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Delayed Umbilical Cord Blood Clamping: First Line of Defense Against Neonatal and Age-Related Disorders

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Abstract

The aging body is unable to maintain homeostasis in cell genesis and function. Stem cell-based regenerative medicine may reverse aging and treat age-related disorders. This perspective article discusses the therapeutic effects of stem cell transplantation on neonatal diseases, which may have long-lasting benefits affecting even the aging process. In particular, the article highlights the potential of the earliest transfer of stem cells between a mother and fetus via the umbilical cord during child birth and how this process may modify the clinical practice of umbilical cord clamping. While such umbilical cord clamping is routinely performed in an expeditious manner after birth for stem cell banking, the present article advances the concept that a delay in clamping the umbilical cord may actually allow more stem cells to be delivered from the mother to the fetus. The authors' overarching hypothesis is that early umbilical cord clamping results in an artificial loss of stem cells at birth and increases the infant's susceptibility to both neonatal and age-related diseases, while delaying umbilical cord clamping is perhaps the most effective and non-invasive way to transplant stem cells in order to treat these diseases.

Keywords

stem cell; transplantation; neonatal disease; aging; age-related disorders; umbilical cord; cord clamping; stem cell banking

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Transplantation of exogenous or induction of endogenous stem cells best describes the main tenet of stem cell-based regenerative medicine (Borlongon, 2009; Sanberg, 2007). Age-related disorders, such as Parkinson's disease, Huntington's disease, Alzheimer's disease, stroke, myocardial infarction, and osteoporosis, have been largely targeted by stem cell therapies because of laboratory and clinical observations demonstrating that aging or diseased organs (e.g., brain, heart, bone) exhibit a reduced capacity of endogenous stem cells to maintain a homeostasis in cell genesis and function (Borlongon, 2009; Lee, 2007; Sanberg, 2007). Recent trends show a shift in stem cell disease candidates to neonatal disorders, primarily due to the notion that the young organ displays robust plasticity thereby actively participating in the recovery process, but also is immune tolerant to exogenous stem cell transplants (Yasuhara, 2010). Acting on this concept that aging and disease states prompt repair mechanisms recapitulating developmental processes, the authors postulate that preventative stem cell transplantation during the most primitive neonatal stage should exert optimal protection against both neonatal and adult diseases. Arguably the earliest stem cell

transplantation occurs at birth in mammals characterized by the offspring connected to the mother via the umbilical cord. Apart from the many nutrients, stem cells are also supplied through umbilical cord blood, which has been tapped into as an abundant source for stem cell banking. The existence of stem cells in fetal circulation indicates that a delay in cord clamping should increase stem cell supply to the baby, providing immediate benefits if neonatal disease is indicated.

Indeed, such delayed cord clamping has been shown to increase cerebral oxygenation (Baenziger, 2007), while decreasing the incidence of sepsis and intraventricular hemorrhage (Mercer 2006), and anemia (Hutton, 2007) in very early pre-term and term-infants, respectively. Whether delayed cord clamping promotes long-term protective effects against age-related disorders remains to be determined. In view of stem cells playing a key role in the development and maturity of many organ systems, including central nervous, respiratory, cardiovascular, hematologic, immunologic and endocrine far before birth, suggest that etiology of many diseases is related to delayed development and immaturity. Hence, the artificial loss of stem cells at birth could potentially impact later development and predispose infants to age-related diseases. A reservoir of cord blood-derived stem cells including hematopoietic stem cells, endothelial cell precursors, mesenchymal progenitors, and pluripotent/multipotent lineage stem cells (Chen, 2005), is likely to produce therapeutic benefits in adulthood. Interestingly, early cord clamping (30–60 seconds after birth) is the recommended active management of child delivery (McDonald et al, 2008) for medical reasons to aid in resuscitation and stabilization of infants, and for stem cell banking to facilitate the harvest of a large amount of cord blood-derived stem cells. In non-human placental mammals, natural birth entails umbilical cord contracting and pumping blood toward the newborn until blood equilibrates, at that time the pulsating action of the cord stops and blood flow ceases. Thus, while cord blood transfusion during birth is allowed to end physiologically in most placental mammals, this phenomenon is curtailed in humans (i.e., at term newborns) by early clamping of the umbilical cord, thus depriving infants of additional stem cells. In summary, the timing of cord clamping is critical for the transfer of those stem cells to the newborn infant, which may have consequent acute, as well as chronic adverse events. Allowing nature to run its course of transplanting stem cells from mother to baby may be the most non-invasive therapeutic science for preventing morbidity and mortality associated with neonatal and adult diseases.

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