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Short-term administration of recombinant human erythropoietin decreases B cell number in human peripheral blood

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ABSTRACT

Objectives: There are conflicting results on the influence of recombinant human erythropoietin (rHuEPO) administration to lymphocytes, especially to B cells.
Methods: We analyzed peripheral white blood cell (WBC) subsets in patients who received one bolus administration of rHuEPO. 119 autologous blood donors were enrolled in this study. Fourty-nine out of them were treated with rHuEPO. Blood samples were obtained before the first phlebotomy and one week later before the second one. By flow cytometry, we measured the numbers of WBC, lymphocytes, dendritic cells, CD4+ T cells, CD8+ T cells, natural killer (NK) cells, B cells, monocytes, and neutrophils, further details of B cell subsets.
Results: In the EPO-treatment group, absolute numbers of lymphocytes, especially CD8+ T cells, NK cells, and B cells, significantly decreased after rHuEPO administration. In B cell subsets, absolute numbers of naïve B cells and $IgD^{-}CD27^{-}$ B cells significantly decreased. Other B cell subsets, such as transitional B cells, memory B cells, and marginal zone B cells, also showed a decreasing trend.
Conclusion: These findings suggest that a single administration of rHuEPO can influence human immune system via reduction of B cell number in peripheral blood.

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1. Introduction

Erythropoietin (EPO) is one of the hematopoietic factors that participates in red blood cell production. It also accelerates proliferation and inhibits apoptosis of erythroblasts [1]. EPO is produced by cells in the kidney and is regulated by the blood oxygen level. When the oxygen level falls, EPO production increases and promotes erythroblast differentiation and maturation [2]. Renal diseases and inflammatory cytokines suppress EPO secretion [3].

Recombinant human erythropoietin (rHuEPO) is used for the treatment of renal anemia and autologous blood donation pre-operation. Epoetin-alpha and Epoetin-beta are representative of rHuEPO; they have different carbohydrate chain structures but show similar treatment efficacies [4].

EPO has been reported to play multiple roles, including an anti-apoptotic role for some cells, an antioxidant role, vascularization and proliferative roles for cardiac myocytes, neuronal progenitor cells, and endothelial cells, in addition to an erythropoiesis stimulatory role [5,6]. Recent studies suggest that the EPO receptor is expressed on vascular endothelial cells, vascular smooth muscle cells, platelets, nerve cells, and erythroblasts [6]; however, its expression in other cell lineages, especially in the blood immune cells, is still debated. In order to determine the effect of EPO on the human immune system, we analyzed peripheral white blood cell subsets such as neutrophils, monocytes, dendritic cells, T cells, Natural killer (NK) cells, and B cells in patients who had received autologous blood donation pre-operation and had been administered short-term rHuEPO.

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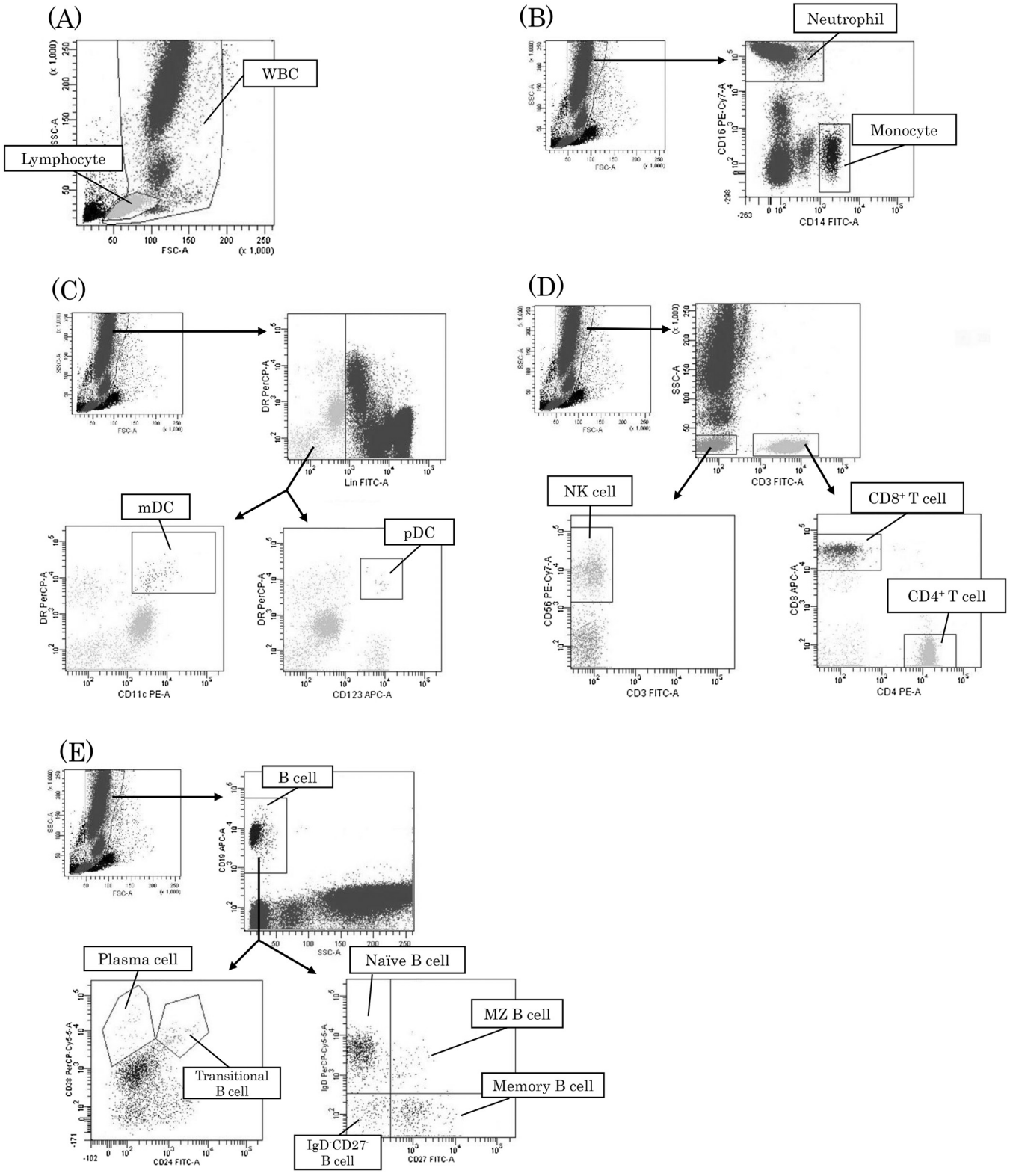

Fig. 1. Flow cytometric analysis.(A) WBCs and lymphocytes, (B) Neutrophils and monocytes, (C) mDCs and pDCs, (D) $CD4^+$ T cells, $CD8^+$ T cells, and NK cells, and (E) B cells.

2. Materials and Methods

2.1. Patients

One hundred nineteen autologous blood donors in Gunma University Hospital were enrolled in this study. This study was approved by the institutional review board of Gunma University Hospital Ethics committee. None of the patients had any infections, inflammation or end stage renal disease. Patients were classified into a treatment group with rHuEPO (EPO-treatment group) and a non-treatment group. Forty-nine patients were treated with rHuEPO (Epoetin alpha or Epoetin beta 24,000 IU) once after

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