ORIGINAL ARTICLE

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Inhibin as a tumor marker in postmenopausal women with ovarian malignancies

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ABSTRACT

Background: Inhibin is a dimeric glycoprotein that has a depressive effect on the anterior hypophyse secretion. The level of this tumor marker is undetectable in menopause women. In patients with gynecological cancer, especially granulosa and epidermal-type (mucinous), ovarian cancers considerable increase in the serum level of Inhibin has been reported. The increased level of Inhibin has been reported in patients with recurrent ovarian cancer.

Methods: We measured total serum Inhibin and CA125 tumor marker level in 38 postmenopausal women with pathologically confirmed ovarian cancer before and after surgery out of 51 suspected women. Our control group were postmenopausal women that attended to our clinic for routine gynecologic checkup. Both tumor markers were measured in these patients too.

Results: Among 38 women with ovarian cancer, 13(34.2%) had elevated serum levels of total Inhibin. Among the 16 women with serous adenocarcinoma, 3 patients (18.8%) had elevated serum levels of Inhibin. All the three women with granulosa cell tumor had elevated serum levels of Inhibin (100%) and 3 of 4(75%) women with mucinous ovarian cancer had the same result. three out of 38 women in control group had elevated serum levels of Inhibin . Among all 38 patients, 6(15.7%) showed tumor recurrence, that all were concomitant with rising of both serum CA125 and Inhibin levels (p=0/001).

Conclusion: Serum Inhibin level is a useful tumor marker in granulosa cell and in mucinous tumor of ovary. In this study combined Inhibin and CA125 assay showed better results in early detection of ovarian cancer in comparison to either CA125 or Inhibin alone.

Keywords: Inhibin, tumor marker, ovarian cancer.

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Introduction

Inhibin is created in a variety of ovarian cancers. Therefore, its precise measurement and control is beneficial in early diagnosis of ovarian cancers, and also in post-op recurrences. It is particularly important in menopausal women for early diagnosis of ovarian cancer because, in normal circumstances, its postmenopausal level is very low.[1] Women's mortality rates due to epithelial ovarian cancer are higher than in other women's cancers. According to the International Obstetrics and Gynecology Association, the prevalence of epithelial ovarian cancer is reported 15 per 100,000 women. These cancers are more diagnosed in advanced stages, and since the 5-year survival rate of women with ovarian cancer declines with progress of disease (stage I, 90%, stage II, 70%, and stage III 37%), thus, early diagnosis leads to patients' increased survival rate.[2, 3] Currently, the most common diagnostic method is ultrasound and tumor marker CA 125,[4] although other diagnostic tumor markers such as CA 19-9 and CA 15-3 are also occasionally used, sensitivity and specificity of each is different. CA 125 is created in more than 80% of non-mucinous ovarian tumors.[5]

Inhibin is a dimeric glycoprotein, secreted by the gonads and is controlled by pituitary gland pulses.[6] Inhibin is composed of two chains. Chain α is made of 3 regions, and chain β is made of two subunits of A and B, with different molecular weights.[7] Inhibin exists in women with active ovaries, Inhibin A, Inhibin B and their subunits are produced by ovarian follicles and corpus luteum. Therefore, they exist in menstrual cycle and during pregnancy, and have a feedback effect on FSH secretion8. With postmenopausal reduction in ovarian follicles, Inhibin level gradually decreases until it becomes immeasurable.[9, 10] This study aims to use Inhibin in diagnosis of early stages of ovarian cancer.

Methods and Methods

In this cross-sectional, descriptive-analytical study, 38 postmenopausal women with suspected ovarian tumor, hospitalized in women's oncology ward of Vali-e-Asr Hospital, awaiting surgery, from April 2004 to November 2008, were investigated. Control group consisted of 38 postmenopausal women that had attended women's clinic for routine examinations, and had shown no signs of ovarian or other types of cancer in clinical examinations and ultrasound. Mean age of patients and control group was 54 years, with at least two years since the onset of menopause. Samples were examined using ELISA method and Biosource kit (Invitrogen-Germany). Total Inhibin and CA 125 were measured for both groups before surgery, and once for patients that had attended oncology clinic for post-op follow-up examinations.

Statistical data were processed with SPSS-16 software, and $\chi 2$ test was used in comparative analysis at significant level $P<0.05$.

