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Should be or Not Use Haematopoietic Growth Factors in the Case of Drug-induced Agranulocytosis

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Drug-induced agranulocytosis is characterized by a severe decrease of neutrophil count of at least <0.5×109/L, in association with the intake of drugs such as: anti-thyroid drugs, antibiotics, ticlopidine, sulfasalazine, and dipyrone [1]. Currently, the incidence of this idiosyncratic adverse effect is estimated to be between 2.4 and 15.4 cases per one million inhabitants. From a clinical perspective, drug-induced agranulocytosis may simply be detected following a routine full blood count, or it may present with the onset of infection with varying degrees of severity, for example, ranging from fever with no clear focus, septicaemia and septic shock, to more localized infections mostly involving the ear nose and throat, the lungs and the skin [1,2].

In oldest studies, the mortality of drug-induced agranulocytosis due to complications resulting from infection ranged from 10% to 16% [2]. At present, this mortality is closer to 5% (between 2.5% and 10%), illustrating the progress that has been made in the recognition and therapeutic management of this condition [1]. Notify that drug-induced agranulocytosis can rapidly become a life threatening condition, hence the importance of optimal clinical management. To our opinion, this includes the use of haematopoietic growth factors such as *Granulocyte Colony-Stimulating Factor (G-CSF)*, which are not yet, in developed countries, licenced for this condition [3].

To date, the efficacy and mainly the usefulness of haematopoietic growth factors in drug-induced agranulocytosis is still a matter of debate. A systematic meta-analysis by Andersohn et al. (n=492) found that since 1985 over two-thirds of reported cases were treated with these agents [2]. Most recent studies demonstrate a significant reduction in the duration of agranulocytosis following the use of these cytokines [2,3]. In our own experience, the administration of *G-CSF*, at a mean dose of 300 µg/day, is associated with a significant reduction in the duration of agranulocytosis, antibiotic use and length of hospital stay, particularly in patients with poor prognostic factors [4,5]. Only one single study showed a survival benefit when using neutrophil growth factors [6]. The most recent data did not find any significant difference in the mortality rate of patients treated or not treated with *G-CSF or GM-CSF:* 5% versus 6% in the study of Andersohn et al.; 8.9% versus 11.4% in the study of Ibanez et al. [2,7]. The prospective, randomized study carried out by Fukata et al. (the only one available to date), was also unable to draw any definitive conclusions regarding the use of neutrophil growth factors [8].

A critical review of the data available support the role of neutrophil growth factors in the presence of at least one of the poor prognostic factors [1,9,10]. In our experience, these factors includes: age over 65 years, neutrophil count at diagnosis of less than 0.1×10^9/L, development of severe intercurrent infection (septicaemia and septic shock) as well as pre-existing co-morbidities (in particular renal impairment, defined by a serum creatinine level >120 µmol/L) [10]. A neutrophil count of $<0.1\times10^9$/L appears to be a particularly important prognostic factor [9,10].

To date, the true impact of the use of haematopoietic growth factors is still being questioned, but these molecules appear to indisputably decrease the duration of agranulocytosis, antibiotic course and length of hospital stay. Finally, it would be beneficial to conduct further public health studies (such as meta-analysis of reported data form the series of Berlin, Barcelona, Strasbourg…) in order to fully confirm the potential use of these agents.

Conflict of Interest

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