RAPID DIAGNOSIS OF CATHETER RELATED SEPSIS IN HEMODIALYSIS PATIENTS

Hemodiyaliz hastalarında katetere bağlı sepsisin hızlı tanısı

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Abstract

Purpose: *To distinguish between infected and non-infected Central Venous Catheters (CVCs) applied to hemodialysis patients without having to wait bacterial cultures, we evaluated the importance of sera C-Reactive Protein (CRP) test results to diagnose Catheter Related Sepsis (CRS) and compared this test with microbiologic cultures.*

Patients and Methods: *Fifty-eight hemodialysis patients (16 Acute Renal Failure and 42 Chronic Renal Failure) and 81 CVCs applied to these patients were followed up. Twenty-six (45%) were female, 32 (55%) male, and the mean age was 46 (SD: 15; range: 15-70) years. When CRS was clinically suspected, catheters were removed and catheter tips cultured using semiquantitative method, or simultaneously blood samples were taken from catheters and peripheral vein for blood cultures. At the same time, peripheral blood samples were taken and sera CRP levels were tested with semiquantitative latex method.*

Results: *Forty suspected and microbiologically confirmed CRS episodes were detected in two year follow up period. The sera CRP test was 95% sensitive and 78% specific (accepted 12 mg/L and higher levels as a CRS) in the diagnosis of microbiologically defined CRS.*

Conclusion: *Results are available in minutes, using CRP test there fore fewer CVCs may have to be removed on suspicion of CRS in hemodialysis patients.*

Key Words: *Catheter, C-reactive protein, Hemodialysis, Patients, Sepsis*

Özet

Amaç: *Hemodiyaliz hastalarına uygulandıktan sonra infekte olan ve olmayan Santral Venöz Kateter (SVK)' lerin bakteriyel kültür sonuçlarını beklemeden ayırımında serum C-Reaktif Protein (CRP)' in değeri araştırıldı. Kateter Bağlantılı Sepsis (KBS) tanısında serum CRP testiyle mikrobiyolojik sonuçlar karşılaştırıldı.*

Hastalar ve Yöntem: *Ellisekiz hemodiyaliz hastası (Akut Böbrek Yetmezliği 16 ve Kronik Böbrek Yetmezliği 42) ve bu hastalara uygulanan 81 SVK takip edildi. Hastalardan 26 (%45)' sı Kadın, 32 (%55)' si Erkek ve ortalama yaş 46 (SD: 15; min:15, maks:70) (yıl) idi. Klinik olarak KBS düşünüldüğünde ya kateter çekilerek kateter ucundan semikantitatif yöntemle kültür alındı ya da hem kateterden hem de periferden eş zamanlı kan kültürü alındı. Aynı zamanda periferden alınan kan örneğinden semikantitatif lateks yöntemi ile serum CRP çalışıldı.*

Bulgular: *İki yıllık takip süresince KBS' den şüphelenilen ve mikrobiyoloji ile kanıtlanan 40 KBS atağı tespit edildi. Mikrobiyoloji ile kanıtlanan KBS ataklarının tanısında serum CRP testi %95 duyarlı ve %78 spesifik (12 mg/L ve üst değerler KBS lehine kabul edildiğinde) bulundu.*

Sonuç: *Hemodiyaliz hastalarında KBS' den şüphe edildiğinde dakikalar içinde alınacak sonuçlarıyla CRP testi ile daha az SVK çıkartılabilir.*

Anahtar Kelimeler: *C-reaktif protein, Hasta, Hemodiyaliz, Kateter, Sepsis*

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Intravascular catheters are indispensable in modern-day medical practice and used in many conditions (1). Central Venous Catheters (CVC) are necessary in some patients without arterio-venous fistula on hemodialysis for Acute Renal Failure (ARF) and Chronic Renal Failure (CRF) (1-4). However, the use of CVC is frequently complicated by a variety of

local or systemic infectious complications. Catheter-related infections, particularly catheter-related sepsis (CRS) are associated with increased morbidity and mortality rates in hemodialysis patients (1, 3, 5, 6). Today, the incidence of CRS ranges from 0.5 to 13 per 1000 patient-days with hemodialysis catheters (3).

