to tumor size within the benign and malignant ovarian tumor groups and found a significant positive correlation between ARE activity and tumor size in the benign ovarian tumor group (R Spearman = 0.46, $p = 0.003$). On the contrary, no correlation was noted between tumor size and ARE activity in the ovarian cancer group (R Spearman = 0.13, $p = 0.324$). There was a statistically significant negative correlation between PON activity and tumor size in the benign ovarian tumor group (R Spearman = −0.50, $p = 0.001$), but there was no correlation between tumor size and PON activity in the ovarian cancer group (R Spearman = 0.132, $p = 0.55$). The PON:ARE ratio was also negatively correlated with tumor size in the benign ovarian tumor group (R Spearman = −0.45, $p = 0.039$) but not correlated with tumor size in the ovarian cancer group (R Spearman = 0.035, $p = 0.87$). We found no differences in ARE and PON activities or PON:ARE ratio according to the histological types of the tumors.

Mean ARE activity in the sera of patients with early stage ovarian cancer (I and II according to FIGO) was 2.02 ± 0.34 U/mL, which was not significantly different from the ARE activity in patients with advanced ovarian cancer stage assessed as III or IV according to FIGO (range, 1.92 ± 0.44 U/mL, $p = 0.63$). Similarly, there were no statistically relevant differences in PON activity among these groups of patients ($p = 0.45$). Median PON activity in early stage ovarian cancer was 76.3 U/mL (range, 25.2–268.3 U/mL), while median PON activity in the sera of patients with advanced stage ovarian cancer was 41.08 U/mL (range, 8.4–219.69 U/mL). The difference in PON:ARE ratio between patients with early stage (median, 32.85; range, 11.45–183.5) and advanced stage (median, 20.99; range, 3.28–155.81) ovarian cancer was not significant ($p = 0.747$).

Moreover, no differences were found between ARE activities, PON activities, and PON:ARE activity ratios according to the histological grade of ovarian cancer ($p = 0.33$, $p = 0.73$, and $p = 0.60$, respectively).

Serum ARE activity was positively correlated with patient age in the benign ovarian tumor group (R Pearson = 0.4, $p = 0.009$). By contrast, there was no correlation between age and ARE activity in the group of patients with ovarian cancer (R Pearson = −0.22, $p = 0.25$). Similarly, there was a negative correlation between PON activity and patient age in the benign ovarian tumor group (R Pearson = −0.34, $p = 0.02$), but there was no correlation in the ovarian cancer group (R Pearson = 0.23, $p = 0.22$). ARE and PON activities were not related to patient BMI in either the ovarian cancer or the benign ovarian tumor group.

Table 1
Histopathological findings among the studied patients.

Benign ovarian tumors (n = 42)	
Endometrioid cysts	14
Serous cystadenoma	8
Mucinous cystadenoma	5
Mature teratoma	5
Other	6
Persistent functional ovarian cysts	4
Ovarian cancers (n = 30)	
Serous adenocarcinoma	13
Mucinous adenocarcinoma	4
Clear cell adenocarcinoma	3
Endometrioid adenocarcinoma	3
Undifferentiated carcinoma	5
Other	2