Spontaneous echo-contrast as an in vivo indicator of rheological imbalance in dilatative cardiomyopathy

V. Turchetti *, M.A. Bellini, D. Ricci, A. Lapi, G. Donati, L. Boschi, L. Trabalzini, M. Guerrini and S. Forconi

Institute of Internal Medicine and Geriatrics, University of Siena, Italy

Received 4 May 2001
Accepted 11 September 2001

Abstract. The aim of this study was to evaluate coagulative and hemorheologic assessment in patients with dilatative cardiomyopathy with or without spontaneous echo contrast (SEC). We studied 45 patients, 35 males and 10 females (mean age 72.1 ± 9.2). We measured whole blood viscosity, plasmatic fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT), D-dimer and red cell morphology with Zipursky–Forconi method. Transthoracic and transesophageal echocardiography was performed in all patients to evaluate the presence of SEC in left atrium. We divided all the patients into two groups: the 1st group of 20 patients with SEC and Atrial Fibrillation (AF) in 80% of cases, and the 2nd group of 25 patients without SEC and AF in 31%. Our results show that in patients with SEC there is a statistically significant increase of whole blood viscosity and plasma fibrinogen in comparison with patients without SEC. Red cell morphology in all patients demonstrates a reversed EMI. D-Dimer, was out of the normal range in about 1/3 of the patients in both groups. An analysis of our results points out that in patients with SEC and AF, with a major risk factor for cardioembolic stroke, we have alterations of hemorheologic assessment with an increase of whole blood viscosity and fibrinogen that seems to be caused by an increase of red cells aggregability favoured by fibrinogen. Our conclusions are that SEC in patients with dilatative cardiomyopathy and AF is an important in vivo indicator of hemorheologic imbalance and an important marker for cardioembolic risk stroke evaluation.

1. Introduction

Cardiac thromboembolism represents a frequent complication in patients affected by idiopathic or post-ischaemic dilated cardiomyopathy [1–3]. In the presence of AF, the risk of strokes increases because these pathologic situations are associated with hypercoagulability and hyperviscosity [4–6]. It is not well understood whether the coagulative and hemorheologic alterations are attributed to dilatation of cardiac chambers and AF (conditions that predispose to venous stasis) or to the initial disease [7–11].

Numerous studies relate alterations of hemorheologic parameters, such as blood and plasma viscosity, erythrocytic stickness, fibrinogenemia, with pathogenesis of cerebrovascular diseases [12,13]. The blood fluidity reduction due to (1) increase of haematocrit (polycythaemic hyperviscosity), (2) fibrinogen (plasmatic hyperviscosity), (3) greater red cell stiffness, is commonly considered a high risk condition for acute or chronic cerebrovascular events. The hemorheologic profile is altered in patients with stroke and TIA with respect to controls [14–17]. Coagulation profile alterations may also predispose the occurrence

* Corresponding author: Dr. Vera Turchetti, Istituto di Medicina Interna e Geriatria, Università degli Studi di Siena, Policlinico Le Scotte, Viale Bracci, 53100 Siena, Italy. Tel.: +39 0577 233319; Fax: +39 0577 233318; E-mail: images@unisi.it.
of cerebral embolic events, as in AF, when it becomes necessary to prophylax with oral anticoagulants [18–21].

SEC is a pathological condition, defined as dynamic smoke-like echoes with characteristic swirling patterns, has been identified as a potential marker for blood stasis. The presence of SEC may be showed by trans-oesophageal echocardiography, which provides excellent visualisation of the left atrium and left atrial appendage [22,23].

The pathogenesis of SEC is unclear, but in vitro studies have suggested that a reduction of blood flow velocity and an increase of erythrocyte stickiness, supported by interaction between plasma proteins and increased platelet adhesiveness, may play an important role [10,11,24].

2. Aim of the study

The aim of this study is to evaluate the behaviour of blood viscosity, fibrinogen, hematocrit, red cells morphology and coagulative parameters (D-dimer, fibrinogen, PT, aPTT) in patients with dilatated cardiomyopathy, due to ischemic or idiopathic origin (ejection fraction = 26 ± 8%). Most of them are associated with chronic AF, with or without SEC. We attempted to identify whether alterations of some parameters may be predictive of major embolic risk and contribute to understanding the genesis of this phenomenon. Patients with major valvular disease were excluded from the study.

