INPLASY PROTOCOL

To cite: Ji et al. Efficacy and safety of hematopoietic stem cell transplantation for hematologic malignancies: A protocol for an overview of systematic reviews and meta-analyses. Inplasy protocol 202150064. doi: 10.37766/inplasy2021.5.0064

Received: 17 May 2021

Published: 17 May 2021

Corresponding author:
Conghua Ji

jchi2005@126.com

Author Affiliation:
Zhejiang Chinese Medical University

Support: **Health Commission of Zhejiang.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Efficacy and safety of hematopoietic stem cell transplantation for hematologic malignancies: A protocol for an overview of systematic reviews and meta-analyses

Ji, C[1]; Dai, R[2]; Wu, H[3]; Li, Q[4]; Liu, S[5]; He, P[6]; Liang, J[7]; Guo, Q[8].

Review question / Objective: **Through this study, we hope to answer which hematologic malignancies is best treated by bone marrow transplantation, peripheral blood stem cell transplantation or cord blood stem cell transplantation; similarly, we also hope to answer which transplantation method is most effective for leukemia, malignant lymphoma and other hematologic malignancies; and whether there is any difference between children and adults.**
Information sources: **We will retrieve eight electronic databases from their inception to May 31, 2021, which include four English databases: PubMed, Cochrane Library, Excerpt Medical Database (Embase), Web of science, and four Chinese databases: China Biology Medicine disc (CBM), VIP database(vip), Wang fang database (WF), China National Knowledge Infrastructure (CNKI). The language will be restricted to English and Chinese.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 May 2021 and was last updated on 17 May 2021 (registration number INPLASY202150064).

INTRODUCTION

Review question / Objective: **Through this study, we hope to answer which hematologic malignancies is best treated by bone marrow transplantation, peripheral blood stem cell transplantation or cord blood stem cell transplantation; similarly, we also hope to answer which transplantation method is most effective for leukemia, malignant lymphoma and other hematologic malignancies; and whether there is any difference between children and adults.**

Condition being studied: Hematopoietic stem cell transplantation (HSCT) is an essential and often the sole treatment strategy for relapsed and refractory hematologic malignancies (HMs), and it is also an important method to treat aplastic anemia. In addition, it can also be used for some genetic diseases, congenital diseases and metabolic diseases[3, 4], such as multiple sclerosis (MS) and neuromyelitis optical spectrum disorders (NMOSD). Hematological malignancies are a diverse group of cancers that are associated with substantial incidence and mortality in all regions of the world. Non-Hodgkin lymphoma (NHL), chronic lymphoid leukemia (CLL), acute myeloid leukemia (AML), acute lymphoid leukemia (ALL), multiple myeloma (MM), Hodgkin lymphoma (HL), and chronic myeloid leukemia (CML) rank 8th, 21st, 22nd, 25th, 26th, 28th, and 30th, respectively in the Global Burden of Cancer report. Hematopoietic stem cell transplantation can improve the overall survival (OS) and relax free survival (RFs) of patients to a certain extent[6], but there are also many adverse reactions. Adverse events after hematopoietic cell transplantation include the immune reaction called graft-versus-host disease (GVHD); bacterial, viral, and fungal infections; hepatic sinusoidal obstruction syndrome; and Venous thromboembolism, etc.

METHODS

Participant or population: Participants who meet the diagnostic criteria of hematologic diseases, Including all kinds of leukemia, malignant lymphoma, myelodysplastic syndrome, etc. There are no restrictions on age, sex, or race of participants.

Intervention: The sources of hematopoietic stem cells include bone marrow, peripheral blood or umbilical cord blood of blood and non-blood donors, and blood donors include HLA identical or haplotype identical.

Comparator: The control group's treatment includes conventional drugs or no treatment which are considered as comparators in SRs and MAs.

Study designs to be included: SRs and MAs that contain more than 1 RCT will be included for further study. SRs and MAs without RCTs, reviews, and other overviews will be excluded.

Eligibility criteria: Population, Intervention, Comparison, Outcome and Study (PICOS) strategy will be employed.

