Introduction

Peripheral blood stem cell transplantation (PBSC) is an alternative to bone marrow transplantation for patients with various malignancies and/or bone marrow disorders. Collecting haematopoietic stem cells from peripheral blood, rather than from bone marrow, provides a larger quantity of cells and a higher rate of engraftment compared to bone marrow transplantation (BMT). PBSC allows the Transplantation team to apply PBSC in patients with severe bone marrow failure (primary or secondary), in haematological malignancies, in solid tumors, and in diseases where stem cell transplantation is the treatment of choice, such as severe aplastic anemia, Fanconi’s anemia, or severe combined immunodeficiency (SCID) syndrome.

Methods

Comparison of efficacy and safety of the evaluated drugs was based on randomized controlled trials (RCTs) identified by means of a systematic review, carried out according to the Cochrane Handbook for Systematic Reviews of Interventions and PRISMA guidelines. The most important medical databases were searched (EMBASE, MEDLINE, PubMed). No language restrictions were used. Two reviewers independently selected trials, assessed their quality and extracted data.

Characteristics of clinical trials

The search in medical databases resulted in total number of 9174 identified publications (including repeated titles). 290 publications were qualified for full text analysis. Finally 7 trials met predefined inclusion criteria and were suitable for further analysis: 4 RCTs comparing PBSC mobilization in healthy donors, 1 RCT comparing PBSC mobilization in patients with breast cancer, and 2 RCTs comparing PBSC mobilization in oncological patients. A total of 2575 patients were included in the 7 selected trials. The mean number of harvested CD34+ cells was assessed in all studies, although methods used differed significantly. Meta-analysis was possible in 6 studies, and an overall comparison of the efficacy of Lenograstim were drawn in from E. coli.

Results

1. Stem cell mobilization in healthy donors

Four similar randomized controlled trials comparing PBSC mobilization with Lenograstim or Filgrastim in healthy donors were identified. Two of the studies had parallel design (Filser 2005, Kishi 2005), another two (Hoglund 1997, Witts 1997) had triple blind design – randomization were applied in all patients with a 4-week wash-out period.

2. Stem cell mobilization in oncological patients

The identified RCTs comparing Lenograstim and Filgrastim in PBSC mobilization in oncological patients. All the studies had parallel design. In one study only patients with breast cancer were included (Kopf 2006), in the other two studies patients with various haematological malignancies were included. The studies were conducted in Europe and indicated for mobilization of PBSC. Lenograstim is a glycosylated cytokine, derived from Chinese hamster ovary cells and Filgrastim is a recombinant human granulocyte colony-stimulating factor, produced in E. coli. The mean number of harvested CD34+ cells was assessed in all studies. None of them showed significant differences between groups with respect to the number of harvested CD34+ cells. Kulkarni et al. (2001) observed that significantly more CD34+ cells were harvested in the Lenograstim group (p=0.01), Kopf et al. (2006) that the median number of aphaeresis procedures in each group was 2, but the median day of the first aphaeresis was significantly shorter in the Lenograstim group (72 vs 135 days, p<0.0001).

Conclusion

In healthy donors lenograstim is more potent than filgrastim in stem cell mobilization in peripheral blood. In oncological patients both drugs have similar impact on stem cell mobilization and lenograstim decreases the risk of platelet transfusion. For oncological patients no differences in the number of subjects who gained target CD34+ cell count were found between treatments for either the target value of CD43+: 1 x 106 per kg of body weight or 2 x 105 per kg of body weight (Table 5). The mean number of harvested CD34+ cells was assessed in all studies. None of them showed significant differences between groups with respect to the number of harvested CD34+ cells. Kulkarni et al. (2001) observed that significantly more CD34+ cells were harvested in the Lenograstim group (p=0.01), Kopf et al. (2006) that the median number of aphaeresis procedures in each group was 2, but the median day of the first aphaeresis was significantly shorter in the Lenograstim group (72 vs 135 days, p<0.0001).

Haematological recovery

Results for haematological recovery are inconsistent. Kulkarni et al. (2000) observed that the median number of days to ANC recovery was shorter in the Lenograstim group than in the Filgrastim group (19 vs 18 days, p=0.02), whereas no differences were noted in the need for supportive care or the number of units of blood or platelet transfusions. Median duration of hospitalization was 24 days in each group.

Non-haematological toxicity

Safety outcomes were reported in one trial (Kopf 2006). The incidence and duration of fever (>38°C) did not differ significantly between the groups. Among lenograstim treated patients one case of diaphramitis and three cases of rash and urticaria were reported. In the filgrastim treated group one patient had diarrhoea. In both groups chemo therapy-related haematological toxicity was reported. No differences between the groups were not evaluated due to low incidence and different chemotherapy regimens used.

1. Selection process according to QUOROM

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Systematic Reviews of Interventions and Polish HTA Guidelines. The methodological credibility of the trials included in the analysis was moderate to high. The Jadad scale. Meta-analysis of head-to-head trials was performed by means of a systematic review, carried out according to the Cochrane Handbook for Systematic Reviews of Interventions and PRISMA guidelines. The most important medical databases were searched (EMBASE, MEDLINE, PubMed). No language restrictions were used. Two reviewers independently selected trials, assessed their quality and extracted data. Clinical trials were performed in order to compare lenograstim and filgrastim in stem cell mobilization in healthy donors (allogenic stem cell transplantation) and in oncological patients (autologous transplantation). The remaining two studies were small – in one of them there was no significant difference, in the other the number of CD34+ cells harvested was higher in the Len-grastim group (Table 5).

2. Methods

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