Short report

Exercise induced mobilisation of the marginated granulocyte pool in the investigation of ethnic neutropenia

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Abstract

This study was designed to determine whether ethnic neutropenia is caused by an increased proportion of neutrophils being present in the marginated granulocyte pool. Thirty two healthy volunteers, half of whom were African or Afro-Caribbean and half of whom were white, exercised vigorously for 10 minutes on a step machine to mobilise granulocytes from the marginated granulocyte pool into the circulating granulocyte pool. The amount of work performed and the pulse rate response of the two ethnic groups were compared to determine whether the exercise carried out was comparable. A full blood count and an automated differential count were performed before and after the exercise. The haemoglobin concentration, platelet count, and absolute counts of total leucocytes and leucocyte subsets before and after exercise were compared in each individual and the values in the two ethnic groups both before and after exercise were compared. The absolute increase in neutrophils in the two ethnic groups was compared. The African/Afro-Caribbean group was found to have a reduced rather than enhanced ability to mobilise neutrophils from the marginated granulocyte pool. Therefore, increased margination of neutrophils is unlikely to be the cause of ethnic neutropenia.

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Several studies from the 1940s onwards have shown that healthy subjects of African ancestry have lower white blood cell counts (WBCs) and neutrophil counts than do white individuals. This has been demonstrated for Afro-Americans,[1] Afro-Caribbeans,[2] East Africans,[3] Central Africans,[4] and West Africans.[5] In healthy white subjects, the neutrophils in the peripheral blood are distributed, more or less equally, between the circulating and the marginated granulocyte pools, the latter pool comprising cells adherent to the endothelium in postcapillary venules.[6] Only the circulating granulocyte pool is sampled when a venous blood specimen is obtained. It has been suggested that ethnic neutropenia is consequent on those of African ancestry having a larger proportion of their neutrophils in the marginated granulocyte pool,[7] but there is no published evidence to confirm or refute this hypothesis.

The marginated granulocyte pool can be mobilised by vigorous exercise of by administration of epinephrine,[6 8] neither of which affects the total blood granulocyte pool, the disappearance time of neutrophils from the blood, or the granulocyte turnover rate.[8] The effects of exercise and epinephrine are very similar and it is likely that exercise mediates its effect by the release of endogenous epinephrine. The action of epinephrine appears to be mediated by increased synthesis of cAMP in vascular endothelial cells, with subsequent release of cAMP into the bloodstream, in turn leading to reduced neutrophil adhesiveness.[9]

We have studied the effect of exercise on the total white blood cell count and the absolute count of neutrophils and other leucocytes in healthy subjects of African or non-African ethnic origin to investigate whether the explanation of ethnic neutropenia is that those of African ancestry have a higher proportion of neutrophils in the marginated granulocyte pool.

Methods

After ethical committee approval, healthy volunteers, mainly medical students and hospital and medical school staff, were recruited to our study. Volunteers were required to be in good health and between the ages of 18 and 46 years. Equal numbers of men and women and equal numbers of Africans/Afro-Caribbeans and white subjects were recruited. The pulse rate was recorded and a venous blood sample was taken immediately before exercise. The volunteer then exercised vigorously for 10 minutes on a step machine in a gymnasium. The amount of exercise was standardised for body weight, but subjects who found the exercise too taxing were permitted to reduce the work load to a level that they found

Table 1 Comparison of biological variables, work performed, and pulse rate before and after exercise in white and African/Afro-Caribbean subjects

Variable	*Whites median (range) or mean (SD)*	*Africans/Afro-Caribbeans median (range) or mean (SD)*	*Difference in mean or median (95% CI)*	*p Value*
Number of men	6	6		1.00
Number of smokers	1	2		1.00
Age (years)	23.5 (22 to 46)	31.5 (22 to 43)	−4 (−9 to 2)	0.18
Power (Watts)	125.31 (25.61)	119.19 (23.89)	6.13 (−11.75 to 24)	0.24
Pre-exercise pulse rate (beats/min)	72 (60 to 88)	76 (68 to 84)	−3.5 (−6 to 4)	0.37
Postexercise pulse rate (beats/min)	106 (92 to 140)	106 (96 to 160)	0 (−12 to 8)	0.73
Increase in pulse rate (%)	42.7 (22.7 to 100)	45.9 (14.3 to 122)	−1.8 (−16.2 to 17.0)	0.81

Data are the mean or median and the 95% range (SD), except for the significance of the difference where the 95% confidence interval (CI) is given.

comfortable. The pulse rate was recorded immediately after finishing the exercise and a further venous blood sample was taken shortly afterwards. A full blood count and differential count were performed on all blood samples, using a Bayer-Technicon H2 automated full blood counter.

The age, sex, and prevalence of cigarette smoking were compared for the two ethnic groups to confirm that the groups were of similar composition. The amount of work done and the postexercise pulse rates were also compared to ascertain whether the exercise performed and the physiological response to it were comparable in the two groups. The total leucocyte counts and absolute counts of different cell types after exercise were compared with pre-exercise values, and values before and after exercise were compared between the two ethnic groups. When data had a Gaussian distribution and similar variance, comparison was by means of an unpaired student's *t* test. When data were non-Gaussian or had dissimilar variance, comparison was by means of a Mann-Whitney U test. Paired data were compared by either a paired *t* test or a Wilcoxon matched pairs test. Proportions were compared by a χ^2 test or Fishers exact test.

Results

We studied 32 subjects, 16 whites and 16 Africans/Afro-Caribbeans. Twelve subjects were men and 20 were women. Comparison of the two ethnic groups showed no significant difference in biological variables (table 1). Comparison of pulse rate before and after exercise and of work performed showed that the amount of exercise and the physiological response to it were similar in the two ethnic groups (table 1).

