Platelet adhesiveness in gout

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Summary

Platelet adhesiveness studies were performed by two techniques in twenty-two gout patients and closely matched controls under carefully standardized conditions. No significant difference in platelet adhesiveness was found between the groups.

A RANGE of plasma lipid levels was recently investigated in twenty-two adult British gout patients and in twenty-two very closely-matched controls, who were hospital patients suffering from a wide variety of conditions. The results of this study have been presented (Darlington, Shaw & Scott, 1971; Darlington & Scott, 1972). Summarized, they showed no significant difference between plasma cholesterol levels, but significantly higher levels of plasma glycerides and phospholipids ($0.01 > P > 0.001$) and very significantly higher levels of plasma unesterified fatty acids in the gout patients ($P < < 0.001$) (Table 1).

TABLE 1. Summary of statistics of lipid studies in twenty-two gout patients and twenty-two controls

	<i>t</i>	<i>P</i>
Cholesterol—gout vs controls	1.260	$> 0.2, < 0.3$
Glycerides—gout vs controls	3.15	$> 0.001, < 0.01$
Phospholipids—gout vs controls	2.966	$> 0.001, < 0.01$
UFA—gout vs controls	4.530	$< < 0.001$

Kerr *et al.* (1965) found that certain phospholipid fractions and free fatty acids caused platelet aggregation; a result confirmed with regard to fatty acids by Hoak, Warner & Connor (1967).

Because of increased levels of phospholipids and unesterified fatty acids in gout patients, and because it has been suggested that there is a high incidence of cardiovascular disease in gout (Weiss & Segaloff, 1959; Hall, 1965), platelet adhesiveness studies have been performed in the gout patients and controls from the study of Darlington *et al.* (1971), and the results are now presented.

Patients, methods and related factors

Two techniques were performed in parallel, using whole blood and platelet-rich plasma, by the method of Shaw, Pegrum & Wolff (1970). In this method, blood and platelet-rich plasma were passed through a standard column of glass microspherules at a constant rate. Adenosine diphosphate was added to the platelet-rich plasma before passage through the column. Platelet adhesiveness was obtained by taking the difference between the platelet count before and after passage through the column and expressing it as a percentage of the initial count. Factors affecting the test conditions, blood sample and the state of the patient were carefully standardized as follows: (1) All subjects had fasted for at least 10 hr before the test, to give a result in the fasting state and to reduce variables of intestinal absorption. Ingestion of glucose and fat increase platelet adhesiveness (Bridges *et al.*, 1965; McDonald & Edgill, 1958). (2) Adhesiveness was determined within 1-2 hr of taking blood, since the time interval after venepuncture is important (Fyfe & Hamilton, 1967). (3) Patients were asked not to smoke for at least 9½ hr before the test since smoking has variable effects which may cause platelet adhesiveness to be affected by fatty acids and glucose in the plasma (Murchison & Fyfe, 1966). (4) No patient or control was receiving aspirin therapy and all subjects were asked to avoid this drug before the test. Aspirin may affect several tests of platelet activity (O'Brien, 1968a) and it appears that, in most circumstances, ADP is not released from platelets exposed to aspirin (O'Brien, 1968b). (5) No patient or control was on any drug known to affect plasma lipids or platelet adhesiveness. (6) Patients were seen early in the morning when exercise had been minimal but accurate assessment of the amount of exercise was nevertheless difficult. Acute, exhaustive exercise increases platelet adhesiveness (Ikkala, Myllylä & Sarajas, 1966) but severe, prolonged exercise caused a fall in platelet adhesiveness (Pegrum *et al.*, 1967).

Following the initial work of Wright (1942), many workers have recorded variations in platelet adhesiveness after surgery and, hence, no abnormal platelet adhesiveness result was accepted until three months or more had elapsed after any trauma or surgery.

Since the work was carried out under the standardized conditions laid down by Shaw *et al.* (1970) and in the same laboratory, their normal values for healthy blood donors were used to give the ranges of normal platelet adhesiveness for whole blood and platelet-rich plasma, i.e. 35–72% and 19–65% respectively.

Results

The platelet adhesiveness values obtained are summarized in Table 2. A regression analysis was performed to determine the significance of these results and is summarized in Table 3. This analysis showed no significant difference in platelet adhesiveness between gout patients and controls by either technique ($P \gg 0.1$).

TABLE 2. Comparison of platelet adhesiveness between gout patients and controls

	Mean $\pm$ SD	
	Whole blood (%)	Plasma (%)
Gout patients	52.2 $\pm$ 12.8	30.3 $\pm$ 12.7
Controls	51.8 $\pm$ 13.6	25.4 $\pm$ 8.0

TABLE 3. Regression analysis

	Coefficient of correlation (r)	P
Gout patients vs controls by whole blood technique	-0.177	$\gg 0.1$
Gout patients vs controls by plasma technique	-0.181	$\gg 0.1$

TABLE 5. Statistics to assess the effect of mobility on platelet adhesiveness

	Mobile patient		Immobile patient		Combined SD	t	P
	Mean	Variance	Mean	Variance			
Whole blood	51.47	165.8	51.5	195	13.2	0.0011	> 0.9
Plasma	29.8	146.5	24.15	50.97	10.89	1.56	> 0.1 < 0.2

TABLE 6.

	Whole blood		Plasma		Combined SD	t	P
	Mean	Variance	Mean	Variance			
Mobile patients	51.7	187	29.4	148	12.9	6.803	< 0.001
Immobile patients	51.5	195	27.6	223	14.5	4.417	< 0.001

Significant correlation between the two techniques was found for both the gout patients and the controls with $r = 0.354$ and 0.407 respectively and $0.02 \geq P > 0.01$ (Table 4). This agrees reasonably with the results of Shaw *et al.* (1970) who found a coefficient of correlation, r of 0.46 between the results from the two methods with $P = 0.001$.

TABLE 4. Significance of correlation between the two techniques

Group	r	P
Control	-0.407	$> 0.01, < 0.02$
Gout	-0.354	$> 0.01, < 0.02$

Since exercise affects platelet adhesiveness it was necessary to ensure that mobility was not having a significant effect on the results obtained by either technique. The gout and control subjects were divided into two groups—those who were mobile and had been bled as out-patients and those who were immobile in-patients.

The results are summarized in Tables 5 and 6, and show that mobility did not significantly affect the results. There was, however, a very significant difference between platelet adhesiveness measurements by the whole blood and the plasma techniques, in both mobile and immobile subjects.

Discussion

This study has demonstrated that the hyperlipidaemia present in many patients with gout is not associated with increased platelet adhesiveness, since this did not differ between groups of gout patients and control subjects, as measured by two different methods. Some of the gout patients were taking treatment which was lowering the plasma concentration of uric acid (uricosuric agents or allopurinol),

but Bluestone, Lewis & Mervant (1971) and Darlington *et al.* (1971) have shown that such therapy does not produce any significant overall fall in lipid levels.

The relationship if any between gout and cardiovascular disease remains obscure, but does not appear to be related to pathological platelet adhesiveness.

Acknowledgments

We wish to thank Miss Charis E. Jocelyn and Miss Bernedette Godhino for skilled technical help. We are grateful to the Sub-committee for Clinical Research, Charing Cross Hospital, for financial support.

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