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Title: Characterisation of cord blood and its potentiality regarding leukaemia: The haematopathological condition.

Abstract

Umbilical cord blood (UCB), often considered a biological waste, is rich in hematopoietic stem and progenitor cells, having unique morphological and functional attributes when compared to the adult peripheral blood (PB). Recently, the therapeutic potential of UCB has ventured and its components are increasingly used in experimental biology and clinical research focussing mainly on translational and regenerative medicine. Cord blood (CB) cellular components have been explored for treating myocardial infarction, neurodegenerative diseases, diabetes, liver cirrhosis, and autoimmune conditions whereas the plasma component is widely used in treating eye anomalies, aging-related issues, neurodegenerative diseases and in cell cultures. The study aimed to establish haematological reference values for UCB of South Asian populations like India specific to the West Bengal cohort, and to examine variations in haematological parameters between urban and rural populations considering different modes of delivery, thus exploring UCB's distinctive cellular characteristics through comparison with adult PB. We also sought to investigate the potential therapeutic property of the plasma component of cord blood when administered as a treatment in leukemic scenarios.

With the advent of industrialisation, carcinogens such as N-nitroso compounds (NOCs) are radially being released into the environment through processed food, contaminated water bodies, tobacco and pesticides and chemical manufacturing units. We used N-ethyl-n-nitrourea (ENU), a potent carcinogenic NOC to induce leukaemia in Swiss Albino mice followed by the induction of cord blood plasma factor (CBPF) as a therapeutic measure to ameliorate the induced leukemic condition in the in-vivo model. The study also aimed to evaluate the efficacy of biologically procured, natural concoction like CBPF as a treatment for leukaemia, while minimising side effects on leukemic profile, which are evident in chemotherapeutic drugs, without claiming it as a 'safer alternative therapy.' Its focus was

solely on assessing its potential benefits and not advocating it as a replacement for current treatments.

Through this study, haematological parameters of the regional population were compared to global standards. The morphological and protein variations were assessed between UCB and PB erythrocytes and leukocytes using scanning electron microscopy (SEM), SDS-PAGE for protein profiling, and flow cytometry for membrane protein expressions and cellular characteristics. Following the characterisation, ENU-induced leukemic mice received CBPF intravenously for 30 days. Pre- and post-treatment effects were analysed across hematopoietic profiles, immune cell cytotoxicity, tissue architecture, bone marrow cellularity, and transcription factor profiling through biochemical staining, cell culture, histology, SEM and flow cytometry.

The cellular components from the cord blood of the West Bengal population showed unique haematological profiles, with elevated WBC and lowered monocyte counts compared to the global scenario. Rural groups expressed higher neutrophil counts, whereas urban groups showed higher lymphocyte and platelet counts. Minor differences in haematological profile were also noted between the vaginal and caesarean delivery modes amidst the urban and rural population. Cellular analysis revealed unique morphological traits in UCB erythrocytes with variations in indentation and altered membrane textures compared to PB cells. Unique metabolic characteristics including low osmotic fragility and reduced lipid peroxidation along with overexpression of GLUT1 and reduced Band 3 proteins were observed in UCB. In the leukaemia study, CBPF administration as a treatment significantly reduced leukemic blasts and abnormal neutrophils in peripheral blood and bone marrow, decreased notable blast infiltration in extra medullary tissues like spleen and liver and enhanced cytotoxic efficacy through increased mature immune cells. Histological analysis verified improved bone marrow architecture and reduced blast cells with significant changes in transcriptional profile further supporting CBPF's role in modulating immune and hematopoietic pathways and reinforcing the anti-leukemic activity of cord blood.

In conclusion, this study established the first UCB haematological reference range for the West Bengal population, revealing notable urban-rural differences along with the reporting of the distinct cellular and protein expression differences in the erythrocyte population of UCB and adult PB. This highlights UCB's unique hematopoietic profile and its potential use in neonatal treatment like transfusion. This work is possibly the first study that reports the use of

CBPF in an ENU-induced leukemic mice model. Through this research, we established that standalone CBPF administration may yield promising anti-leukemic effects, including reduced blast cell burden, increased hematopoietic differentiation, and improved tissue architecture with minimal toxic effect, indicating its potential use in haematopathological and regenerative medicine. This research accentuates UCB's clinical relevance and encourages further exploration of CBPF's role, potentially in combination with standard therapies, to improve therapeutic outcomes in haematological disorders.

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