CRS is simply defined as peripheral bacteraemia caused by the same microorganism as cultured (semiquantitative or quantitative) from the catheter. Conventional methods to diagnose generally require removal of the catheter so that the microorganisms colonising can be cultured (1). However, in more than half the patients these culture results are negative, despite clinical suspicion of catheter-related infection (7, 8) and culture results are not available before 24 hours.

C-Reactive Protein (CRP) is one of the acute-phase proteins (9). This study was planned to distinguish infected and non-infected CVCs without waiting for bacterial cultures. We evaluated sera CRP test results to diagnose CRS by comparing this test with microbiology.

PATIENTS AND METHODS

In the period between 1 October 1994 and 30 September 1996, newly inserted hemodialysis catheters in hemodialysis patients in the Department of Infectious Diseases and Internal Medicine at our hospital (an 800 bed university hospital) were studied prospectively.

Catheters: The double-lumen hemodialysis catheter (MEDCOMP 11.5 F DUO-FLOW) was used for hemodialysis. This is a 15-cm polyurethane and noncuffed catheter.

Catheter insertion and maintenance: All catheters were inserted by Cardiovascular Surgery medical staff. Details concerning the underlying illness, location within the hospital, current treatment, catheter insertion site, and date of insertion and removal were recorded for each patient. Catheter insertion was performed using the Seldinger technique (10). The entry side was prepared with 10% povidone-iodine, and a subclavian or jugular vein was used for catheterization. A povidone-iodine gauze dressing was applied to the skin entry side. The dressing was removed before each dialysis or if leakage or local discomfort occurred. The insertion site was inspected and cleaned with 10% povidone-iodine, then redressed before each hemodialysis run. The catheter was flushed with 5 ml of heparin solution (5,000 U) after each use.

Catheter removal: Before removal of the catheter, a sample of blood was drawn from a peripheral vein for culture and to test for serum CRP level. The skin exit site was inspected for evidence of local infection, cleaned with 10% povidone-iodine, and allowed to dry. The catheter was carefully removed avoiding skin contact, distal segment was removed aseptically and cultured of Maki et al (11) according to the reasons for removal and the patients' clinical condition were recorded. Catheters were removed for these reasons: 1) no need of catheter, 2) suspected CRS, 3) dysfunction and occlusion of the catheter.

Cultures of catheter distal segment: All catheter distal segment cultures on blood agar plates were incubated aerobically at 37°C for at least 48 hours. Counts of each colonial type present were recorded for each plate and microorganisms isolated from plates identified phenotypically according to standard methods.

Cultures of blood: Cultures of blood (Castenada) were incubated aerobically at 370C for periods of up to seven days. They were subcultured when turbid or after seven days, onto blood agar and incubated aerobically at 37°C for at least 48 hours. Microorganisms isolated from the blood were identified phenotypically according to the standard methods.

Definition of Catheter-related Sepsis (CRS): Isolation of the same organism from a semiquantitative culture (growth of 15 colony-forming units) of a catheter distal segment and from the peripheral blood of a patient with accompanying clinical symptoms of bloodstream infection and no other apparent source of infection.

Assay of sera CRP: The CRP levels in sera were tested with semiquantitative latex agglutination method which is commercially available as latex test kits (AVITEX-CRP; Omega Diagnostics, Alloa, U. K.). The CRP results were tested for each patient and recorded.

The five properties of the CRP diagnostic tests were then calculated microbiologically, defined as CRS: sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. These properties are shown in Fig. I and the results are reported as a percentage.