The expected ethnic differences were seen in the pre-exercise total WBC and neutrophil count (table 2). The haemoglobin concentration and the lymphocyte, monocyte, and eosinophil counts did not differ significantly and the difference in the platelet count (lower in Africans/Afro-Caribbeans) was of only marginal significance.

In both ethnic groups, exercise led to a significant increase in the total WBC and the neutrophil, eosinophil, and monocyte counts (table 2). After exercise, the ethnic differences in the WBC and neutrophil counts were greater than they had been before exercise (table 2). The percentage rise tended to be less rather than greater in the African/Afro-Caribbean group, although this was of only marginal significance ($p = 0.27$ for the WBC and $p = 0.17$ for the neutrophil count). The absolute increase in neutrophils was significantly less in the African/Afro-Caribbean group (0.49 *v* 0.84×10^9/litre; $p = 0.036$). In neither ethnic group was the response of the neutrophil count to exercise greater in those with the lowest counts before exercise. For both groups, the correlation between the exercise induced increment and the pre-exercise count tended to be positive rather than negative ($r = 0.14$ for white subjects; $r = 0.34$ for Africans/Afro-Caribbeans), although this was not significant. After exercise, a significant ethnic difference was present in the monocyte count (mean, 0.5×10^9/litre for white subjects; 0.4×10^9/litre for Africans/Afro-Caribbeans;

Table 2 Haematological variables before and after exercise in healthy white and African/Afro-Caribbean subjects

Variable	*Caucasians mean (SD) or median (range)*	*Africans/Afro-Caribbeans mean (SD) or median (range)*	*Differences in mean or median (95% CI)*	*p Value*
Pre-exercise WBC	5.73 (1.44)	4.82 (0.26)	0.91 (0–1.81)	**0.049**
Postexercise WBC	8.11 (2.14)***	6.51 (1.80)***	1.61 (0.18–3.03)	**0.028**
% Increase in WBC	40.1 (12.7–93.1)***	25.95 (7.7–126.1)***	10.5 (−6.4 to 25)	0.27
Pre-exercise neutrophil count	3.34 (1.02)	2.36 (0.21)	0.98 (0.03–1.65)	**0.006**
Postexercise neutrophil count	4.18 (1.22)***	2.86 (1.01)***	1.33 (0.52–2.13)	**0.002**
% Increase in neutrophil count	26.4 (−2.4 to 57.1)	13.96 (5.9 to 88.9)	6.8 (−5.5 to 19.05)	0.169
Absolute increase in neutrophil count	0.84 (0.53)	0.49 (0.48)	0.35 (0.02 to 0.68)	**0.036**
Pre-exercise monocyte count	0.36 (0.10)	0.34 (0.08)	0.02 (−0.04 to 0.09)	0.449
Postexercise monocyte count	0.50 (0.30 to 1.00)***	0.40 (0.30 to 0.60)**	0.10 (0 to 0.20)	**0.026**
% Increase in monocyte count	49.4 (36.0)	23.75 (24.5)	25.6 (3.4 to 47.9)	**0.025**
Absolute increase in monocyte count	0.1 (0 to 0.4)	0.1 (−0.1 to 0.2)	0.1 (0.05 to 0.15)	0.144
Pre-exercise eosinophil count	0.11 (0.07 to 0.31)***	0.11 (0.04 to 0.74)*	0.01 (−0.05 to 0.05)	0.63
Postexercise eosinophil count	0.15 (0.08 to 0.42)	0.13 (0.02 to 0.75)	0.03 (−0.02 to 0.07)	0.29
% Increase in eosinophil count	36.0 (30.65)	14.7 (30.1)	21.3 (−0.65 to 43.2)	0.057

Cell counts are given as $\times 10^9$ cells/litre.
p Values of < 0.05 are shown in bold type.
*p < 0.05 for the difference from the pre-exercise value; **p < 0.01 for the difference from the pre-exercise value; ***p < 0.001 for the difference from the pre-exercise value.

p = 0.026). Both the percentage and the absolute increase in the monocyte count were significantly less in the African/Afro-Caribbean group.

The haemoglobin concentration, lymphocyte count, and platelet count all rose significantly with exercise, the rise being similar in the two ethnic groups. The ethnic difference in the platelet count persisted but remained of only marginal significance.

Discussion

We studied mobilisation of neutrophils from the marginated granulocyte pool in healthy volunteers of different ethnic origins to investigate the cause of ethnic neutropenia. We found that a group of healthy Africans and Afro-Caribbeans, whose mean neutrophil counts were significantly lower than those of a group of healthy white subjects, mobilised significantly fewer neutrophils in response to exercise. Furthermore, the response of the neutrophil count to exercise was no greater in those with the lowest counts before exercise. These findings in healthy volunteers differ from those in patients, of unstated ethnic origin, who were investigated for idiopathic or disease related neutropenia.[10] These patients were heterogeneous in their responses but many of them, particularly those with the lowest counts, had a pronounced increase in neutrophil count after exercise, indicating that their neutropenia was at least in part caused by increased margination.

The African/Afro-Caribbean group also mobilised fewer monocytes in response to exercise, suggesting that the total circulating monocyte pool might also show an ethnic difference.

Our results suggest that ethnic neutropenia is unlikely to be caused by increased neutrophil margination. The absolute number of neutrophils mobilisable from the marginated granulocyte pool is less than in white subjects and, because the neutrophil count in the resting state is also lower, it appears likely that the total blood granulocyte pool is lower than in whites. We cannot totally exclude the possibility that those of African ancestry have both increased margination and impaired ability to mobilise neutrophils, but this appears unlikely. Because our data do not support increased neutrophil margination as the cause of ethnic neutropenia, we suggest an alternative hypothesis—that there is an ethnic difference in bone marrow neutrophil production or release.

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