Information sources: We will retrieve eight electronic databases from their inception to May 31, 2021, which include four English databases: PubMed, Cochrane Library, Excerpt Medical Database (Embase), Web of science, and four Chinese databases: China Biology Medicine disc (CBM), VIP database(vip), Wang fang database (WF), China National Knowledge Infrastructure (CNKI). The language will be restricted to English and Chinese.

Main outcome(s): The primary endpoints are overall survival (OS) and relapse-free survival (RFS) at 6 months, 1 year, 2 years and 3 years, measured from the time of HSCT. The secondary endpoints are the cumulative incidence of relapse (CIR) and non-relapse mortality (NRM). The safety index mainly include the incidence of graft versus host disease(GVHD) and infection.

Quality assessment / Risk of bias analysis: (1) Evaluation of the reporting quality of the included studies PRISMA will be applied to assess report quality of SRs and MAs. Two authors (QL and SL) will evaluate the reports' quality of each study using PRISMA, which contains 27 item list. Each checklist item will be evaluated as yes, no, or partially Yes to indicate compliance. (2) Evaluation of the evidence quality of the included studies The evaluation of the evidence quality of the included studies will be conducted by two reviewers (PH and CD), using the GRADE approach. GRADE specifies four categories: high, moderate, low, and very low. Two reviewers will evaluate the evidence quality of the outcomes of the included SRs and MAs independently, and describe the

downgraded or upgraded factors that may affect the evidence quality to guarantee the reliability and transparency of results. If there are any disagreements, they will be solved by introducing a third researcher (CJ) for judgment. (3) Evaluation of the risk of bias of the included studies Two authors of this review (PH and CD) will assess the risk of bias of the included studies, using ROBIS tool. The ROBIS is a tool to assess the risk of bias of SRs, which involves assessment of four domains: study eligibility criteria; identification and selection of studies; data collection and study appraisal; and synthesis and findings. The evaluation of the risk of bias is associated with each domain which will be judged as "low risk", "high risk" or "unclear risk".

Strategy of data synthesis: This overview will analyze SRs and MAs for hematopoietic stem cell transplantation. General characteristics of the included studies include the total sample size of SRs and MAs, interventions, name of disease and their effect size and related 95% CIs. Data from individual studies are likely to be pooled multiple times across the reviews included in our overview. As a result, we will not conduct a meta-analysis of results; rather, we will present a narrative synthesis of the findings from the included meta-analyses reviewed.AMSTAR2 will be used for the SRs and MRs methodological quality assessment, PRISMA will be applied to assess report quality, and GRADE for the quality of evidence and ROBIS for the bias, which will be conducted in tabular form for each review. The quality of evidence will be detailed in the form of tables. We will combine the reviews in a narrative summary, structured around the type and content of interventions and the reported results. Efficacy and safety of hematopoietic stem cell transplantation in the treatment of hematologic malignancies will be assessed at SRs and MAs level. We will extract pooled relative risk (RR) or pooled odds ratio (OR) for dichotomous outcomes, and pooled weighted mean difference or standardized mean difference for continuous outcomes which will be also reported with 95% confidence interval (CI) and will be presented graphically using a forest plot.

Subgroup analysis: Subgroup analysis was performed according to adults and children

Sensitivity analysis: The I2 values will be described for reporting heterogeneity across RCTs, with 0% to 25% representing low heterogeneity, 26% to 50% representing medium heterogeneity, and above 50% representing high heterogeneity.

Country(ies) involved: China.

Keywords: hematopoietic stem cell transplantation, bone marrow, peripheral stem cells, cord blood stem cells, hematologic malignancies, AMSTAR-2, PRISMA, GRADEE, overview.

Contributions of each author:
Author 1 - Conghua Ji.
Author 2 - Rong'chen Dai.
Author 3 - Hanting Wu.
Author 4 - Qiushuang Li.
Author 5 - Shan Liu.
Author 6 - Peijie He.
Author 7 - Juan Liang.
Author 8 - Qing Guo.