RESULTS

In the period between 1 October 1994 and 30 September 1996, 81 newly inserted CVCs in 58 hemodialysis patients were followed up. In this period, 40 suspected and microbiologically confirmed CRS were detected. Details on patients are given in Table I. The mean duration of CVC placement was 14 days (range 3-53). Causative microorganisms (mostly coagulase negative staphylococci) are given in Table II. In addition, peripheral blood cultures were negative and no clinical symptoms of bloodstream infection of patients inserted with 41 CVC were detected (15 colonised, 21 non-colonised and 5, exit site infection).

The sera CRP testing results of the patients with and without CRS are presented in Table III. The test was found positive (accepted 12 mg/L as a CRS) in 38 of the 40 patients who had microbiologically defined CRS, and had an overall sensitivity of 95% and specificity of 78%, with a positive predictive value of 81%, a negative predictive value of 94%, and an accuracy of 86% (Table IV).

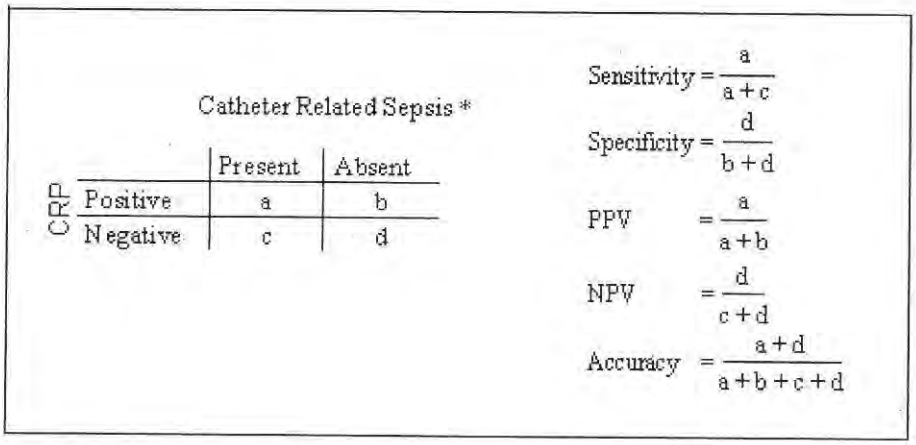

Figure 1. Definition of terms for describing usefulness of serum C-reactive protein testing with catheter-related sepsis

* Isolation of the same organism from a semiquantitative culture (growth of 15 colony-forming units) of a catheter distal segment and from the peripheral blood of a patient with accompanying clinical symptoms of bloodstream infection and no other apparent source of infection. PPV: positive predictive value, NPV: negative predictive value.

Table I. Characteristics of Hemodialysis Patients

	With CRS* (n=30)	Without CRS (n=28)	Total (n=58)
Mean age, year (range)	45 (15 - 70)	48 (22 - 70)	46 (15 - 70)
Male, n (%)	18 (28)	14 (62)	32 (55)
Female, n (%)	12 (29)	14 (71)	26 (45)
Acute renal failure, n (%)	5 (31)	11 (69)	16 (28)
Chronic renal failure, n (%)	25 (45)	17 (55)	42 (72)

* *Catheter-related sepsis*

Table II. Causative Microorganisms of Catheter-related sepsis in 40 Hemodialysis Catheters

Microorganism	number	%
Coag. Negative Staphylococci	12	30.0
Enterobacter spp	8	20.0
Escherichia coli	8	20.0
Staphylococcus aureus	3	7.5
Citrobacter spp	2	5.0
Acinetobacter spp	2	5.0
Pseudomonas aeruginosa	1	2.5
Flavobacterium spp	1	2.5
Streptococcus pneumoniae	1	2.5
Enterococcus faecium	1	2.5
Candida albicans	1	2.5
Total	40	100.0

Table III. Sera C-reactive protein testing results of patients

CRP (mg/L)	With CRS Number	%	Without CRS Number	%
5 and ↓	0	0.0	20	48.8
6-11	2	5.0	12	29.3
12-23	12	30.0	6	14.7
24-47	9	22.5	1	2.4
48-95	7	17.5	1	2.4
96-191	6	15.0	1	2.4
192 and ↑	4	10.0	0	0.0
Total	40	100.0	41	100.0

