



Value and significance of tumor markers as CEA, CA125, SCC-Ag, CA199 and CYFRA21-1 in the diagnosis of cervical cancer

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ABSTRACT

Objective: To investigate the value and significance of serum CEA, CA125, SCC-Ag, CA199 and CYFRA21-1 in the diagnosis of cervical cancer by comparing the detection of five serum markers. **Methods:** A total of 108 cases were divided into three groups, including 60 cervical cancer patients and 20 cervical intraepithelial neoplasia patients treated in our hospital from September 2015 to September 2016 and 28 healthy women. Radioimmunoassay was used to detect and compare the serum levels of CA125, CA199, CYFRA21-1 and ELISA method was used to detect and compare the serum levels of SCC-Ag, CEA. **Results:** (1) There was no statistically significant difference in the serum CEA, CA125, SCC-Ag, CA199, CYFRA21-1 levels between CIN group and control group. The serums CEA, CA125, SCC-Ag, CA199, CYFRA21-1 levels of cervical cancer patients were significantly higher than the other two groups. The differences were statistically significant. (2) There were statistically significant differences in the serum CEA, CA125, SCC-Ag, CA199, CYFRA21-1 levels between different cervical pathological type groups. The serum CA125, CA199, CEA levels of cervical glandular cancer patients were significantly higher than the other two groups. The differences were statistically significant. The serum SCC-Ag, CYFRA21-1 levels of cervical squamous cancer patients were significantly higher than the other two groups. The differences were statistically significant. **Conclusion:** The serums CEA, CA125, SCC-Ag, CA199, CYFRA21-1 levels of cervical cancer patients were significantly higher than cervical intraepithelial neoplasia patients and healthy women. The serum CA125, CA199, CEA levels of cervical glandular cancer patients were significantly higher and the serum SCC-Ag, CYFRA21-1 levels of cervical squamous cancer patients were significantly higher. The five tumor markers can be used in diagnosis of cervical cancer and they are also worthy in distinguishing cervical pathological types.

1. Introduction

Cervical cancer is one of the most common malignancies in the

female reproductive system, second only to breast cancer[1]. High risk human papillomavirus (HPV) infection is the leading cause of cervical cancer. About 300 thousand women die each year from cervical cancer, and they tend to be younger[2,3]. Because of the location of the lesion is obscure, and there is no obvious clinical symptom in the early stage, most patients are in advanced stage and therefore seriously affect the treatment outcome and prognosis. At present, in addition to the use of cervical biopsy and imaging examination in the diagnosis of cervical cancer, the application of serum tumor marker (TM) examination is also particularly important. Serum tumor markers commonly used in diagnostic

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monitoring include carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), squamous cell carcinoma antibody (SCC-Ag), carbohydrate antigen 199 (CA199), and cytokeratin 21-1 (CYFRA21-1). Therefore, the purpose of this study is to investigate the value and significance of serum CEA, CA125, SCC-Ag, CA199 and CYFRA21-1 in the diagnosis of cervical cancer by comparing the detection of five serum markers.

2. Informations and methods

2.1. General information

A total of 108 patients were divided into three groups according to the type of disease, among them, include 60 cervical cancer patients and 20 cervical intraepithelial neoplasia. Patients treated in our hospital from September 2015 to September 2016 and 28 healthy women. In the cervical cancer group, the average age was (48.15 ± 9.72) years old; Pathological stage: 10 cases were stage I, 19 cases were stage II, 23 cases were stage III, and 5 cases were stage IV; Tissue type: 38 cases of squamous carcinoma, 16 cases of prostate cancer, 6 cases of squamous adenocarcinoma. The average age of CIN group was (50.28 ± 7.46) years old; Statistical methods were used to compare the general data of the three groups, and the difference was not statistically significant ($P>0.05$). The inclusion criteria was as follows: Clinically diagnosed patients with cervical cancer and cervical intraepithelial neoplasia; People with good compliance, informed and signed informed consent to the study; No serious diseases such as heart, liver, kidney and other important organs were found; No combination of other diseases of the uterus may have an impact on the study target.

