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Variations of the Platelet Aggregation During the Cycle of Menstruation *

J. A. Aznar, J. Aznar and A. Fernández-Pavón

Laboratorio de Hemostasia y Trombosis
and Laboratorio Clínico y Bioquímica
Ciudad Sanitaria «La Fe»
Valencia (Spain)

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The platelet aggregation during the menstrual cycle has been studied. They have found a significant decrease of the aggregation on the 13th-14th days of the menstrual cycle.

The significant of the preliminary results are briefly discussed.

It seems likely that between the blood hormonal measure and a certain tendency to thrombophilia, there are reasons for correlation which are not well established. A proof of it can be the anomalies of the hemostasia appearing in the last months of pregnancy (21), which seem to be related to the estrogenic measure (21). It can also be connected with this fact the tendency to thromboembolic accidents found by some authors in women getting oral anticonceptives (7, 18, 31), or even more precisely the increases of the platelet adhesion subsidiary to such therapeutics (9, 20, 22). It is just in the anticonceptive therapeutics called sequential where these alterations seem to be more evident (19). Consequently, and considering the similarity of its hormonal cadence to the cycle of menstruation, we thought it would be interesting to study the aggregation of the platelets during such a cycle, with a view to finding out whether there is any relationship between the thrombocytary function and the said cycle.

Materials and Methods

For this study, we have chosen a group of 13 healthy nurses, of an age from 18 to 25, none of whom showed any previous alteration of the hemostatic system.

As a technique of study, it has been chosen Born's modified photocolorimetric technique (3).

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Results

By valuing the platelet aggregation activated with ADP and adrenaline (Table I), we notice how the former is smaller on the 13th-14th days of the menstrual cycle. This is also verified by cosidering the aggregation indexes (Table II), finding that the differences between the various days are significant.

By studying the platelet aggregation in a group of men, of an age similar to that given above for women, we notice that their average aggregation index is most similar to that obtained in the group of women during the first days of the menstrual cycle (Table I). This can be quite interesting if we bear in mind that the feminine hormonal measure is minimum in the first days of the menstrual cycle.

Discussion

Judging by the present knowledge, it seems undoubtable that the platelet hyperfunction plays an important part in the pathogeny of thrombosis (23). Likewise, it is also admitted by many authors that some states of hormonal disequilibrium may favour the appearance of thromboembolic phenomena. Such is the case, for instance, with the last months of pregnancy (21), when most probably depending on an increase of estrone and progesterone (21) measure we have been able to find an increase in the incidence of thromboembolic phenomena, as well as an increase of the platelet adhesion (28). This last fact has not been proved by other authors (24). It also seems that during the hormonal anticonceptive the-

Table I. *Curves of platelet aggregation with A.D.P. (0.4 μg/ml) and adrenaline (1 μg/ml).* The curves are expressed in absorption units. Before beginin the experiments the galvanometer record was calibrated to zero of O.D. with distilled water and to 40 with the plasma problema. The curves represent the average of 13 healthy female group of 18 to 25 years old during the menstrual cycle and 25 healthy men of the same age.

Sex	Days of menstrual cycle	Aggregation Curve O.D.											
		A.D.P.					Adrenaline						
Woman	1-2	21.6	16.7	15.7	15.9	16	30.9	27.3	24.4	21.6	19.6	18.2	16.7
	13-14	27.3	23.3	22.7	23.4	24.6	32.2	30.8	29.6	27.1	25.6	24.2	23
	23-24	24.9	19.6	18.3	18	18.6	32.7	29.4	25.9	23.1	20.8	19.2	17.7
Man	—	21.5	16.6	15.6	15.1	16.6	28	23.3	20	17.5	16.1	15	14.5

Table II. *Values of the mean aggregation indexes corresponding to the 1-2, 14-15 and 23-24 days of menstrual cycle.*
The experiments were made in a group of 13 healthy women.

Days of menstrual cycle	Aggregation Indexes			
	Adrenaline		A.D.P.	
1-2	65.46 ±5.96	P=0.0044	62.23 ±6.25	P < 0.001
14-15	48.07 ±9.25	P=0.08	44.38 ±6.29	P < 0.001
23-24	60.69 ±9.24		56.46 ±4.51	

rapeutics, there exists a greater tendency to the appearance of thromboembolic phenomena (2, 7, 18, 19, 31, 32, 35, 36), above all when such therapeutics has an estrogenic basis (10, 17), contrary to what happens using progesterone fundamentally (29). It has also been indirectly confirmed when noticing an increase in the incidence of thromboembolic phenomena in women to whom lactation has been suppressed with estrones (11, 12). This interdependence between anticonceptives and thromboembolic phenomena is not unanimously accepted (1, 13, 14, 33, 37, 38).

Another interesting aspect in this probable hormones/thrombosis/platelet interrelation is the fact that women, during their fertile periods, seem in some way protected against infarct of myocardium (21), which in our opinion has to be prudently interpreted, thinking that just which the setting up of the menopause there can be other factors added depending on the age and wich in some way or other might influence in the appearance of the thromboembolic accidents.

Everything mentioned above makes us think that there may exist some relationship between hormonal measure and thromboembolic accidents in general, and thrombocytary function in particular, which is also corroborated by an increase of the platelet adhesion (9, 20, 22) or an accelerated aggregation (28) in patients having oral anticonceptives, though this aspect as it always happens has not been confirmed by other authors (16, 25, 30).

