A step towards the cure of Burkitt's lymphoma in developing countries

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The outcome of sporadic Burkitt's lymphoma (BL) in high-income countries may be considered excellent due to its overall cure rate of roughly 90%[1-4]. Three major US and European childhood cancer groups [Lymphoma malignancy B-cell (LMB), Berlin-Frankfurt-Munster (BFM), Children's Cancer Group/Children Oncology Group (CCG/COG)] contributed to the most effective treatment strategies to date. Nevertheless, the treatment has pronounced toxic effects such as long periods of mucositis, hematological toxic effects as well as the potential risk of severe infection. Assuredly, the improvement of supportive care has contributed to these better outcomes[1-4]. On the other hand, in low-income countries, therapeutic schemes need to be modified in accordance with local conditions in order to avoid unacceptable treatment-related mortality[5].

In this issue Cunha et al.[6] present a retrospective study of 50 cases of BL in children and adolescents who were treated with chemotherapy regimens containing intermediate methotrexate doses (500 mg/m^2). The probability of overall survival was 73% (median follow-up of 35 months). The data show a favorable step with improvement in the results of BL treatment in Brazil even considering the high mortality rate (23.8%) observed in the study. Reinforcing the predicted tumor burden value in the prognosis of BL patients, survival was significantly lower for patients with uric acid levels $\geq$ 7 mg/dL. In addition, these results may also show that the impact of methotrexate on the overall success may be of less importance in patients with lower tumor load compared with those with larger tumor masses[7]. Thus, the efficacy of treatment may depend as much on the number of drugs used (at least 4-6 drugs systemically) as on their doses and so lower dose multidrug regimens may improve outcome without comparable increases in toxicity[8].

Although the study by Cunha et al.[6] provides important information on the approach to BL care in Brazil, there are still several areas to be addressed. Differences among survival rates in a large country such as Brazil are worthy of comment. The mean tumor burden at diagnosis has an important impact on the outcome[9]. Even though the Brazilian Government Healthcare System (SUS – *Sistema Único de Saúde*) covers most chemotherapy drug costs, primary healthcare should be improved for earlier diagnosis. Moreover, supportive care facilities remain inadequate in some Brazilian regions where resources are limited. Enhancement of laboratory monitoring, aggressive hydratation and the use of urate oxidase in patients with high risk of tumor lysis syndrome will result in fewer toxic events and better treatment outcomes[10].

The availability of rituximab in the SUS to treat B-cell lymphomas in adult patients has led to the possibility of obtaining excellent results in children with less toxicity by combining this drug with chemotherapy. However, there is a question as to whether rituximab is an effective drug in pediatric B-cell non-Hodgkin lymphoma (B-NHL). This drug was tested in a phase II short-window study showing that it can be safely added to a pediatric chemotherapeutic regimen[11]. Even so, only controlled clinical trials will allow an evaluation of the role of this drug in the treatment of pediatric B-NHL.

Taking these considerations into account, results like those of high-income countries may be achieved by directing research towards designing protocol regimens in formal clinical trials with chemotherapy tailored by tumor burden. The primary goal of therapy studies in developing countries today is to define risk groups as accurately as possible, so that the patients receive therapy consistent with the best possible outcome while further reduction of acute and chronic toxicity may be achieved.

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