CRP: C-reactive protein, CRS: Catheter-related sepsis

Table IV. Accuracy of C-reactive protein in the diagnosis of catheter related sepsis

C-reactive protein*	Number of catheters With sepsis	Without sepsis	Total
Positive	38	9	47
Negative	2	32	34
Total	40	41	81

**Positive: ≥ 12 mg/L.*
Sensitivity 95%; Specificity 78%;
Positive Predictive Value 81%;
Negative Predictive Value 94%; Accuracy 86 %

DISCUSSION

In the United States, 332,000 and in Turkey 33,000 patients are treated annually because of renal failure (12, 13). CVCs are a major advance in end-stage renal disease patient care until the burden of catheter-related complications such as CRS become obvious. CRS is one of the major causes of morbidity, with potential hazards in hemodialysis patients (3, 5). Today the definition of CRS is based on culture techniques which have significant diagnostic limitations (1). Furthermore, the culture results reguire at least 24 hours to beome available. Though the pathophysiology of the condition changes with time, diagnosis of CRS remains problematic. The most widely used laboratory technique for diagnosis of catheter-related infection is the roll-plate method described by Maki et al.

(11). However, most CVCs removed after suspicions of CRS are not confirmed as the source of infection (7, 8). Thus, diagnosis of CRS needs rapid and specific diagnostic tests.

Previously, direct gram staining of catheters on removal was shown as a rapid method of defining CRS. However, this technique was accepted impractical for routine diagnostic use (1). Acridine-orange staining of catheters has been proposed as a modification of the gram staining technique. This test was found 87% sensitive and 94% specific in paediatric patients, and 96% sensitive and 92% specific in surgical patients in the diagnosis of CRS (14, 15).

A large number of homeostatic mechanisms that are operative in vertebrates under normal circumstances are altered substantially following tissue injury or infection. These alterations constitute the acute-phase response (16). CRP is one of the best-studied and most dramatic example of acute-phase protein (9). The CRP is primarily produced by the hepatocytes, but also by activated mononuclear cells and its synthesis increases within hours of acute injury or the onset of inflammation (9, 17). Previously, it was shown that the measurement of sera CRP was useful in the diagnosis and management of infectious diseases (17). In addition, CRP is an effective indicator of infection or inflammation even in the presence of ARF and CRF (18, 19). Harrison et al (18) demonstrated that ARF itself did not cause the CRP to increase significantly without the coexistence of infection or tissue damage, and dialysis did not alter concentrations of CRP.

The sera CRP test is sensitive (95%) and specific (78%) (accepted 12 mg/L as CRS) on microbiologically defined CRS in hemodialysis patients (Table IV). This test has not previously been studied on the diagnosis of CRS in hemodialysis patients. However the CRP has been studied in patients with CRF. Lindgren et al (19) found that acute-phase proteins including plasma CRP were not affected by renal failure, and synthesis increased during the course of inflammation and declined at the end of inflammatory stimuli. Rushforth et al (14) reported that the CRP test was less sensitive (45%) and specific (61%) in the diagnosis of CRS by quantitative blood culture in paediatric patients. They suggest that the CRP test is useful to monitor treatment after the diagnosis of CRS. The CRP can rise to peak levels within 24 to 48 hours (17). This trend of CRP is of most value, single measures giving only limited information but it may well be the earliest indicator of sepsis available to the physician (17, 18).

This study includes a single-day measurement test of the sera CRP to diagnose CRS in hemodialysis patients, and the study demonstrated that it is sensitive to CRS in hemodialysis patients. To test the acute-phase reactant proteins is quick and readily available for the physicians. We think that using the CRP results, which are available in minutes, we can remove less CVCs because of suspicion of CRS in hemodialysis patients. However, to confirm our results, further studies with a greater number of patients and more sensitive CRP tests are necessary.

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