3. Subjects and methods

We studied 45 patients, 35 males and 10 females, aged from 45 to 88 (mean age 72.15 ± 9.28) affected by idiopathic dilated or post-ischaemic cardiomyopathy associated or not with AF. All patients were treated with digitalis, ACE-inhibitors, nitro-derivatives and diuretics; patients suffering from post-ischemic dilated cardiomyopathy were also treated with thrombocytic antiaggregants.

Patients with severe arterial hypertension, lipoidoproteinosis, chronic renal failure, diabetes mellitus, severe ATS cerebrovasculopathy and patients in treatment with oral anticoagulants were excluded from the study.

We divided patients into two groups and then compared them to a control group C:

Group A: 20 patients, 16 males and 4 females, mean age 76.3 ± 6.9, with SEC in left atrium (AF in 80% of cases).

Group B: 25 patients, 19 males and 6 females, mean age 69.2 ± 9.6 without SEC in left atrium (AF in 31% of cases).

Group C: 30 healthy subjects (control group), 20 males and 10 females, mean age 68.3 ± 7.8.

In all patients we measured:

- whole blood viscosity with plane-cone rheometer Carri-Med in cPs at a shear rate of 10 s⁻¹ [25];
- plasma fibrinogen, PT and aPTT with coagulative method (Behring Coagulation Timer); hemocrome with Coulter Counter;
- red cells morphology with Zipursky–Forconi method, that is based on 3-dimensional observation of red cells with optical microscope [26,27];
- D-dimer (NycoCard D-Dimer) using the immune-filtration method [28].
We also assessed coagulative profile (PT and aPTT) and protein profile with albumin/globulin ratio.

The statistical analysis of the data was performed with Student’s t test for non-paired data. Trans-esophageal echocardiography was performed in all patients to consider the presence of SEC in the left atrium [22,23].

4. Results

In Table 1 are the electrocardiographic and ecographic characteristics of the subjects. We see that in group A, 80% of cases have AF. In group B 31% of cases. The presence of AF is highly significant with respect to the control group, where sinus rhythm prevailed. There is also a statistically significant difference between group A and group B. Ejection fraction (EF) is significantly reduced in both pathologic groups with respect to the control group, but not reduced between group A and B.

In Table 2 we collected coagulation and haematological parameters of the three groups and observe that there are not statistically significant differences of examined parameters except D-dimer which is significantly increased in patients affected by dilated cardiomyopathy with respect to controls, but it does not discriminate between the two groups with or without SEC; standard parameters of coagulative assessment do not show alterations in the three groups.

Table 1

| ECG and echocardiographic parameters in patients suffering from dilative cardiomyopathy with (SEC+) and without (SEC−) spontaneous echo contrast and controls |
|---------------------------------|-----------------|-----------------|
| (A) SEC+ | (B) SEC− | (C) Controls |
| n = 20 | n = 25 | n = 30 |
| Sinus rhythm | 20% | 69% | 100% |
| Atrial fibrillation | 80% | 31% | 0 |
| Ejection fraction | 24 ± 6% | 28 ± 5% | 55 ± 5% |
| Left atrial dimension (AP mm/m²) | 33 ± 6 | 30 ± 5 | 20 ± 4 |

Table 2

| Haematologic and coagulative parameters in patients suffering from dilatative cardiomyopathy with (SEC+) and without (SEC−) spontaneous echo contrast and controls |
|--------------------|-----------------|-----------------|-----------------|
| (A) SEC+ | (B) SEC− | (C) Controls |
| n = 20 | n = 25 | n = 30 |
| PT (sec) | 11.8 ± 0.7 | 11.6 ± 1.01 | 12 ± 0.75 |
| aPTT (sec) | 30.7 ± 3.5 | 30.7 ± 2.4 | 33.5 ± 2.28 |
| D-dimer (ng/ml) | 390 ± 52.3 | 380 ± 40.5 | 178.5 ± 22.5 |
| RC (×10¹² l⁻¹) | 4.92 ± 0.92 | 4.88 ± 0.8 | 4.7 ± 0.65 |
| MCV (fl) | 85.75 ± 6.4 | 86.5 ± 6.1 | 85.2 ± 5.4 |
| WC (×10⁸ l⁻¹) | 7.1 ± 1.7 | 7.2 ± 1.8 | 6.5 ± 1.3 |
| PTL (×10⁹ l⁻¹) | 243 ± 70.8 | 226 ± 69.5 | 199 ± 40.5 |
| Tot. protein (g/dl) | 6.89 ± 0.7 | 6.95 ± 0.68 | 7.1 ± 0.45 |
| Albumin/globulin | 1.58 ± 0.29 | 1.63 ± 0.32 | 1.76 ± 0.25 |

