The effect of continuous ambulatory peritoneal dialysis on serum CA-125 levels

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Summary

Malignant and non-malignant serosal fluids were found to be associated with high serum levels of CA-125, suggesting that the presence of fluid in the serosal cavities may stimulate its release. In this study, we investigated the relationship between serum CA-125 levels and peritoneal irritation during continuous ambulatory peritoneal dialysis (CAPD). We performed a clinical study in 24 stable patients (15 amenstrual females and 9 males), aged 46 ± 14 years on CAPD. The control group consisted of 32 healthy volunteers (20 females, 12 males) aged 44 ± 12 years. CA-125 levels were determined prior to the CAPD dwell (without dialysate in abdomen) and during the CAPD dwell (dialysate in abdomen 4 hours after). As a result, serum CA-125 levels were found to be 14.86 ± 5.98 U/ml and 15.23 ± 6.05 U/ml respectively, whereas it was 8.32 ± 5.54 U/ml in the control group. Serum CA-125 levels were found to be significantly elevated in CAPD patients when compared with healthy volunteers. However, serum CA-125 levels detected prior to and after CAPD did not differ between the groups. Interestingly, all of the patients in our study group were detected to have normal serum CA-125 levels (< 35 U/ml). We concluded that CAPD-induced abdominal artificial ascites did not affect serum levels of CA-125. Moreover, short and non-inflammatory mechanical pressures in the CAPD procedure do not have any effect on serum CA-125 levels.

Key words: Continuous ambulatory peritoneal dialysis; CA-125.

Introduction

The Cancer antigen 125 (CA-125), an ovarian tumor marker, is used especially in the follow-up of ovarian cancer for monitoring the efficacy of therapy and for early detection of recurrence. CA-125 is a very sensitive marker for the monitoring of ovarian cancer, but like all other cancer markers, it has restricted value by the fact that antigen CA-125 is produced by normal epithelia of the peritoneum, endometrium and benign ovarian cysts and not only by ovarian cancer cells [1-4]. The peritoneum is an important source of CA-125. During peritoneal irritation (hyperstimulation, salpingitis, ruptured ectopic pregnancy, laparotomy), peritoneally derived CA-125 significantly contributes to circulating CA-125 concentrations, giving elevated CA-125 values [3, 4]. In a number of previous studies, we found elevated levels of serum CA-125 in patients with nephrotic syndrome [5] and chronic renal failure (CRF) in the presence of peritoneal, pleural, or pericardial fluids [6]. Interestingly, normal serum CA-125 levels were detected in hemodialysis patients with hepatitis in the absence of serosal fluid [7]. Thus our results suggested that elevated serum CA-125 levels are possibly due to the presence of fluid in the peritoneum, pleura, or pericardium rather than the primary etiology. Finally, in our last two studies, we concluded that the cause of stable serum CA-125 levels before and after abdominal and pelvic physical examination and transvaginal ultrasonography was probably due to an insufficient peritoneal irritation unlike abdominal surgery [8, 9]. We also attempted to elaborate the probable relationship between CA-125 and artificial serosal fluids in patients on CAPD. Thus, we designed a clinical study to investigate the serum levels of CA-125 in that patient group.

Patients and Methods

Study Participants

Twenty-four stable patients (15 amenstrual females and 9 males) on CAPD: mean age was 46 ± 14 years (range 11-70 years), mean serum creatinine 5.9 ± 3.8 mg/dl (range, 2.1-10.2 mg/dl), and mean time on CAPD 18.43 ± 7.84 months (range, 3-36 months) were included in the study. None of the patients had clinical or radiologic evidence of malignancy or other non-malignant conditions possibly affecting the concentration of CA-125 apart from renal failure. Especially the patients who had peritonitis attacks, abdominal surgery or peritoneal dialysis catheter implantation within had three months were excluded from this study. The etiology of chronic failure was chronic glomerulonephritis (n = 18) and amyloidosis (n = 6). The control group consisted of 32 age- and sex-matched healthy volunteers (20 healthy female volunteers at the preovulatory phase of the menstrual cycle and 12 males) aged 44 ± 12 years (range, 19-68 years). Informed consents were obtained from the patients and volunteers.

Serum CA-125 Measurement

Peripheral venous blood was collected prior to the CAPD session and at the end of the fourth hour of the CAPD dwell (dialysate in abdomen) and the serum was separated immediately. Serum CA-125 levels were evaluated two times based on the presence and absence of dialysate fluid in the abdominal cavities.

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Serum CA-125 level was determined by Immulite OM-MA [Diagnostic Products Corporation (DPC), Gwynedd, United Kingdom], which was a solid phase, chemiluminescent enzyme immunometric assay. It was used with the Immulite DPC automated analyzer.

