Transient ischaemic attacks and increased platelet aggregability associated with oral contraceptives

Treatment with dipyridamole and aspirin

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SUMMARY A 24 year old woman after using birth control pills for two months began to suffer from frequent migraine-like attacks, which turned eventually into typical transient ischaemic attacks (TIAs). A significant increase in spontaneous platelet aggregation was found, and combined treatment with dipyridamole and aspirin was started. After two months of treatment spontaneous platelet aggregation rate fell to normal limits and the TIAs disappeared. A causal relationship between increased platelet aggregability and TIAs is supposed.

Since increased platelet aggregability in patients with cerebral vascular disease was found (Sano *et al.*, 1971; Danta, 1973), its causal role in cerebral ischaemia and thrombosis was postulated (Kalandovsky *et al.*, 1975). To prove this assumption additional studies on large numbers of cases should be undertaken, but well-investigated individual cases, such as the following, can demonstrate a certain relationship between increased platelet aggregability and cerebral ischaemia.

Report of a case

A 24 year old woman started to take birth control pills² one year before her admission. She had always been healthy; her present history and her family history showed no incidence of migraine. Ten months before her admission attacks of paroxysmal headache appeared which lasted from two to 24 hours with a frequency of about four to five times a month. Seven months later transient numbness over her right arm and right half of her face appeared, which subsided after half an hour and was followed by a severe generalised headache lasting a few hours. She was seen by a neurologist the same day. No pathological signs were found in the neurological

examination; EEG, echoencephalogram, and isotope brainscan were normal. A local vascular lesion in the left cerebral hemisphere was suspected and she was referred for admission, for left carotid arteriography. Her birth control pills were immediately discontinued. During the following three months until her admission she experienced approximately 12 to 15 attacks of transient numbness which was usually limited to the right arm and right half of the face but sometimes also spread to the right leg. Most, but not all, of the attacks were followed by severe generalised headache lasting for two to three hours. On some occasions the patient suffered from paroxysmal headache for a few hours, without previous numbness.

On admission, repeated EEG examinations (one of them performed during one of her typical attacks) did not reveal any abnormalities. Left carotid arteriography revealed an area of decreased vascularity and swelling in the left suprasylvian region. All blood coagulation tests were normal except for the platelet aggregation test which showed a significant increase in spontaneous aggregation (79%, see Table), while the normal level by the method used in our laboratory (Holdrinet *et al.*, 1969) is up to 25%. Combined treatment with dipyridamole 100 mg and aspirin 1 g daily was started. After one month of treatment spontaneous platelet aggregation was still increased (68%) but she experienced only two attacks of transient numbness. After the second month of treatment her spontaneous platelet aggregation was normal (27%). Seen three months after her discharge

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² Madinon-S, sequential regime: Mestranol 80 µg for 11 days followed by mestranol 80 µg and chlormadinone 2 mg for 10 days.

Accepted 24 August 1976

Table Platelet aggregability before and during treatment with dipyridamole and aspirin

Platelet aggregability tests	Before treatment (%)	4th week of treatment (%)	8th week of treatment (%)
Spontaneous aggregation	79.3	68.2	27.3
ADP-induced aggregation	84.9	89.2	76.7

from the department, she reported that she was free from any attacks of numbness for at least two months.

Comment

Studies conducted to determine the relation between the use of oral contraceptives and the occurrence of stroke in young women estimate that the relative risk of cerebral ischaemia or thrombosis is from six to nine times greater for women who use oral contraceptives than for those who do not (Masi and Dugdale, 1970; Collaborative Group for Study of Stroke in Young Women, 1973). In the search for mechanisms underlying strokes in women who are taking oral contraceptives, the blood clotting factors and blood coagulability in these cases were thoroughly investigated and an increased rate of platelet aggregation in a number of cases was definitely established (Kalendovsky *et al.*, 1975). From these findings three possibilities can be assumed:

1. Increased platelet aggregation in such cases may be a secondary reflection of the appearance of damaged brain tissue (major cerebral infarction, for example).

2. The same common factor (oral contraceptives) influences the simultaneous appearance of both increased platelet aggregation and thrombosis, but there is *no causal* relationship between them.

3. Cerebral ischaemia or thrombosis in these cases is a consequence of the tendency to increased blood coagulability, in particular, increased platelet aggregability.

The first suggestion seems unlikely, as it was found that platelet aggregation was significantly accelerated in women taking oral contraceptives without any clinical or laboratory signs of an ischaemic or thrombotic event. Prospective follow-up studies, taking into account blood clotting factors and changes in platelet activity in women taking oral

contraceptives, showed an inevitable acceleration of platelet aggregation rate appearing already during the third month of combined oestrogen-progestogen oral contraception (Poller *et al.*, 1969). These findings, together with the fact of high incidence of cerebral ischaemia and thrombosis during oral contraception, make the causal relationship between accelerated aggregation and thrombosis quite feasible, but the possibility of their simultaneous appearance due to a factor common to both of them (use of oral contraceptives), without causal relationship between them, should also be considered.

In our case, there were seen a decrease in frequency and later disappearance of transient ischaemic attacks simultaneously with the decreasing and eventual normalisation of previously highly abnormal platelet aggregability during the combined treatment with dipyridamole and aspirin. It may be concluded that the increased platelet aggregation was one of the factors which influenced the appearance of the transient ischaemic attacks. It is worth while to point out the excellent therapeutic effect of treatment with dipyridamole and aspirin.

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