

Platelet size in patients with chronic airflow obstruction with and without hypoxaemia

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ABSTRACT Platelet size, expressed as mean platelet volume, was estimated in 35 patients with chronic airflow obstruction and a wide range of arterial oxygen tension (PaO_2) values. In these patients there was a negative correlation between MPV and PaO_2 ($r = -0.70$). Mean platelet volume was greater (9.41 (0.86) fl) in 20 patients with an arterial PaO_2 of 8 kPa (60 mm Hg) or less than in 18 normal subjects (8.21 (0.63) fl; $p < 0.001$). After 24 hours of supplemental oxygen treatment there was a small fall in mean platelet volume, from 9.47 (1.06) to 8.96 (0.8) fl ($p < 0.05$) in 12 hypoxaemic patients (PaO_2 breathing air ≤ 8 kPa) but no change in nine non-hypoxaemic patients. Larger platelets are considered to be haemostatically more active, leading to abnormal platelet function, which may contribute to the development of pulmonary vascular damage in chronic hypoxaemia. Supplemental oxygen may partially reverse these changes by modifying platelet size and activity.

Platelets play an important part in thrombosis and vascular damage, but their role in the pulmonary vascular changes of patients with chronic hypoxic lung disease is uncertain. Pulmonary thromboembolism has frequently been found at necropsy in patients with chronic lung disease¹ and increased platelet activity could contribute to the thrombotic events. Platelet aggregation has been shown to be increased in patients with hypoxaemia and chronic airflow obstruction,² with falls in platelet survival time, suggesting that hypoxia may increase platelet consumption.³ Evidence from work with the isolated rat lung has suggested that platelets may potentiate the hypoxic vasoconstrictor response of the pulmonary circulation, and this could contribute to the development of pulmonary hypertension.⁴

Larger platelets, as reflected by an increased mean platelet volume, appear to be haemostatically more active, with an increased aggregating ability.^{5,6} Studies in patients with myocardial infarction have shown platelet size to be increased, and this abnormal platelet function may lead to the development of coronary thrombosis.^{7,8} In patients with chronic lung disease larger, more active platelets could contribute to the development of pulmonary vascular changes.

In this study we have measured mean platelet

volume in patients with chronic airflow obstruction, with and without hypoxaemia, and investigated the short term effects of oxygen supplementation on platelet size.

Methods

We studied 35 patients (29 of them men) with chronic airflow obstruction and a wide range of arterial blood gas tensions (from PaO_2 5.54 kPa (42 mm Hg) to 11.5 kPa (86 mm Hg)). All the patients were stable clinically throughout the study period, with no exacerbations of airflow obstruction for at least two weeks before the study. None of the patients had been treated with supplemental oxygen, none was taking any medication that is known to affect platelet function, and none was smoking during the study periods. The study was approved by the London Hospital ethics committee.

The FEV_1 and the FVC were measured with a Morgan dry spirometer. Venous blood was taken without stasis and collected into potassium edetic acid. Blood was taken from the radial artery after the venous sample and analysed for gas tensions on a Radiometer ABL 1 analyser. The haemoglobin concentration, platelet count, and mean platelet volume were returned with the Coulter counter (Model S Plus IV). The Coulter counter extrapolates from the histogram of all particles measured in the range 2-20 fl the best fit log normal curve, and the platelet count and mean platelet volume were determined from the

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extrapolation. Measurements were made 30 minutes to two hours after the samples had been taken, as the mean platelet volume varies slightly with time from sampling.⁹

Twelve patients with a P_{aO_2} of 8 kPa (60 mm Hg) or less and nine patients with a P_{aO_2} of more than 8 kPa (60 mm Hg) were treated in hospital with continuous supplemental oxygen via a face mask at 4 l min^{-1} for 24 hours. Arterial blood gas tensions, platelet count, and mean platelet volume were determined before and after the 24 hours of oxygen treatment. There were no alterations in the patients' medication during the study period.

Student's *t* test (two tailed), paired or unpaired as appropriate, was used for comparison of means for parametric data and the linear correlation coefficient (*r*) was calculated. Values of *p* below 0.05 were taken as significant.

Results

Table 1 shows the clinical details of the patients studied. The relationship between P_{aO_2} and mean platelet volume for the patients is shown in figure 1, mean platelet volume increasing with the fall in P_{aO_2} ($r = -0.70$; $p < 0.001$). The mean of the mean platelet volumes (9.41 (0.86) fl) for 20 patients with arterial hypoxaemia ($P_{aO_2} \leq 8 \text{ kPa}$ (60 mm Hg)) was significantly greater than the mean (7.83 (0.60) fl) for 15 patients without hypoxaemia ($p < 0.001$). The mean for the hypoxic group was also greater than the mean for a group of 18 normal subjects without chronic airflow obstruction (8.21 (0.63) fl; $p < 0.001$). There was no significant correlation between mean platelet volume and P_{aCO_2} .

