Elevation of plasma D-dimer is closely associated with venous thrombosis produced by double-lumen catheter in pre-dialysis patients

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Abstract

Background. A double-lumen catheter (DLC) is used as a temporary blood access in emergency haemodialysis and continuous haemodialysis. There are various reports concerning thrombosis related to use of DLC and other catheters. The objective of this study is to assess the incidence of venous thrombosis when using DLC in patients undergoing blood purification.

Method. Forty-eight Japanese patients, hospitalized in the Saitama Medical University hospital from December 2004 to April 2005, who had DLC insertion as a temporary blood access for blood purification. The existence of a thrombus was determined using ultrasonography, before catheter insertion, and every 2 days after insertion up to 3 weeks. At the time of DLC insertion, general blood tests including plasma D-dimer, and serum C-reactive protein (CRP) were performed. When DLC was removed, plasma D-dimer and serum CRP were measured.

Results. In 30 of 48 (62.5%) patients with DLC insertion as a temporary blood access for haemodialysis, venous thrombi with diameters >1.1 mm were detected by venous ultrasonography. No predictive factors were recognized except an increase in plasma D-dimer that was significantly higher in the patients with venous thrombus. The changes in plasma D-dimer were 3.54 (SE 0.8) μg/dl in patient with thrombus, and 0.29 (0.30) μg/dl in patient without thrombus (P = 0.004).

Conclusions. The study suggests that changes in plasma D-dimer after the insertion of the catheter may be used to predict thrombus formation and is more accurate than baseline measurements, and easier than other new markers.

Keywords: D-dimer; double-lumen catheter (DLC); haemodialysis; pulmonary embolism; thrombosis

Introduction

A double-lumen catheter (DLC) is used as a temporary blood access for emergency haemodialysis and continuous haemodialysis. There are various reports concerning thrombosis related to the use of DLC and other catheters. The risk of thrombus formation appears to increase with longer duration of catheter insertion and the diameter of the catheter employed [1]. Also factors related to patients, such as infection, malignant tumour and heart failure, may increase the risk of thrombus formation [2–4]. Although DLC can be used as a simple and quick temporary blood access in blood purification therapy, recently it has also been used on a more permanent basis for blood access to limited cases. As thrombus formation accompanying long-term catheter insertion may serve as a risk of pulmonary embolism, catheter retention to central vein is classified as a risk factor of the second-line level in a deep-vein-thrombosis prevention guideline [5]. Moreover, in cases with high-risk of venous thrombus embolism, avoiding the central venous catheter insertion from the legs, such as a femoral vein (FV), is advisable. In spite of the apparent higher risks due to thicker diameter, there has been little investigation concerning the relationship between DLC and thrombosis [6,7]. In this study, we investigated the prevalence of venous thrombosis after the insertion of DLC in patients receiving haemodialysis.

Patients and methods

Forty-eight Japanese patients, hospitalized in the Saitama Medical University hospital from December 2004 to April 2005 were inserted with DLCs as a temporary blood access for blood purification. All DLCs used in the present study were made of polyurethane (Niagara: end-hole type, Medicon Inc., Osaka, Japan). Insertion of a catheter was performed in sterile manner using a gown technique into the right internal jugular vein (IJV). For insertion into the IJV, a straight type, 15 cm length DLC was used. At the time of
DLC insertion, general blood tests including plasma D-dimer, and serum C-reactive Protein (CRP) were performed. The ultrasonic diagnostic equipment was ProSoundII SSD-6500SV (Aloka, Tokyo, Japan) with 7.5 Mz probes. The existence of a thrombus was evaluated using a linear probe, before insertion, and every 2 days after insertion for up to 3 weeks. The areas of scanning were from the insertion point to the supraclavicular fossa of the same side as the DLC insertion. The inserted DLC was seen as a higher luminosity linear echo image in the vein and the circumference of the thrombus was seen as a lower luminosity echo image (Figure 1). The occurrence of catheter infection was monitored by physical examination, local findings of the catheter insertion point, serial measurement of white blood cell count and serum CRP. DLC removal was considered if the DLC became occluded or there was remarkable reduction in blood flows, or in the event of infection, or secession from haemodialysis. When the DLC was removed, plasma D-dimer and serum CRP were measured. If the patient was receiving anticoagulant drugs such as aspirin, and showed coagulation abnormalities (D-dimer \(>10 \mu g/ml\), inflammation (CRP \(>2.5 \text{mg/dl}\)) and disseminated intravascular coagulation (DIC) or nephrotic syndrome at the time of catheter insertion, the patient was excluded from the study. The analysis was performed by dividing the patients into two groups; in one group, patients did not have thrombi for at least 3 weeks, and in the other, patients had thromb, measuring \(>1.1 \text{mm}\) in diameter which is the minimum size that can be detected by ultrasound.