2.2. Observation indexes^[4]

All of the subjects were fasting for 8 h, 3 mL venous blood was extracted for centrifugal process. Serum levels of CA125 (carbohydrate antigen 125), CA199 (carbohydrate antigen 199) and CYFRA21-1 (cytokeratin 21-1) were detected by radioimmunoassay in three groups of subjects; Serum SCC-Ag (squamous cell carcinoma antibody) and CEA (carcinoembryonic antigen) levels were detected by ELISA (enzyme-linked immunosorbent assay).

Table 1.

Comparison of serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA levels among three groups.

Group	n	CA125 (U/L)	CA199 (U/L)	CYFRA21-1 (μg/L)	SCC-Ag (μg/L)	CEA (μg/L)
Cervical cancer group	60	43.15±28.64 [#]	52.23±47.87 [#]	9.18±7.91 [#]	4.52±3.79 [#]	14.94±5.15 [#]
CIN group	20	20.67±9.35	13.88±17.34	1.12±0.66	0.81±0.55	5.46±0.83
healthy control group	28	21.23±6.51	14.36±9.24	1.39±0.98	0.51±0.38	3.51±1.27

Note: compared with the normal group, ^{*} $P<0.05$; compared with the CIN group, [#] $P<0.05$.

2.3. Statistical processing

We Used SPSS 21.0 software package to process the test result data, mean ± standard deviation ($\bar{x}\pm s$) represents measurement data, the use of t test was to compare the difference between groups, with $P<0.05$ as a statistically significant.

3. Results

3.1 Comparison of serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA levels among three groups

The results showed that the levels of serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA in CIN group were (20.67±9.35) U/L, (13.88±17.34) U/L, (1.12±0.66) μg/L, (0.81±0.55) μg/L, (5.46±0.83) μg/L. There was no significant difference in serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA levels among the three groups ($P>0.05$); The levels of serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA in the cervical cancer group were (43.15±28.64) U/L, (52.23±47.87) U/L, (9.18±7.91) μg/L, (4.52±3.79) μg/L, (14.94±5.15) μg/L, which were significantly higher than the healthy control group and the CIN group, and the difference was significant ($P<0.05$). Please look at Table 1.

3.2. Comparison of CA125, CA199, CYFRA21-1, SCC-Ag and CEA levels in patients with different types of cervical cancer

In different tissue type of cervical cancer patients, the serum levels of CA125, CA199, CYFRA21-1, SCC-Ag and CEA were statistically significant ($P<0.05$). The levels of CA125, CA199 and CEA in adenocarcinoma were significantly higher than those in squamous cell carcinoma and squamous cell carcinoma, and the difference was statistically significant ($P<0.05$). There was no significant difference between squamous cell carcinoma and squamous cell carcinoma ($P>0.05$); The content of CYFRA21-1 and SCC-Ag in squamous cell carcinoma was significantly higher than that in adenocarcinoma and squamous adenocarcinoma, and

Table 2.

Comparison of CA125, CA199, CYFRA21-1, SCC-Ag and CEA levels in patients with different types of cervical cancer.

Group	n	CA125 (U/L)	CA199 (U/L)	CYFRA21-1 (μg/L)	SCC-Ag (μg/L)	CEA (μg/L)
Squamous cell carcinoma	38	28.46±11.24	37.48±16.95	11.06±5.90 ^{#△}	5.41±2.68 ^{#△}	10.97±5.88
Adenocarcinoma	16	48.73±15.46 ^{*△}	58.36±19.07 ^{*△}	8.54±3.84	1.85±0.95	17.46±8.30 ^{*△}
Squamous adenocarcinoma	6	30.31±16.29	41.55±20.54	8.06±4.15	1.51±0.66	11.42±7.04

Note: compared with squamous cell carcinoma, ^{*}P<0.05; compared with adenocarcinoma [#]P<0.05; compared with squamous adenocarcinoma, [△]P<0.05.

the difference was statistically significant ($P<0.05$). There was no significant difference between adenocarcinoma and squamous cell carcinoma ($P>0.05$). Please look at table 2.