Statistical analysis

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

Results

Serum CA-125 level was found to be 14.86 ± 5.98 U/ml and 15.23 ± 6.05 U/ml in the CAPD group, respectively, whereas it was 8.32 ± 5.54 U/ml in the control group. Significantly high serum CA-125 levels were encountered in CAPD patients both in the presence or absence of dialysate in the abdomen when compared with the age- and sex-matched healthy volunteers (both p values were < 0.05). However, serum CA-125 levels detected prior to and after CAPD sessions were statistically insignificant ($p > 0.05$). In all of the patients in our study group, serum CA-125 levels were found to be lower than 35 U/ml (Table 1).

When CAPD patients were considered according to sex, no statistically significant difference was observed. There was also no correlation between serum CA-125 levels and duration of CAPD.

Table 1. — *Serum CA-125 levels and characteristics of study participants.*

Groups	No. (f/m)	Age (Years)	Duration of CAPD (Months)	CA-125 (U/ml)
Prior to the CAPD dwell	24 (15/9)	46 ± 14	18.43 ± 7.84	14.86 ± 5.98
During the CAPD dwell	24 (15/9)	46 ± 14	18.43 ± 7.84	15.23 ± 6.05
Control	32 (20/12)	44 ± 12	-	8.32 ± 5.54

Discussion

The antigen CA-125 is produced by normal epithelia of the peritoneum, pleura, pericardium, endometrium, and benign ovarian cysts and not only by ovarian cancer cells [1-4]. Malignant and non-malignant serosal fluids were also found to be associated with high serum levels of CA-125, suggesting that the presence of fluid in the serosal cavities may stimulate its release [10]. Therefore, measurement of the serum CA-125 level could become a diagnostic marker of irritation of the coelomic epithelium such as the pericardium, peritoneum, or pleura.

Now, it is time to ask such questions like 'Is only irritation of the peritoneum enough for elevated serum CA-125 levels?' or 'Which kind of irritation is necessary for elevated serum CA-125 levels?' or 'How long should be the irritation time for the peritoneum to secrete CA-125?'.

The elevated levels of serum CA-125 in patients with nephrotic syndrome and CRF [5, 6] suggest that the presence of fluid in the peritoneum, pleura, or pericardium rather than the primary etiology itself were the causative factor for the elevated serum CA-125 levels. Interestingly, it seems that CA-125 levels were elevated to a greater extent in patients with peritoneal fluids than in those with pleural or pericardial fluids [6]. This can be attributed to the higher surface area of the peritoneum or to the amount of fluid in the peritoneum. These studies suggest that serum CA-125 levels were elevated in patients with serosal fluids regardless of the underlying etiology. Serum CA-125 levels were also found to be elevated in patients who underwent abdominal surgery. This elevation was more pronounced at the 24th hour postoperatively and decreased slightly over time and reached normal values by the 7th day [9].

Normal and low serum CA-125 levels in patients with CRF on CAPD have been found in different studies. Bastani et al found that while the serum CA-125 level were within the normal limits in stable CAPD patients, it could also be raised in unstable CAPD patients due to peritoneal irritation, either from peritonitis, peritoneal dialysis catheter implantation or intraabdominal surgery [10]. Interestingly, Kawabe *et al.* found low serum CA-125 concentrations in patients on CAPD [11].

Mesothelial changes occur during CAPD. Passadakis *et al.* found a statistically significant difference between dialysate CA-125 concentrations at 0 minutes and 240 minutes. These results suggest that longer dwell times on CAPD increases dialysate CA-125 concentrations. However, they reported that serum CA-125 concentrations were not changed with duration of CAPD [12]. Lai *et al.* demonstrated no correlation between dialysate CA-125 levels and number of mesothelial and other cells. This result may be related to the early loss of peritoneal transport properties as a result of the use of hypertonic dialysate [13]. Similarly, Pannekeet *et al.* observed a negative dialysate CA-125 trend with duration of CAPD. They explained the relationship between low dialysate CA-125 levels and duration of CAPD by the possible vanishing of the mesothelial layer [14, 15]. Koomen *et al.* reported that CA-125 was locally produced in the peritoneal cavity during CAPD and that the mesothelial cells were the major source of this CA-125. They also observed however that plasma CA-125 levels did not change with the duration of CAPD [16].

In our study, significantly high serum CA-125 levels were found in CAPD patients both in the presence or absence of dialysate in the abdomen when compared with the control group. But, the serum CA-125 levels detected prior to CAPD sessions were statistically insignificant when compared with CAPD solution in the abdomen four hours after. However, in all patients in our study group, serum CA-125 levels were found to be lower than 35 U/ml. In addition, there was no correlation between serum CA-125 level and the duration of CAPD. These results suggest that only the presence of fluid without inflammation in the peritoneal cavity on stable CAPD patients may not stimulate its release. On the other hand,

because of hypertonic dialysate, CAPD patients may be not proper examples for artificial ascites.

In conclusion, serum CA-125 levels should be evaluated with caution in CAPD patients. Serum CA-125 level may not be a useful marker for peritoneal irritation and it may cause controversy for evaluation of malignancy in CAPD patients. Still, new studies are needed to highlight the pathophysiologic basis of CA-125 and its relation to peritoneal irritation.

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