The effects of abdominal and bimanual pelvic examination and transvaginal ultrasonography on serum CA-125 levels

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Summary

The need for the early detection of ovarian cancer continues to be one of the most important issues in women's health care. The three most extensively evaluated screening methods for ovarian cancer are pelvic examination, transvaginal ultrasonography, and serum CA-125 levels. The answers to questions such as should the levels of CA-125 be measured before bimanual pelvic examination or transvaginal ultrasonography or do abdominal examinations effect the levels of CA-125 are obscure. Fifty-four otherwise healthy female volunteers at the preovulatory phase of the menstrual cycle complaining of vaginal candidiasis were divided into 3 groups. Abdominal (group 1), bimanual pelvic (group 2), and transvaginal ultrasonography (group 3) examination was performed and serum CA-125 levels were evaluated prior to examination and 10 minutes, 6 hours, and 24 hours after the examination. As a result, serum CA-125 levels (U/ml) were found to be 8.13±4.76, 8.23±5.05, 8.32±4.88, and 8.33±4.94 in the group of abdominal examination, respectively, 8.23±4.89, 8.45±5.15, 8.77±4.96, and 8.79±5.50 in the group of bimanual pelvic examination, respectively, and 8.19±4.56, 8.30±5.10, 8.81±5.56, and 8.88±5.71 in the group of transvaginal ultrasonography, respectively.

The serum CA-125 levels detected prior to examinations were statistically insignificant when compared with the results obtained at 10 minutes, 6 hours, and 24 hours later in all three groups. We concluded that physical examination, either abdominal or pelvic, and transvaginal ultrasonography do not change the serum levels of CA-125.

Key words: Frozen shoulder syndrome; Menopause; Kanzo; Shakuyaku.

Introduction

The Cancer Antigen-125 (CA-125) is expressed in amnion and its derivatives of fetal coelomic epithelia such as Müllerian epithelia, peritoneum, pleura and pericardium and in many adult tissues such as the epithelium of the fallopian tubes, endometrium, endocervix, pleura and peritoneum [1]. The normal endometrium produces CA-125 and this production can contribute significantly to the level of circulating CA-125 at the time of menstruation [2, 3]. During peritoneal irritation (hyperstimulation, salphingitis, ruptured ectopic pregnancy, laparotomy), peritoneally derived CA-125 significantly contributes to circulating CA-125 concentrations, giving elevated CA-125 values [4]. The use of the CA-125 serum assay as a single diagnostic tool is restricted by the fact that the antigen CA-125 is produced by normal epithelia of the peritoneum, endometrium and benign ovarian cysts and not only by the ovarian cancer cell [5]. It is now widely accepted that CA-125 is a very good marker for the monitoring of ovarian cancer, but like all other cancer markers it has restricted diagnostic value. Serum CA-125 levels have been reported to be elevated after diagnostic applications such as laparoscopy or laparotomy [6]. However, the effects of abdominal and pelvic examinations and transvaginal ultrasonography on serum CA-125 levels have not been reported in the literature. Because physical examination and transvaginal ultrasonography are generally done before obtaining serum CA-125 levels, it is not known whether peritoneal irritation affects serum CA-125 levels or not. Therefore we investigated the effects of these circumstances on serum CA-125 levels in healthy subjects.

Patients and Methods

Study Participants

Fifty-four otherwise (mean age 36.53±14.20 years) healthy female volunteers at the preovulatory phase of the menstrual cycle complaining of vaginal candidiasis were divided into 3 groups. Abdominal (group 1), bimanual pelvic (group 2), and transvaginal ultrasonography (group 3) examinations were performed and serum CA-125 levels were evaluated prior to examination and 10 minutes, 6 hours, and 24 hours after the examination. Physical examinations and transvaginal ultrasonography were done by the same gynecologist.

CA-125 Measurement

CA-125 was determined by Immulite OM-MA, Diagnostic Products Corporation (DPC, Gwynedd, U.K.) which was a solid-phase, chemiluminescent enzyme immunometric assay. It was used with the Immulite, DPC automated analyser.

Statistical Analysis

Statistical analysis was done by SPSS® statistical software. Data are presented as the means-standard deviations. The comparisons were done using the Mann-Whitney U and Kruskal-Wallis tests with $p<0.05$ considered as statistically significant.

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Results

Abdominal (group 1), bimanual pelvic (group 2), and transvaginal ultrasonography (group 3) examinations were performed and serum CA-125 levels (U/ml) were evaluated prior to examination and 10 minutes, 6 hours, and 24 hours after the examination. As a result, serum CA-125 levels were found to be 8.13±4.76, 8.23±5.05, 8.32±4.88, and 8.33±4.94 in the group of abdominal examination, respectively, 8.23±4.89, 8.45±5.15, 8.77±4.96, and 8.79±5.50 in the group of bimanual pelvic examination, respectively, and 8.19±4.56, 8.30±5.10, 8.81±5.56, and 8.88±5.71 in the group of transvaginal ultrasonography, respectively. Serum CA-125 levels prior to examinations were statistically insignificant when compared with the results obtained at 10 minutes, 6 hours, and 24 hours later in the three groups (Table 1).