4. Discussion

Cervical cancer is one of the most common gynecologic malignancies, mostly occurs in women aged 30-55 years. Cervical cancer is caused by the slow progression of cervical intraepithelial neoplasia, but it usually has no obvious clinical symptoms at the early stage, thus affecting the early diagnosis of cervical cancer[5]. In the type of cervical cancer tissues, about 85% are squamous cell carcinoma, 10%-15% are adenocarcinoma, about 3% are squamous cell carcinoma, and a few are small cell carcinoma or neuroendocrine tumor[3,6]. The detection of serum tumor markers not only can be used in the diagnosis of cervical cancer, but also can be used to judge whether there is lymph node metastasis, follow-up monitoring, treatment effect, and so on. It is of great significance[7].

The present study showed that serum tumor markers that have clinical value in cervical cancer patients include squamous cell carcinoma antibody (SCC-Ag), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199) and cytokeratin 21-1 (CYFRA21-1). Among them, squamous cell carcinoma antibody (SCC-Ag) is the most valuable serological marker in the diagnosis of squamous cell carcinoma of the cervix, Carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199) and carcinoembryonic antigen (CEA) are of greater value in the detection of cervical adenocarcinoma[8]. CC-Ag is a serine protease inhibitor found by Kato[9] in 1977, it exists in the cytoplasm of squamous cell such as cervix, lung and so on. The content of SCC-Ag in serum of healthy women is not more than 1.9 μg/L[8], and research shows that about 28%-88% of cervical squamous cell carcinoma patients were detected serum SCC-Ag content increased before treatment[6]. Since cervical cancer is mostly squamous cell carcinoma, many studies have used SCC-Ag as the first marker for the diagnosis of cervical cancer. CYFRA21-1 is a fragment of keratin 19 found in cervical epithelial cells, it is an epithelial tumor marker and a tumor marker of squamous cell carcinoma of the lung, when tumor cells are cleaved and lysed,

CYFRA21-1 can be released into the bloodstream[10,11]. The results showed that the levels of serum SCC-Ag and CYFRA21-1 in patients with cervical cancer were significantly higher than those in CIN group and healthy control group, and squamous cell carcinoma patients were higher than those of adenocarcinoma and squamous adenocarcinoma patients, which was consistent with the results of Zhong Yan's research[12]. However, it was reported that the sensitivity of simultaneous detection of serum SCC-Ag and CYFRA21-1 levels was no higher than that of serum SCC-Ag alone[13].

CA125 and CA199 are tumor markers of high molecular mucin type carbohydrate protein. CA125 and CA199 are also serum markers of many malignant tumors, such as lung cancer, pancreatic cancer[14-16], among them, CA199 is the most sensitive marker for pancreatic cancer so far[17]. Luo Yelin and other studies, with 35 U/mL and 27 U/mL as thresholds, detected elevated levels of blood CA125 and CA199 in patients with cervical cancer, and the positive rate of cervical adenocarcinoma was higher than that of squamous cell carcinoma of the cervix, And positively correlated with clinical stage. CEA is a glycoprotein antigen that was first discovered and widely used as a tumor marker[18], Especially for colorectal cancer, breast cancer and lung cancer, the efficacy of monitoring and monitoring has a high specificity, mainly in colorectal cancer tissues[19]. Studies have shown that it is associated with clinical staging, lymph node metastasis, and prognostic estimates of cervical cancer[20]. The results of this study show that the levels of serum CA125, CA199 and CEA in patients with cervical cancer were significantly higher than those in CIN group and healthy control group, and the patients with cervical adenocarcinoma were higher than those of squamous cell carcinoma and squamous cell carcinoma, which was consistent with the results of studies in china[21,22].

In summary, the levels of serum CA125, CA199, CYFRA21-1, SCC-Ag and CEA in patients with cervical cancer were significantly higher than those in patients with cervical intraepithelial neoplasia and healthy subjects, SCC-Ag and CYFRA21-1 levels were higher in patients with squamous cell carcinoma of the cervix, CA125, CA199 and CEA are more useful in the diagnosis of cervical adenocarcinoma. These five kinds of tumor markers can be used as indicators for the diagnosis of cervical cancer. It is also valuable for the differential diagnosis of cervical cancer.

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