Fibrinolysis in idiopathic menorrhagia

Maida Shamseddin*, Muna A. Kashmool**

Departments of *Obstetric-gynecology, **Hematology-pathology, Mosul Medical College, University of Mosul


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ABSTRACT

Objective: the role of fibrinolysis in idiopathic dysfunctional uterine bleeding (IDUB).
Design: prospective clinic-haematological study.
Setting: patients were collected in Alaliya maternity teaching hospital; a haematological study was conducted in Ibn Sina teaching hospital in Mosul from 10th January to 10th of June 2004.

Participants: 53 patients with mean age of 40.5 years and a range of 15-54 years, complaining of idiopathic dysfunctional uterine bleedings(IDUB) served as experimental group, and 30 presumed healthy women served as a control group, their ages were between 16-45 years.

After exclusion of organic causes, drugs, IUCD, medical causes, and bleeding tendency, blood samples were tested for haemoglobin, plasma D-dimer test and plasma fibrinogen.

Results: D-dimer test was positive in 16 out of 53 cases (30.2%) of experimental group (Group I). It was significantly positive (p< 0.005) in cases of idiopathic menorrhagia compared to the control group. D-dimer test was significantly positive in those with prolonged duration of vaginal bleeding >7days, compared to those with heavy periods and short duration of vaginal bleeding (p<0.05). D-dimer test was negative in the remaining cases (group II). The fibrinogen level was significantly lower in patients with positive D-dimer (p<0.05). Antifibrinolytic agent tranexamic acid was given to all patients in both groups; 95% of women responded to the treatment in group I, while the response in group II was 54%.

Conclusion: Idiopathic menorrhagias appear to be due to increased fibrinolytic activity, such patients are likely to benefit from antifibrinolytic agents.

Keywords: Menometrorrhagia, dysfunctional uterine bleeding, fibrinolysis
enorma gia is defined as blood loss of 80ml or more per period[2]. It is still one of the common symptoms that bring patients to the gynecological clinic[3]. One of the fascinating aspects of menstruation is that menstrual blood does not clot and the endometrium has a high fibrinolytic activity; the fibrinolytic activity is enhanced in women with idiopathic dysfunctional uterine bleeding[4,5]. Metronorma has been attributed to a number of different causes. The incidence of coagulation disorders has been found to be almost 20% in adolescents with IDUB[6]. The endometrium possesses an active fibrinolytic system, as fibrinolytic activity is greater in the endometrium of women with menorrhagia than it is in the endometrium of women with menorrhagia blood loss in the normal range[7]. The former patients had defect in the regulation of the fibrinolytic system, accurate diagnosis of such disorder is essential to the design of appropriate therapeutic regimen[7]. Haemostasis of the endometrium is directly related to the functions of platelets and fibrin. Deficiencies in either of these components result in menorrhagia. Thrombi are seen in the functional layers but are limited to the shedding surface of the tissue. Fibrinolysis limits the fibrin deposits in the unshed layer. Accurate diagnosis of such disorder is essential to the design of appropriate therapeutic regimen as suggested by taking fibrinolytic inhibitors (e.g. tranexamic acid)[8,9]. Anti fibrinolytic agents provide a rational and effective treatment, reducing the degree of menstrual blood loss by about 50%[10,11]. The D-dimer test utilizes a monoclonal antibody that recognizes a cross-linked fibrin epitope. The D-dimer assay is often used to assess the presence of disseminated intravascular coagulation (DIC). Generation of D-dimer requires action of both thrombin and plasmin and thus is specific for clot formation followed by lysis. Thus, the D-dimer assay is more specific for DIC than the fibrinogen/fibrin degradation product assay[12].

**SUBJECTS AND METHODS**

**Subjects:** Fifty three women were selected with a mean age of 40.5 years and a range of 15-54 years from the out patient clinic with idiopathic menorrhagia (the studied group). Patients were evaluated by taking a comprehensive history, including details of quantity, rhythm and duration of bleeding, medical problems such as diabetes mellitus and hypertension were considered, the method of contraception, pregnancy complications and drug history. We selected our cases after general and local examination for organic and endocrinological abnormalities, pelvic ultrasonography, luteal phase progesterone, thyroid function studies, and diagnostic curettage were done. Control group: 30 presumed healthy women aged between 18-45 years, they were not taking any medications.