The two groups were compared for the following: history of taking an antihyperlipidaemic drug, or angiotensin receptor blocker (ARB)/angiotensin-converting enzyme inhibitor (ACEi), diabetes, being overweight (BMI \(>25\)), sex, the plasma level of D-dimer and serum CRP.

**Statistical analyses**

Paired \(t\)-test was used to assess the changes during the DLC insertion, and unpaired \(t\)-test and chi-square test were also employed to determine any differences between the two groups. A significant difference was defined as \(P<0.05\) in each evaluation.

**Result**

The patients consisted of 29 men and 19 women, and their mean age was 68 (SE 14) years old. The primary diseases of renal insufficiency were: 18 diabetic nephropathy, 16 chronic glomerular nephritis and 14 hypertensive benign nephrosclerosis. The rate of formation of the thrombus was 62.5%. There was no significant difference between the two groups with respect to age, sex, being overweight, the history of hyperlipidaemia, diabetes mellitus, taking statin derivatives and ARB/ACEi, plasma level of D-dimer, serum albumin and CRP level at catheter insertion (Table 1). The time to detection of thrombus was an average of 9.5 days (range 2–30 days). The sizes of thrombi varied from 1.5 to 36 mm in the major axis and 1.1 to 15 mm in the minor axis. A significant difference was not found in the time that the catheter was in place and changes in serum CRP (Table 2); however, the change in plasma level of D-dimer was statistically significantly higher in the group with thrombus \((P=0.004)\). Moreover, plasma D-dimer was significantly increased in patients with thrombus after the DLC insertion \((P=0.0001)\). There was no significant difference in serum CRP level between pre-and post-DLC-insertion in patients with and without thrombus (Figure 2).

**Discussion**

When the DLC was inserted into a central vein, thrombi measuring 1.1 mm or more were observed in 62.5% of patients with renal failure, by ultrasonic diagnosis; the thrombus was formed in an average of 9.5 days after catheter insertion. In the patients who had thrombus, plasma level of D-dimer significantly increased at the time of occurrence of thrombus compared with baseline.

There is a tendency for thrombus to form during long-term catheter insertion and as the diameter of the catheter increases. It was suggested that bed rest of more than 2 days is also a risk-factor for clot formation [1]. Longer catheter length and wider contact area to vessel wall due to anatomical flexion...
Table 1. Comparison of clinical profiles between patients with or without thrombus. Data are expressed in mean with SE.

<table>
<thead>
<tr>
<th></th>
<th>Thrombus (+)</th>
<th>Thrombus (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69.3 (2.5)</td>
<td>64.7 (3.3)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>19/11</td>
<td>10/8</td>
</tr>
<tr>
<td>Obesity (yes/no)</td>
<td>6/24</td>
<td>3/15</td>
</tr>
<tr>
<td>Hyperlipidaemia (yes/no)</td>
<td>10/20</td>
<td>3/15</td>
</tr>
<tr>
<td>Basal D-dimer (mU/ml)</td>
<td>2.75 (0.52)</td>
<td>2.56 (0.55)</td>
</tr>
<tr>
<td>Basal CRP (mg/dl)</td>
<td>0.59 (0.10)</td>
<td>0.55 (0.12)</td>
</tr>
<tr>
<td>Basal albumin (g/dl)</td>
<td>3.0 (0.1)</td>
<td>3.1 (0.2)</td>
</tr>
<tr>
<td>History of diabetes (yes/no)</td>
<td>12/18</td>
<td>8/10</td>
</tr>
<tr>
<td>Taking antihyperlipidaemic agents (yes/no)</td>
<td>6/24</td>
<td>0/18</td>
</tr>
<tr>
<td>Taking ARB/ACEi (yes/no)</td>
<td>19/11</td>
<td>10/8</td>
</tr>
</tbody>
</table>

