Increased blood viscosity in young women using oral contraceptives

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Blood viscosity and its major determinants (hematocrit, plasma fibrinogen, and plasma viscosity) were measured in 25 men, 25 women who were not using oral contraceptives, and 25 women who had been using oral contraceptives for at least 3 months. Mean blood viscosity and hematocrit were significantly higher in women using oral contraceptives than in women who were not ($p < 0.001$), and use of oral contraceptives abolished the normal sex difference in blood viscosity and hematocrit. After correction to a standard hematocrit of 45%, blood viscosity was still higher in users of oral contraceptives, as was plasma fibrinogen ($p < 0.05$). Plasma viscosity was not significantly increased in users of oral contraceptives. (AM. J. OBSTET. GYNECOL. 137:840, 1980.)

USE OF estrogen-containing oral contraceptives is associated with increased risk of venous thromboembolism, occlusive arterial disease, and hypertension.[1] Increased blood viscosity is also associated with these disorders.[2] In subjects commencing use of oral contraceptives there are sequential increases in blood viscosity[3] and its major determinants, hematocrit[3] and plasma fibrinogen.[4] We performed a cross-sectional study of blood viscosity, hematocrit, fibrinogen, and plasma viscosity in young women, with respect to use of oral contraceptives.

Methods

We studied 75 healthy volunteers from the hospital staff, aged 18-29 years: 25 were male and 50 were female. Only women who had been using estrogen-containing oral contraceptives for at least 3 months (users) and women who had never used oral contraceptives (nonusers) were studied. No subject was receiving other medication. A midmorning, nonfasting venous blood sample was taken after 10 minutes' rest. Women were studied at the midpoint of the menstrual cycle (day 13 to day 15), to minimize menstrual variations in blood viscosity and its determinants.[5] Blood was anticoagulated with ethylenediaminetetra-acetic acid (1 mg/ml) for measurement of blood viscosity at 37° C, with a shear rate of 100 sec^{-1}, in a rotational viscosimeter.[6] Plasma viscosity (37° C, BS M3 capillary viscosimeter) and microhematocrit (Hawksley, 13,000 × g for 5 minutes) were measured on the same sample. Fibrinogen was measured in citrated plasma by the method of Clauss,[7] with a Dade fibrometer and standards. Differences in means were analyzed by Student's t test, and correlations were determined by the method of least squares.

Results

Table I shows that mean blood viscosity and mean hematocrit were significantly higher in men than in women not using oral contraceptives ($p < 0.001$). In women using oral contraceptives, mean blood viscosity and mean hematocrit were significantly higher than in nonusers ($p < 0.001$) and not significantly different from male values ($p > 0.1$).

Blood viscosity correlated linearly with hematocrit ($r = 0.7$). After correction to a standard hematocrit of 45% by use of this regression curve,[2] mean blood viscosity was significantly higher in women using oral contraceptives than in nonusers or in men ($p < 0.05$). Plasma fibrinogen was significantly increased in users of oral contraceptives compared to nonusers ($p < 0.05$) but not compared to men ($p > 0.1$). Plasma viscosity

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Received for publication October 24, 1979.

Accepted February 14, 1980.

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0002-9378/80/150840+03$00.30/0

Table I. Clinical details and blood viscosity factors in subjects studied (mean ± SEM)

	Men	*Women (nonusers)*	*Women (users)*
No.	25	25	25
Age (years)	23.9 ± 0.6	22.7 ± 0.5	22.8 ± 0.5
Smokers	10	9	8
Blood viscosity (cp)	6.60 ± 0.09	6.01 ± 0.10	6.71 ± 0.11
Hematocrit (%)	45.0 ± 0.5	40.3 ± 0.7	44.0 ± 0.5
Blood viscosity (cp) (hematocrit 45%)	6.60 ± 0.07	6.57 ± 0.08	6.84 ± 0.08
Fibrinogen (gm/L)	2.46 ± 0.08	2.31 ± 0.09	2.71 ± 0.13
Plasma viscosity (cp)	1.36 ± 0.02	1.35 ± 0.03	1.39 ± 0.03

cp = Centipoise.

was not significantly elevated in users of oral contraceptives ($p > 0.1$). Fibrinogen correlated with corrected blood viscosity ($r = 0.38$) and plasma viscosity ($r = 0.55$). No significant differences in blood viscosity or its determinants were found when women who smoked were compared with nonsmokers or when users of oral contraceptives containing 30 μg of estrogen ($n = 10$) were compared with users of 50 μg preparations ($n = 15$).

Comment

The major determinant of blood viscosity is the unit volume of packed red cells, or hematocrit.[2] It is well known that menstruating women have a lower hematocrit and, hence, lower blood viscosity than men.[8] It has been suggested that this lower blood viscosity may be one factor protecting female subjects from atherosclerotic vascular disease before the menopause.[8] In the present study, we have confirmed this sex difference in hematocrit and blood viscosity. We also have shown that women who have been using estrogen-containing oral contraceptives for at least 3 months have increased midcycle levels of hematocrit and blood viscosity as compared to nonusers and that use of oral contraceptives abolishes the normal sex difference in these variables. The results from this cross-sectional study are in accordance with the sequential study of Aronson and associates,[3] who found increases in blood viscosity and hematocrit in subjects commencing oral contraceptive use. Our finding of an increased hematocrit in women using oral contraceptives is supported by data from a large study of women attending a family planning clinic, which show a statistically highly significant increased mean hemoglobin level in subjects using oral contraceptives.[9] It is likely that oral contraceptives give rise to increased hematocrit and hemoglobin levels by decreasing menstrual blood loss and protecting against the development of iron-deficiency anemia.[9, 10] The resulting increase in red cell mass must presumably outweigh the increase in plasma volume produced by oral contraceptive use.[11]

When blood viscosity is corrected to a standard hematocrit, it correlates with the plasma fibrinogen level, and fibrinogen is thought to be the second major determinant of blood viscosity.[2] In this study we found that, after correction for hematocrit, blood viscosity was higher in users of oral contraceptives than in nonusers or in men. This may be due in part to the increased fibrinogen level in users of oral contraceptives, which has also been documented in previous studies.[4] However, the correlation between fibrinogen and blood viscosity was not high, and other determinants of viscosity may be involved, such as alpha-2 macroglobulin[4] or red cell deformability.[12] Nevertheless, we have shown that the two major determinants of blood viscosity, the hematocrit and the plasma fibrinogen level, are both increased in users of oral contraceptives and combine to increase blood viscosity.

Increased blood viscosity tends to increase blood pressure and is associated with arterial and venous occlusive diseases.[2] While further studies are required to determine the role of blood viscosity in the development of circulatory complications of oral contraceptive use, the effects of oral contraceptives should be considered in studies of blood viscosity and its determinants.

We thank Staff Nurse M. McColl for her assistance.

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