Table 2 compares the subjects who were treated with 24 hours of supplemental oxygen—12 hypoxaemic patients and 9 non-hypoxaemic patients. Mean P_{aCO_2} and packed cell volume were both greater in the hypoxaemic patients ($p < 0.01$), while mean P_{aO_2} was significantly lower in the hypoxaemic group (7.27 (0.88) kPa (54.5 \pm 6.6 mm Hg)) than in the non-

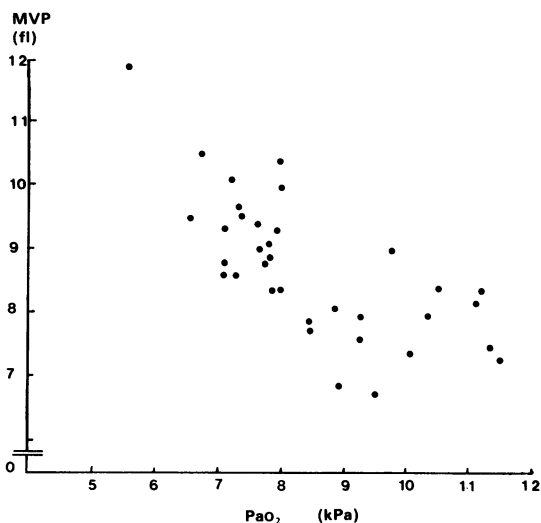


Fig 1 Relationship between mean platelet volume (MPV) and arterial oxygen tension (P_{aO_2}) in the 35 patients studied. Conversion: SI to traditional units: 1 kPa = 7.5 mm Hg.

hypoxaemic group (9.93 (1.12) kPa (74.5 (8.4) mm Hg); $p < 0.001$). After oxygen treatment there was a significant rise in mean P_{aO_2} in both groups ($p < 0.001$). There was a small fall in the mean mean platelet volume in the hypoxaemic group—from 9.47 (1.06) fl before treatment to 8.96 (0.8) fl ($p < 0.05$) after 24 hours of oxygen treatment—but no significant change in the non-hypoxaemic group after oxygen (fig 2).

The mean platelet count was lower for the 12 hypoxaemic patients than for the nine non-hypoxaemic subjects ($p < 0.05$; table 2). When the platelet counts were assessed for all 35 patients, however, there was a weak correlation with P_{aO_2} ($r = 0.41$; $p < 0.05$) and with mean platelet volume ($r = -0.46$; $p < 0.01$). The 20 hypoxaemic patients had a lower mean platelet count (254.5 (91.9) $\times 10^9/l$) than the 15 non-hypoxaemic patients (316.5 (90.6) $\times 10^9/l$), but this difference was not significant. There was no change in the platelet counts after 24 hours of oxygen treatment.

Discussion

We have shown that platelet size as reflected by the mean platelet volume increases with increasing hypoxaemia in patients with chronic airflow obstruction. Larger platelets are thought to be more active⁶ and thus hypoxaemic patients will show increased platelet aggregation, leading to the release of more platelet vasoactive substances.¹⁰ This could contribute to the development of pulmonary vascular damage.

Table 1 Clinical details of the 35 patients studied

	Mean	Range
Age (y)	65.2	45–80
FEV ₁ (l)	0.84	0.43–1.8
Forced vital capacity (l)	1.97	1.04–3.25
P_{aO_2} (kPa)	8.46	5.54–11.5
P_{aCO_2} (kPa)	5.74	4.19–8.13
Haemoglobin (g/dl)	14.5	10.7–19.5
Packed cell volume	0.44	0.32–0.57
Platelet count ($\times 10^9/l$)	281	132–479

Conversion: SI to traditional units—Arterial oxygen (P_{aO_2}) and carbon dioxide tension (P_{aCO_2}): 1 kPa = 7.5 mm Hg.