Table 1. — *Serum CA-125 levels in three groups on four blood samples.*

Groups	Prior to examination (U/ml)	10 minutes after examination (U/ml)	6 hours after examination (U/ml)	24 hours after examination (U/ml)
Abdominal examination	8.13±4.76	8.23±5.05	8.32±4.88	8.33±4.94
Pelvic examination	8.23±4.89	8.45±5.15	8.77±4.96	8.79±5.50
Transvaginal ultrasonography	8.19±4.56	8.30±5.10	8.81±5.56	8.88±5.71

Discussion

In this study, we investigated the effects of abdominal and pelvic examinations and transvaginal ultrasonography on serum CA-125 levels. Because physical examination and transvaginal ultrasonography are generally done before obtaining serum CA-125 levels, it is not known whether peritoneal irritation affects serum CA-125 levels or not.

CA-125 is a sensitive, but not a specific tumour marker especially used in the follow-up of ovarian cancer for monitoring of the efficacy of therapy and for early detection of recurrence but like all other cancer markers it has restricted diagnostic value [6]. Elevated serum CA-125 levels have been demonstrated in a number of benign gynaecologic as well as benign and malignant non-gynaecologic conditions [5]. High serum CA-125 levels may also be encountered in cirrhosis, peritonitis, pancreatitis, endometriosis, uterine leiomyomas, benign ovarian cysts, and in pelvic inflammatory disease other than ovarian tumours [7, 8].

Two of the important sources of CA-125 are epithelium of the ovary and peritoneum [6]. However, there is also a contribution of the pleura, pericardium, cervix, endometrium, fallopian tube, colon, kidneys, and epithelial cells of the stomach [1, 9-11]. The use of the CA-125 serum assay as a single diagnostic tool is restricted by the fact that antigen CA-125 is produced by normal epithelia of the peritoneum, pleura, pericardium, endometrium, and benign ovarian cysts and not only by the ovarian cancer cell. Therefore, measurement of serum CA-125 levels could become a diagnostic marker for the irritation of the coelomic epithelium such as the pericardium, peritoneum or pleura. As peritoneum is one of the tissues that expresses CA-125, peritoneally derived CA-125 significantly contributes to circulating CA-125 concentrations giving elevated serum CA-125 values during peritoneal irritation such as hyperstimulation, salpingitis, ruptured ectopic pregnancy, laparoscopy, and laparotomy. To investigate the extent of CA-125 release by human peritoneal mesothelial cells, Zeimet *et al.* [12] measured CA-125 shedding of human peritoneal mesothelial cells and compared the results by ovarian cancer cell lines and observed five times more CA-125 shedding in human peritoneal mesothelial cells. In another study, interestingly, the surface epithelium of normal fetal and adult ovaries, thought to be derived from coelomic epithelium, did not express CA-125 determinant, except in inclusion cysts, areas of metaplasia, and papillary excrescences [1, 10]. There can be other reasons for elevated CA-125 levels such as overproduction, or a probable defect in elimination or metabolisation of CA-125 in renal failure and chronic liver diseases which are frequently associated with false positivity but the common finding was the presence of serosal fluid either in the pericardium, pleura, or peritoneum [13-16]. Non-malignant ascites was also found to be associated with high serum levels of CA-125, suggesting that the presence of fluid in the peritoneal cavity may stimulate its release. Abnormal levels of CA-125 were detected in 49% of ovarian cancer patients whereas elevated CA-125 levels were found to be higher in 89% of these same patients with ascites. There was pathological CA-125 values in 94% of patients with ascites (mean 566±528 U/ml, $p<0.001$) in 373 patients with various liver diseases [17]. Miladinovic *et al.* [18] found elevated CA-125 values in patients with peritoneal affection (malignant or benign). In a group of studies also designed in our hospital, we found elevated levels of serum CA-125 in patients with nephrotic syndrome and chronic renal failure (unpublished observations) in the presence of ascites.

The effects of abdominal and pelvic examinations and transvaginal ultrasonography on serum CA-125 levels have not been reported in the literature. The relationship between serum CA-125 levels and peritoneal irritation during physical examination was investigated; we found that either abdominal or pelvic examination or transvaginal ultrasonography did not change the levels of CA-125 in the first 24 hours. We conclude that, serum CA-125 levels were not affected by short and indirect mechanical pressure and the serum CA-125 levels detected before or after these examinations in outpatient clinics did not differ statistically.

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