On account of it all, we thought it would be quite interesting to value the thrombocytary aggregation during the menstrual cycle on the one hand, because during same very definite variations of the feminine hormonal measures occur, and on other because when going through literature within our reach we have hardly found any reference to this subject. EGEBERG and OWREN (15) study the variations of different plasmatic factors in connection with the menstrual cycle and do not find any anomalies worth mentioning. BOLTON (6) studies the platelet function in connection with the menstrual cycle in two women and finds no variation of the platelets constants which could be attributed to the menstrual cycle. We have, however, found a significant decrease of the platelet aggregation precisely coinciding with the intermediate days of the cycle. Regarding this fact, OLIVER findings (8, 26) can be interesting, since they find a notable depression of the plasmatic phospholypids precisely during the central days of the menstruation, which could bear some relationship with the role that perhaps the said platelet phospholypids may play in the mechanism of trombocytary aggregation. But in any case, we think ti would be rather hazardous to establish any pathogenic hypothesis and we could only point out the fact that we have found a significant decrease of the platelet aggregation, coinciding precisely with the days of ovulation.

References

1. AMRIS, C. J. and STARUP, J.: *Acta Obst. Gynec. Scandinav.*, **46**, 78, 1967.
2. ASK-UPMARK, E., GLAS, J. E. and STERAM, U.: *Acta Med. Scand.*, **185**, 479, 1969.
3. AZNAR, J. and ALBEROLA, V.: *Coagulation*, **3**, 153, 1970.
4. BERKARDA, B., AKOKAM, G. and DERMAN, V.: *J. Atheroscler. Res.*, **5**, 595, 1965.
5. BLACKBURN, E. K.: *Brit. Med. J.*, **2**, 159, 1963.
6. BOLTON, C. H., HAMPTON, J. R. and MITCHELL, J. R. A.: *Lancet*, **1**, 1336, 1968.
7. BRITISH MEDICAL RESEARCH COUNCIL: *Brit. Med. J.*, **2**, 355, 1967.
8. BROWN, J. B.: *Lancet*, **1**, 320, 1955.
9. CASPARY, E. A. and PEBERDY, M.: *Lancet*, **1**, 1142, 1965.
10. COMMITTEE ON SAFETY OF DRUGS: C. n.° 9, 1969.
11. DANIEL, D. G., CAMPBELL, H. and TURNBULL, A. C.: *Lancet*, **11**, 287, 1967.
12. DANIEL, D. G., BLOOM, A. L., GIDDINGS,

J. C., CAMPBELL, H. and TURNBULL, A. C.: *Brit. Med. J.*, **1**, 801, 1968.
13. DRILL, V. A.: Oral Contraceptives. Mc Graw-Hill Book, Co., Inc., New York, 1966.
14. DRILL, V. A. and CALHOUN, D. W.: *JAMA*, **206**, 77, 1968.
15. EGEBERG, O. and OWREN, P. A.: *Brit. Med. J.*, **1**, 220, 1963.
16. HAM, J. M. and ROSE, R.: *Amer. J. Obst. Gynec.*, **105**, 628, 1969.
17. HILL, H.: *Practitioner*, **205**, 5, 1970.
18. INMAN, W. H. and VESSEY, M. P.: *Brit. Med. J.*, **2**, 193, 1968.
19. INMAN, W. H., VESSEY, M. P., WESTERHOLM, B. and ENGELUNDS, A.: *Brit. Med. J.*, **2**, 203, 1970
20. MARGULIS, R. R., AMBRUS, J. L., MINK, L. B. and STRYKER, J. C.: *Am. J. Obst. Gynec.*, **93**, 161, 1965.
21. MESSER, R. H.; *Med. Clin. N. Amer.*, **53**, 1085, 1969.
22. MILLER, S. P., LEE, S. L. and RITZ, N.: *Metabolism*, **14**, 398, 1965.
23. MUSTARD, J. F., ROWSELL, H. C. and MURPHY, E. A.: *Amer. J. Med. Sc.*, **248**, 469, 1967.
24. NILSSON, I. M. and KULLANDER, S.: *Acta Obst. Gynec. Scandinav.*, **46**, 273, 1967.
25. NILSSON, I. M. and KULLANDER, S.: *Acta Obst. Gynec. Scandinav.*, **46**, 286, 1967.
26. OLIVER, M. F. and BOYD, G. S.: *Clin. Sci.*, **12**, 217, 1953.
27. OLIVER, M. K. and BOYD, G. S.: *Lancet*, **11**, 690, 1959.
28. POLLER, L., PRIEST, C. M. and THOMSON, J. M.: *Brit. Med. J.*, **4**, 273, 1969.
29. POLLER, L., THOMSON, J. M., TABIOWO, A. and PRIEST, C. M.: *Brit. Med. J.*, **1**, 554, 1969.
30. ROBINSON, R. W.: *Am. J. Obst. Gynec.*, **99**, 163, 1967.
31. SARTWELL, P. E., MASI, A. T., ARTHES, F. G., GREENE, G. R. and SMITH, H. E.: *Amer. J. Epidem.*, **90**, 365, 1969.
32. SEIGEL, D. G. and MARKUSH, R. E.: *Amer. J. Epidem.*, **90**, 11, 1969.
33. SWYER, G. I. M.: *Brit. Med. J.*, **1**, 355, 1966.
34. ULUTIN, O.: Chapter in «Recent Advances in Blood Coagulation». Edit. by Poller. Churchill, London, 1969.
35. VESSEY, M. P. and DOLL, R.: *Brit. Med. J.*, **2**, 199, 1968.
36. VESSEY, M. P. and DOLL, R.: *Brit. Med. J.*, **2**, 651, 1969.
37. WHO: *Techn. Rep. Ser.*, **326**, 1, 1966.
38. WINTER, I. C.: *Metabolism.*, **14**, 422, 1965.