Table 2 Comparison of patients with and without hypoxaemia treated with supplemental oxygen (mean (SEM) values)

	Hypoxaemic (n = 12)	Non-hypoxaemic (n = 9)	Significance
Age (y)	67.8 (7.29)	66.9 (11.2)	NS
FEV ₁ (l)	0.77 (0.27)	0.94 (0.43)	NS
Forced vital capacity (l)	1.90 (0.48)	1.97 (0.66)	NS
Pao ₂ (kPa), breathing air	7.27 (0.88)	9.93 (1.12)	p < 0.001
Paco ₂ (kPa), breathing air	9.58 (1.59)	13.1 (2.48)	p < 0.001
Pao ₂ (kPa), oxygen	6.21 (1.03)	4.85 (0.95)	p < 0.01
Paco ₂ (kPa), oxygen	7.01 (1.29)	4.95 (0.44)	p < 0.001
Packed cell volume	0.45 (0.05)	0.38 (0.04)	p < 0.01
Platelet count (× 10 ⁹ /l)	268.8 (94.2)	361.9 (82.6)	p < 0.05
Mean platelet volume (fl)	9.47 (1.06)	7.52 (0.50)	p < 0.001

Conversion: SI to traditional units—Arterial oxygen (Pao₂) and carbon dioxide (Paco₂) tension: 1 kPa = 7.5 mm Hg.

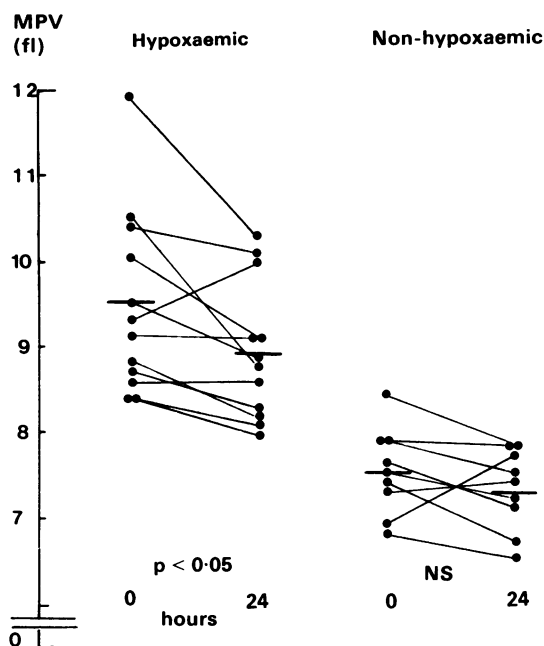


Fig 2 Changes in mean platelet volume (MPV) in 12 hypoxaemic patients and nine non-hypoxaemic patients before and after 24 hours of oxygen treatment.

The mechanisms causing the increase in platelet size are not clear but hypoxia may have a direct effect on platelet production, with the release of larger, metabolically more active platelets. The change in platelet size could also be produced by a selective consumption of smaller platelets in hypoxaemic con-

ditions, leaving the larger platelets in the circulation. In hypoxic rabbits at simulated high altitude platelets are sequestered in the lung.¹¹ Platelet survival times are decreased in hypoxaemic patients, but increase with oxygen treatment,⁴ suggesting that the faster platelet consumption can be reversed with supplemental oxygen. With short term (24 hour) oxygen treatment we found a reduction in platelet size, indicating that these changes are also reversible with oxygen. Hypoxia may cause endothelial injury¹² in the pulmonary circulation, which could further increase platelet aggregation and consumption.

Recent evidence has suggested that platelets are produced by physical fragmentation in the pulmonary circulation and not by megakaryocyte budding in the bone marrow.^{13,14} Alteration of the pulmonary vasculature in chronic airflow obstruction could lead to a decrease in the number of fragmentation steps and thus the formation of larger platelets. Although it was initially reported that larger platelets are "younger,"¹⁵ recent evidence suggests that there is no significant relationship between platelet size and age, and thus the variation in platelet volume will be more dependent on the mechanisms of platelet formation.¹⁶ Supplemental oxygen could reverse hypoxic vasoconstriction and increase the number of megakaryocyte fragmentations, resulting in the formation of smaller platelets. This mechanism could explain the effects of the relatively short term oxygen treatment on platelet size that were found in this study. Further studies are required to assess the effects of long term oxygen treatment on platelet size and function.

Exposure to chronic hypoxia in mice produces thrombocytopenia but also stimulates the development of polycythaemia, which through stem cell competition may have caused the reduction in platelet count.¹⁷ A similar mechanism may be operating in our group of 12 hypoxaemic patients, who had a lower platelet count than the non-hypoxaemic patients, as the packed cell volume was higher in the hypoxaemic group. Platelet trapping and consumption in hypoxaemic lungs could also explain the reduced platelet count, though we observed no changes in the counts after oxygen treatment.

This study shows that platelet behaviour is altered in patients with chronic hypoxaemia. Possibly changes in platelet activity, produced either by supplemental oxygen or by pharmacological methods, would reduce pulmonary vascular damage and improve survival in patients with chronic lung disease.

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