CLINICAL RESEARCH

Platelet size in myocardial infarction

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Abstract

The mean platelet volume and platelet count were measured serially in 100 patients soon after myocardial infarction and again at a follow up clinic about seven weeks later. The results were compared with those in age matched controls. The mean platelet volume after infarction (mean 9·07 fl (SE 0·08)) was significantly greater than in the controls (8·32 fl (SE 0·07); $p < 0·001$), and was still raised at the follow up clinic (8·69 fl (SE 0·10); $p < 0·01$). The mean platelet count on admission (275×10^9/l (SE 7)) was significantly lower than in the control group (295×10^9/l (SE 5); $p < 0·05$) and fell significantly during admission, with a mean change of -36×10^9/l (95% confidence limits −26, −45; $p < 0·01$). At the follow up clinic the platelet count had risen to a level not significantly different from the admission value.

As larger platelets are haemostatically more active, the finding of an increased mean platelet volume after myocardial infarction provides further evidence that abnormal platelet behaviour may be implicated in the process of infarction.

Introduction

There has been considerable interest in the possible role of abnormal platelet behaviour in the pathogenesis and prognosis of myocardial infarction, based mainly on the assessment of changes in platelet aggregation, survival time, or release reactions. With the Coulter Counter, Model S Plus, it is now possible to get from routine blood samples an estimate of platelet size, expressed as the mean platelet volume.[1] Larger platelets, as reflected by an increased mean platelet volume, appear to be more active when measured by conventional tests of platelet activity,[2-5] and in particular have an increased aggregation ability.[6 7]

The clinical importance of an increased mean platelet volume measured in this way has been shown in several studies. Nelson and Kehl found that the mean platelet volume was higher in patients with cancer who had thrombocytopenia resulting from platelet loss or consumption than in those with thrombocytopenia secondary to failure of the bone marrow.[8] Eldor *et al* showed that thrombocytopenic patients with a high mean platelet volume had a reduced chance of haemorrhage compared with patients with a low value, owing to the haemostatic superiority of larger platelets.[9]

At this centre Giles examined the mean platelet volume and platelet count in 5000 unselected patients and found varying patterns of platelet volume distribution in different clinical disorders.[10] Unpublished data associated with his work suggested the possibility of a change in mean platelet volume with myocardial infarction. We therefore performed a prospective controlled study to examine this concept.

Patients and methods

One hundred and thirteen men admitted consecutively to a coronary care unit after myocardial infarction were studied. Infarction was diagnosed on the basis of the history and characteristic electrocardiographic changes or increased cardiac enzyme activities.

Two patients were excluded: one had taken aspirin, a drug known to affect platelet behaviour, in the 72 hours before admission; the other suffered from idiopathic thrombocytopenic purpura. Eleven patients died before samples could be taken for platelet analysis. The remaining 100 patients comprised the fully investigated group, of whom seven died in hospital. The patients studied had a mean age of 55·9 (range 33-75), and their characteristics are shown in the table together with a separate breakdown of the features for those patients who died during the study and those alive at the time of follow up.

Routine anticoagulation was not used. Four patients received indomethacin for pericarditis during their three day period of blood sampling, the earliest starting 36 hours after infarction. No other drug known to affect platelet behaviour had been taken in the week before admission, nor were any used during the patients' stay in hospital. For analysis blood samples were timed from the onset of symptoms and the results grouped together in 12 hour periods.

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Details of patients studied. Results are shown according to whether the patients were alive at the time of the follow up clinic

	Patients with myocardial infarction			
	All patients	Patients alive	Patients dead	Controls
No of patients	100	86	14	200
Mean age	55·9	55·9	56·0	57·8
No with:				
Transmural infarction	77	65	12	
Non-transmural infarction	18	17	1	
Site of infarction not known	5	4	1	
Previous infarct	23	21	2	
Diabetes	8	8	0	
No who smoked on admission	48	39	7	
Mean (SE) peak lactate dehydrogenase	860 (47)	799 (46)	1262 (134)	
No taking drugs on admission:				
Digoxin	3	1	2	
Diuretics	9	8	1	
Beta-blockers	15	14	1	

On the first three days of admission early morning blood samples were taken for measuring plasma urea and electrolyte concentrations and cardiac enzyme activities. At the same time samples were collected into edetic acid for measuring haemoglobin, platelet count, and mean platelet volume with a Model S Plus Coulter Counter, which was subject to continuous quality control. All specimens were examined 30 minutes to six hours after venesection because of the slight variation in mean platelet volume that occurs during storage.[10]

Each patient was age matched with two male controls. The control subjects were hospital outpatients with no acute illness or history of myocardial infarction who had normal values for haemoglobin and white cell and platelet counts. The mean of the two control readings of platelet count and mean platelet volume were then used in the statistical analysis.

