

Dose intensity and autologous stem cell transplantation as salvage therapy for pediatric primary CNS malignancies

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Dear editor

We have read with great interest the work of Lu et al published recently in the *International Journal of Nanomedicine*,¹ in which the authors describe different strategies for an efficient delivery of drugs to the central nervous system (CNS) across the blood–brain and blood–cerebrospinal fluid barriers. The paper describes in a very organized and efficient manner the current approaches to improve the penetration of various drugs across the blood–brain barrier, of key importance in CNS malignancies.

Several methods have been proposed as improved ways to surpass the problems related to poor delivery and resistance of CNS malignancies to chemotherapy. The dose intensity is defined as high-dose chemotherapy followed by an autologous stem cell transplantation, and represents an efficient salvage protocol for a primary CNS malignancy treated with a carmustine-based, carboplatin-based or thiotepa-based regimen, along with autologous stem cell rescue.^{2,3} The result is reduced mortality and a prolonged disease-free interval. However, the efficiency of dose intensity in pediatric neurooncology is still unknown. Whether defined as high-dose chemotherapy, autologous bone marrow rescue, hematopoietic stem cell rescue, or myeloablative chemotherapy, very conclusive data have yet to be published supporting the superiority of dose intensity over less aggressive consolidation chemotherapy.

Myeloablative chemotherapy is somewhat biased regarding the more favorable outcomes, as clinical trials either support or refute these protocols.^{4,5} This is why further trials, that enroll more patients, are expected to decide the efficacy of this approach, as dose intensity alone seems to lack the strength to treat pediatric CNS malignancy. In the case of neuroblastomas, Kesheleva et al⁶ have proven that acquired resistance to chemotherapy increases progressively to the intensity of the delivered in vivo dosage. This resistance is probably linked to the number of malignant cells that acquire genetic or epigenetic alterations during standard protocols used in the clinic.

Thus, it is important to mention the issue of dose intensity in hematopoietic transplantation in pediatric hematooncology. This is because it seems to be of crucial importance in the treatment of children with primary CNS cancers or resistant disease with various chemoenhancers, as is the case of autologous stem cell transplantation in order to achieve a long-term remission or at least an improved therapeutic ratio.

Disclosure

The authors have no conflicts of interest to declare in relation to this communication.

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