ARB, Angiotensin receptor blocker; ACEi, angiotensin-converting enzyme inhibitor.
Numbers in parenthesis denote SEs.

Table 2. Changes in serum CRP and plasma D-dimer levels in patients with or without thrombus.

<table>
<thead>
<tr>
<th></th>
<th>Thrombus (+)</th>
<th>Thrombus (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of insertion</td>
<td>16.1 (1.7)</td>
<td>12.9 (1.7)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.87 (0.38)</td>
<td>0.28 (0.24)</td>
</tr>
<tr>
<td>D-dimer (μg/ml)</td>
<td>3.54 (0.80)</td>
<td>0.29 (0.30)</td>
</tr>
</tbody>
</table>

Data are expressed as mean with SE. Changes in CRP and D-dimer show the differences between the value at the time of catheter insertion and at the time of observation of the thrombus in the thrombus-positive group. In the thrombus-negative group, changes in CRP and D-dimer show the differences between the values at the time of catheter insertion and at its removal. Numbers in parenthesis denote SEs.

would also cause thrombus formation in the FV [8]. However, the frequency of the thrombus formation varied according to the study location, patient group and type of catheter used. Kimata et al. [6] reported that 22 of 23 (95.7%) patients with FV DLC insertion were positive for thrombosis. Meanwhile, Montagnac et al. [7] reported that thrombus were observed in 29 of 55 (52.7%) patients. Moreover, Wanscher et al. [1] and others found thrombus in 56 of 91 patients with DLC insertion in the subclavian vein, and the average time of insertion was reported to be 27 days. Patient-related factors include mainly acceleration of coagulation accompanying a malignant tumour, catheter infection and heart failure [2–4].

It is considered essential to diagnose this important complication in catheter insertion time early in the procedure. Goodacre et al., [9] recommended that the ultrasonography be used for patients with high Wells score or positive for D-dimer test. It was reported that the combination of ultrasonography and pre-test probability [10] or CT scan [11] would increase the accuracy of the diagnosis. However, in general, these image scanning tests, including MRI or scintigram, are carried out in the second line after a blood test is performed [12]. A blood test usually determines the basal value of D-dimer [13]; although opinions vary, some believe it is useful [14,15] and some not [16,17]. In the study of Kearon et al., [18] they compared the usefulness of plasma levels of D-dimer and repeated ultrasonography to detect deep venous thrombosis in suspected patients. The D-dimer testing had acceptable safety, and was comparable in safety to anticoagulant therapy and routinely repeated ultrasonography. Moreover, they confirmed the usefulness of D-dimer testing in the diagnosis of pulmonary embolism in 1126 patients [18]. Increase in serum P-selectin [19], prothrombin [20], sialic acid [21] and soluble fibrin [22] have also predicted the existence of deep-vein thrombosis. However, the basal value of these markers might be modified by aging [23], and co-measurement of these markers would be useful to increase the accuracy of diagnosis [24].

In this study, plasma level of D-dimer at the time of thrombus formation increased markedly compared with the time of insertion in patients with a thrombus. There has been no study of changes in D-dimer test, not a single measurement at insertion. This indicator offers more accurate information than the single measurement at insertion. Moreover, plasma D-dimer test is now routine and can be measured easily and without special equipment compared with other new markers.
As noted, in the patient with DLC insertion, it was necessary to measure the changes in plasma D-dimer level, followed with ultrasonography even it was a short-term insertion. Moreover, when thrombus formation is found, anticoagulant therapy using low-molecular heparin, etc. should be considered immediately [25,26].

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Conflict of interest statement. None declared.

References


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