*p < 0.05 Student’s “t” test.
Table 3

Hemorheologic parameters in patients suffering from dilatative cardiomyopathy with (SEC+) and without (SEC−) spontaneous echo contrast and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(A) SEC+ n = 20</th>
<th>(B) SEC− n = 25</th>
<th>(C) Controls n = 30</th>
<th>A vs C</th>
<th>B vs C</th>
<th>A vs B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viscosity (cPs)</td>
<td>8.56 ± 1.61</td>
<td>7.25 ± 1.59</td>
<td>6.32 ± 0.34</td>
<td>**</td>
<td>*</td>
<td>**</td>
</tr>
<tr>
<td>Shear rate 10 s⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen (mg%)</td>
<td>438.31 ± 96.04</td>
<td>377.86 ± 89.66</td>
<td>250.85 ± 34.5</td>
<td>**</td>
<td>*</td>
<td>**</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>43.47 ± 4.28</td>
<td>41.9 ± 4.79</td>
<td>41.87 ± 2.2</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>EMI</td>
<td>0.69 ± 0.13</td>
<td>0.72 ± 0.12</td>
<td>1.2 ± 0.09</td>
<td>**</td>
<td>**</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

*p < 0.05 Student’s “t” test.

**p < 0.01 Student’s “t” test.

In Table 3 and Figure 1 we correlated hemorheologic parameters and observe that patients affected by dilated cardiomyopathy have an altered hemorheologic assessment with respect to controls of age-related healthy subjects, demonstrated by a statistically significant increase of blood viscosity and plasma fibrinogen. In presence of SEC we found a further statistically significant increase in whole blood viscosity.
and plasma fibrinogen with respect to those without SEC. Red cell morphology put in evidence in all patients an increase of discocytes if compared with bowls, with an inverted EMI (erythrocyte morphological index), in groups A and B with respect to group C, but without substantial differences between both pathologic groups.

5. Conclusions

An analysis of our results points out that patients affected by dilatative cardiomiopathy with SEC show alterations of hemorheologic assessment that predispose to a major risk of cerebral embolism [3, 7, 10, 17, 29, 30]: the hemorheologic alterations we find, are essentially attributed to an increase of total blood viscosity and fibrinogen; those parameters we find altered in ischaemic cerebrovascular diseases [31]. When the diameter of the left atrium increases, the reduced speed of blood flow may cause, by haematic stasis, an increase of red cells aggregability that associated to a situation of hyperfibrinogenaemia, which alter both blood and plasma viscosity [32, 33]. Transesophageal echocardiography help us to find the presence of SEC that according to certain authors is the morphologic representation of these aggregations [17, 34–37].

The study of red cells morphology, even if it shows a rise of discocytes and a reduction of EMI as in patients with ischaemic vasculopathy, is not able to be differentiated between the two groups. Increased values of D-dimer, expression of fibrinolitic activation, are present in equal percentages in both groups: these data support us in hypothesizing that both alterations, erytrocytic deformability and coagulation–fibrinolytics system, are related to diseases that cause dilatative cardiomypathy. In pathogenesis of SEC we must take hemorheologic alteration into consideration [16, 38–42].

The presence of AF, according to data in the literature, considerably increases the possibility of finding of SEC and therefore of thromboembolic risk. In this condition we observe that hemorheologic alterations are more evident and are statistically significant with respect to patients affected by dilatative cardiomypathy in sinus rhythm [23, 33–37, 43–46]. Analyzing of our data we may draw two conclusions:

- The presence of spontaneous echo-contrast, founded by transesophageal echocardiography, may help us to visualize in vivo hemorheologic alterations favoured by hyperfibrinogenaemia and low flow.
- In patients affected by dilatative cardiomypathy associated with AF, the presence of altered hemorheologic parameters is a potent risk factor for ischemic accidents.

These evaluations are very important in the follow up of patients with dilatative cardiomypathy [3, 17, 32, 46–52].

Acknowledgements

This research was supported by a grant of the University of Siena (P.A.R. 2000).

References


[30] D.G. Nabavi, S. Arato, D.W. Droste, G. Schulte-Altedorneburg, V. Kemeny, H. Reinecke, M. Borggreve, G. Breithardt and E.B. Ringelstein, Microembolic load in asymptomatic patients with cardiac aneurysm, severe ventricular dysfunction,


