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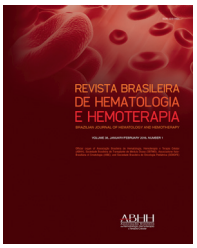

Scientific Comment

Use of biomarkers in the management of febrile neutropenia episodes in children with cancer☆

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Although the diagnosis and treatment of febrile neutropenia episodes have improved significantly over the past two decades, sepsis is still a major cause of mortality and morbidity in patients undergoing chemotherapy regimens that cause intensive myelosuppression.[1–4] Even in institutions where early initiation of antibiotic therapy and advances in supportive measures have significantly reduced the mortality associated with infections, there is great concern about the morbidity related to these complications.[5] Other important aspects to be considered are the high costs associated with treatment and impaired quality of life of the patients and their family, attributable to the need for prolonged or repeated hospitalizations.[6]

Therefore, it is extremely important to develop risk-stratification models that can predict the following conditions early, that is, at admission or within 48 h of evaluation: (1) children at low risk for developing severe infections who can have a reduced intensity of antibiotic therapy and/or a shorter hospital stay; and (2) children at high risk of developing complications and death who need more aggressive therapeutic measures.[3,7]

Although their use is well established in adult patients, there is still no consensus on scores and strategies for predicting the risk for infection and complications in children with cancer who present with febrile neutropenia.[7] The use of reliable and reproducible scores would allow the identification of patients who could benefit from the de-escalation of intravenous antibiotic therapy to oral administration, would help to identify the best time for this change in procedure, and would also contribute to safe decision-making about the place of treatment – hospital or home.[3,7]

The results of research on these predictive models reinforce the importance of developing instruments designed for the pediatric population, including parameters that can be easily measured. However, there is great variability in the methods adopted for assessments, and they are often based only on clinical data, without sufficient discriminatory power.[3,7,8] The elements used in the composition of these scores include patient-related factors (such as age, type of cancer, and status of the underlying disease), parameters referring to the treatment followed, the presence of clinical complications (hemodynamic or respiratory instability, high fever) and laboratory findings suggestive of myelosuppression.[7,8]

In order to move forward and define parameters for these predictive models, serum biomarker studies seem to becoming more important.[6,7] The biomarkers that are most frequently evaluated and appear to have a greater discriminatory power are the following: C-reactive protein (CRP), procalcitonin (PCT), interleukin 6, and interleukin 8.[6]

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☆ See paper by Barbosa et al. in Rev Bras Hematol Hemoter. 2015;37(6):395–9.
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In a systematic review and meta-analysis carried out by Hauesler et al., a marked heterogeneity was found among the 37 studies selected with regard to the diagnosis of the patients included (hematologic malignancies or solid tumors), the definition of febrile neutropenia, and the outcomes evaluated (severe sepsis, severe inflammatory response syndrome, or admission to an intensive care unit). The findings of this study suggest a greater discrimination power of PCT when compared to CRP. However, these authors emphasized that the heterogeneity of the studies complicates comparisons and prevented them from reaching definitive conclusions, which limits the clinical application of the results.[6]

Barbosa et al. conducted a study to determine whether the levels of CD64, a surface marker expressed by activated neutrophils, could be used as a predictor of positive cultures in children with febrile neutropenia episodes. Although this biomarker has been considered promising in studies conducted with adults and newborns, the results obtained by the Brazilian researchers did not identify CD64 as a biomarker that can be used to identify febrile neutropenia patients with a high risk for developing severe infections. The limitations of this study are similar to those previously described in the literature, and, as highlighted by the researchers, it is important to conduct a complementary investigation before reaching definitive conclusions.[9]

It is clear that many questions need to be answered before reaching a consensus on the clinical relevance of biomarkers in the management of children with febrile neutropenia, either to guide immediate measures or to assist in the monitoring and evaluation of the response to the treatment. Despite promising evidence, there is still the need for consistent and reproducible studies to validate the use of these tests and demonstrate that they can be complementary to evaluations based on traditional clinical criteria.[6,9]

Conflicts of interest

The author declares no conflicts of interest.

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