Results

Among 38 women with confirmed pathological malignancies and ovarian cancer, 13 (34.2%) had high levels of total Inhibin. Sixteen (18.8%) patients had pathological serous adenocarcinoma, 3 of whom had elevated total Inhibin. After surgery, 4 patients were found to have mucinous adenocarcinoma, 3 (75%) of whom had elevated total Inhibin. Three out of 38 patients had granulosa tumor, and all 3 (100%) had elevated total Inhibin. Generally, this marker was significantly higher in patients than in control group (P=0.005) (**table 1**). Tumor marker CA 125 was measured in all patients, and serum total Inhibin in patients with granulosa tumor and mucinous carcinoma was significantly higher than other ovarian tumors. Of the total of 38 patients, 6 (15.7%) had recurrent disease, and all had significantly high total Inhibin (15.7%).

Discussion

A study by Robertson in 2002 showed that Inhibin is

Table 1. Frequency distribution of positive Inhibin A and B in malignant and control groups.

Group	Inhibin A, B		Total
	+	-	
Malignant	13 (34.2%)	25 (65.8%)	38 (100%)
Control	3 (7.9%)	35 (92.1%	38 (100%)
Total	16 (21.1%)	60 (78.9%)	76 (100%)

measurable in women with stage I and II mucinous ovarian cancer. It has also been found that serum Inhibin increases in recurrent cases of granulosa cell tumor. Thus it is recommended as a sensitive test that may be useful especially in early stages of diagnosis. This study showed that measuring Inhibin may be useful in patients with suspected early tumor, and also in assessment of recurrence after treatment.[11] Another study by Robertson in 2004 showed that Inhibin is secreted and produced by various ovarian tumors. Measuring its serum levels, using immunoassay, may be an effective diagnostic help in early stages of disease; it can also be effective as a tumor marker in diagnosis of recurrence of tumors after surgery. These markers are particularly useful in postmenopausal women with normally low or even negative levels of Inhibin. Total Inhibin can be measured using ELISA, which is rather helpful in cases of granulosa cell tumors and mucinous tumors.[12]

In a study by Tsigkou in 2008 on total Inhibin , blood samples were collected from postmenopausal women in stages II and III of epithelial ovarian cancer group (89 patients), 25 had benign tumors, 10 had breast cancer, 10 colon, and 10 stomach cancer, and also from 95 women in the control group. In epithelial ovarian cancer group, blood samples were also measured after surgery. In 4 cases with stage IIc mucinous tumor, follow-up blood samples were also measured.[13]

Study results showed that total Inhibin level was significantly higher than benign, non-ovarian, or control group (P<0.001). The 40 patients with serous carcinoma, or 17 with mucinous carcinoma showed the highest levels of total Inhibin (P<0.001). With 95% specificity, total Inhibin confirmed 37 (93%) out of 40 patients with serous tumor, and 16 (94%) out of 17 patients with mucinous tumor. There was a clear reduction in total Inhibin in women with serous and mucinous cancers after surgery (P<0.001). The 4 women followed up by Inhibin, showed increased total Inhibin at recurrence.[13] Serum Inhibin is a sensitive marker for diagnosis and control of patients with granulosa and ovarian mucinous tumors, whose level significantly reduces after surgery. This marker can be useful in diagnosis of recurrent ovarian cancer,[14] especially in the above two cancers.

In this study, of the 38 patients with pathologically confirmed ovarian cancers, 16 were with pathological serous adenocarcinoma, of whom 3 had high levels of A and B Inhibin s (18.8%). Also, in mucinous tumor group, 3 out of 4 patients showed increasing Inhibin s A and B (75%), and in granulose tumors, serum Inhibin B was significantly higher than in any other group (100%).

It was found in this study that association of Inhibin with CA 125, especially in mucinous and granulosa tumors was significantly higher (P=0.005). After surgery, study subjects showed a significant reduction in CA 125 and Inhibin A and B (P=0.001).

In this study, there were 6 cases of recurrent tumor: One granulose tumor, 3 cases of serous adeno-carcinoma, one mucinous adenocarcinoma, and one case of clear cell. In this study a reduction in Inhibin s A and B, and an increase in patients with recurrent tumors were observed after surgery. Inhibin can also be useful in diagnosis of this group (P=0.001).

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