**Methods:** Plasma D-dimer test was done by using a commercially available kit (biomek/fibronorm-68452/France) that depends on the clot-based method of Claus[13]. Haemoglobin and platelet count were done according to Dacie and Lewis. Thromboembolic patients were excluded from the study. The control group were tested for plasma fibrinogen and D-dimer. Statistical analysis was done by using the chi square test and the t student test.

**Results:** The mean haemoglobin level was 105g/dl with a range of 69-135g/dl. Anaemia was observed in 30/53 (56.6%) of cases. Most women were married, four women were single unmarried. Plasma fibrinogen, hib levels and platelet counts of patients and controls are shown in (Table 1).

<table>
<thead>
<tr>
<th>Table (1): Plasma fibrinogen, haemoglobin levels and platelet count in different groups.</th>
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<tr>
<td><strong>Group I (No.16)</strong></td>
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<tr>
<td><strong>Plasma fibrinogen(L)</strong></td>
</tr>
<tr>
<td>1.7-2.5</td>
</tr>
<tr>
<td>Hb (g/L)</td>
</tr>
<tr>
<td>Platelet count X 10^11/L</td>
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During this study we identified 2 subgroups of patients in the studied group. Group 1, including 16 out of 53 (30.2%) with positive plasma D-dimer test (>0.5mg/ml), the normal range of D-dimer test is (<0.5mg/ml). The mean plasma fibrinogen levels was 2.1g/l with a range of (1.7-2.5g/L), the mean haemoglobin level was 108g/l with a range of 81-135g/L, as shown in table 1. Anaemia was seen in 9 out of 16 patients (56.2%) in group 1.

Group II included 37 out of 53 patients (69.8%) with negative plasma D-dimer test (<0.5mg/ml) and a mean plasma fibrinogen level of 3.2g/L and a range of (2.4-4.6g/L). The mean haemoglobin level was 102g/L with a range of (69-136g/L). Anaemia was seen in 21out of 57-sides (56.7%). The D-dimer was significantly positive in patients with idiopathic menorrhagia compared to the control group with (p<0.005). The D-dimer test was negative in all women in control group. Positive D-dimer was significantly seen in those with prolonged duration of menstruations (>7days) compared to those with short duration of cycles with (p<0.05) as shown in Figure1.

Plasma fibrinogen level was significantly lower in patients with positive D-dimer with (p<0.05) (Table 1). Significant negative correlation was found between plasma fibrinogen level and duration of menstrual cycle (Figure 2) (p<0.05).

Antifibrinolytic agent (tranexamic acid) was given to all patients, 15/16 (93%) of women responded to the treatment in group I, while the response in the group II was in 20/37 (54%). The drug was used for three cycles starting from the first day of the cycle and for 5days in a dose of 500mg three times per day.

Figure(1): The significance of positive D-dimer reaction in patients with prolonged duration of menstrual cycle.

Figure(2): Correlation between plasma fibrinogen level and duration of menstrual cycle.
DISCUSSION

In this study positive plasma D-dimer test (level >0.5 mg/ml) was found in 19/53 (36.2%) of cases with idiopathic menorrhagia. The D-dimer is a marker of fibrinolysis, and has been mentioned in many studies. Bish et al mentioned that the fibrinolytic activity could be a cause of idiopathic menorrhagia, using the serum fibrin/fibrinogen degradation products (FDP) as a guide.

Positive plasma D-dimer test was more significantly seen in our patients with prolonged duration of the cycle (>7days) figure (1), positive correlation between duration of bleeding and FDP level was observed by others. In the present study significantly lower plasma fibrinogen level was found in patients with positive plasma D-dimer reaction group I compared to both (group II) and the control group (table 1) (p<0.05), and this may be attributed to excessive fibrinolytic activity present in such cases. The significantly low plasma fibrinogen level found in those with long cycle indicates increased fibrinolysis in these patients (figure 2). Bleeding in group II may be due to increased fibrinolytic activity in uterus, secondary to plasmogen activator. Such patients (group I and group II) are likely to be benefited with antifibrinolytic agents also as mentioned by others. Antifibrinolytic agent reduced the menstrual loss by about 50%. In our study we have 82.5% women with anaemia, and this was most probably due to the large amount of blood loss during menstruations.

CONCLUSIONS AND RECOMMENDATIONS

Increased fibrinolytic activity may cause idiopathic DUB, which could be assessed by D-dimer test and plasma fibrinogen assay.

REFERENCES