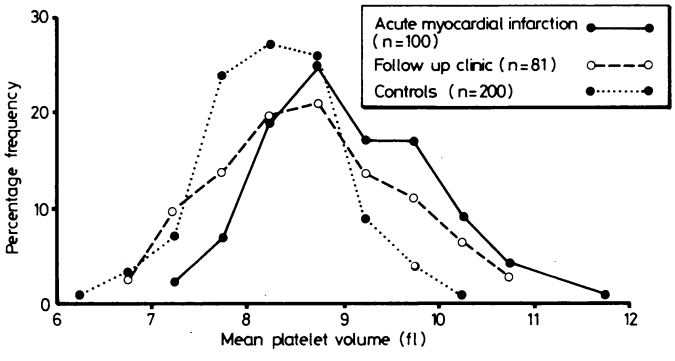
After discharge the platelet count and mean platelet volume were estimated in blood samples taken from those surviving at a follow up clinic which occurred a mean of 46 days after infarction. By this stage a further seven patients had died, and five patients did not attend the clinic for other reasons.

We used Student's paired *t* test for comparing the group means and examined correlation using the Pearson product-moment correlation coefficient.

Results

There was no significant change in the mean platelet volume during the period of blood sampling in hospital, so the mean of the three readings for each patient was used in the analysis.

The mean platelet volume during admission (mean 9·07 fl (SE 0·08)) was significantly larger than the mean of the control group (8·32 fl (SE 0·07); $p < 0·001$). At the follow up clinic the mean platelet volume of the survivors was still raised (8·69 fl (SE 0·10); $p < 0·01$), although there had been a significant fall in the value between admission and follow up ($p < 0·01$). The figure shows the percentage frequency distributions of these values and shows that the distribution of mean platelet volumes in patients with infarcts was shifted significantly to the right of that in controls.



Percentage frequency distribution of mean platelet volumes among patients after acute myocardial infarction (mean=9·07 fl), at the follow up clinic (mean=8·69 fl), and among control subjects (mean=8·32 fl).

There was no significant difference in the mean platelet volume between the patients who died during the study and those who survived. There was no significant correlation between the mean platelet volume recorded during admission and the age of the patient, the site or type of infarct, or peak values of plasma urea, lactate dehydrogenase, or alanine transaminase. The mean platelet volume was not significantly different in patients with diabetes or in patients who smoked, had received indomethacin, or had had a previous myocardial infarct.

The mean of the first platelet counts after admission (275×10^9/l (SE 7)) in the patients with myocardial infarction was significantly lower than that in the controls (295×10^9/l (SE 5); $p < 0·05$). There was a significant fall in the patients' platelet counts during admission, with a mean change of -36×10^9/l (95% confidence limits -26, -45; $p < 0·01$). There was no significant difference in platelet count between patients who died during the study and those who survived. By the time of the follow up clinic the count had risen again to a value not significantly different from that on admission.

Discussion

Our results show that the mean platelet volume was increased in association with myocardial infarction and was still raised seven weeks later. The platelet count fell during the early phase after infarction but had risen again by the time of the follow up attendance. Not all acute illnesses are associated with a raised mean platelet volume,[10] so the recorded effect seems to be more than a non-specific reaction to severe illness.

The increase in mean platelet volume did not appear to provide any prognostic information on mortality during the period of the study; the value in patients who died was no different from that of the survivors. The mean platelet volume did not correlate with the more established factors determining prognosis after infarction, such as the size or type of infarct.

Our finding of increased platelet size in patients with myocardial infarction agrees with the work of Enticknap *et al*, who measured the calculated geometric platelet volume.[11] They also found that the platelet size was increased to a lesser degree in patients with chronic angina, and Daniel *et al* have shown an increased mean platelet volume in a group of patients more than three months after infarction.[12] These findings support the idea that changes in platelet size may be linked to the development of infarction. In our study the raised mean platelet volume recorded within hours of infarction must, in part, have been derived from platelets circulating before the onset of symptoms.

Conflicting evidence has been obtained from studies of platelet behaviour after myocardial infarction.[13–16] Even so, many of these findings agree with what is known about the activity of larger platelets from studies of subjects without infarction: the adhesive capacity,[5] sensitivity to aggregating agents,[2 3] and serotonin uptake and release[17] of larger platelets are all increased. Heptinstall *et al* found that patients dying within a year of infarction had had a greater platelet serotonin release reaction during admission than the survivors.[18] It will be interesting to see if a larger mean platelet volume is associated with a less favourable long term prognosis.

When platelets appear in the circulation they are probably of varying sizes,[19] and changes in size may not just be related purely to aging.[20] The fall in platelet count and increased mean platelet volume in our study might suggest that smaller platelets had been consumed preferentially. A shortened platelet survival time soon after infarction has been shown,[21] but further work on platelet turnover and volume distribution in myocardial infarction is required before the mechanism of our observation can be elucidated. Larger platelets have appeared with infarction, and in view of their characteristics they may have a specific role in the production of infarction. As larger platelets are haemostatically more active it is an appealing, though unproved, idea to link the presence of large platelets with "coronary thrombosis."

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Failure of bromocriptine to maintain reduction in size of a macroprolactinoma

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Abstract

A patient with a macroprolactinoma was treated with bromocriptine 15 mg daily. Both the size of the tumour as shown by computed tomography and the serum prolactin concentration decreased over several months but then increased. The dose of bromocriptine was increased to 40 mg daily but tumour growth continued, and the tumour was resected. Production of prolactin by cultured cells was not inhibited by high concentrations of bromocriptine, suggesting that regrowth of the tumour was due to cells resistant to dopamine agonist action.

This case of regrowth of a prolactinoma during bromocriptine treatment after an initial reduction in size indicates the need for close surveillance especially of patients whose serum prolactin concentration fails to fall into the normal range with bromocriptine treatment.

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Introduction

Treatment with bromocriptine reduces the size of macroprolactinomas[1 2] and is advocated as the initial treatment of choice.[2 3] Clearly, the tumour may enlarge when bromocriptine treatment is stopped,[4] but no case has been reported in which the size of the tumour decreased initially with bromocriptine treatment but subsequently increased despite continuing treatment. We now report such a case.

Case report

A 47 year old man presented in November 1981 with a history of failing vision for five months and headaches for one month. Libido and potency had waned over the past five years, and he had had diminished energy and cold intolerance for several months. On examination he had reduced visual acuity (right 6/24, left 6/36) and bitemporal hemianopia. Both testes were soft and 12 ml in volume.

X ray examination of the skull showed an enlarged and eroded pituitary fossa. A computed tomograph of the head showed a large contrast enhancing pituitary tumour with suprasellar extension (fig (A)). Serum prolactin concentration was 135 000 mU/l (normal < 500 mU/l). Serum follicle stimulating hormone concentration was 2 IU/l (normal 3-20 IU/l), luteinising hormone concentration 3 IU/l (normal 5-20 IU/l), and testosterone concentration 3 nmol/l (0·87 ng/ml) (normal in men 10-35 nmol/l (2·9-10·1 ng/ml)). Serum thyroxine concentration was 40 nmol/l (3·1 μg/100 ml) (normal 60-150 nmol/l (4·7-11·7 μg/100 ml)), free thyroxine index 31 (normal 50-140), and serum thyroid stimulating hormone concentration 1 mU/l (normal < 4 mU/l). Plasma cortisol concentration was 47 nmol/l (1·7 μg/100 ml) (normal value at 0800 > 150 nmol/l (> 5·4 μg/100 ml)).

Adrenal and thyroid hormone replacement was begun. Bromocriptine treatment was started at 2·5 mg daily increasing to 15 mg daily in divided doses over one week; this was continued uninterrupted throughout his care. Subjective visual improvement occurred within