Immunity against hepatitis B and measles vaccination after chemotherapy for acute lymphoblastic leukaemia in children: revaccination policy

Francesca Fioredda

Istituto Giannina Gaslini, Genoa, Italy

In this issue Viana et al.[1] discuss immunity after chemotherapy for acute lymphoblastic leukemia whose recostitution does not garantee protection against vaccine preventable disease. Current treatment for acute lymphoblastic leukaemia (ALL) cures the majority of patients but as a consequence it causes severe immunosuppression which may even last after completing chemotherapy. After the end of treatment, immune reconstitution can take several months to be completed. According to many authors the immune system fully recovers, while other scientists sustain that a permanent deficit, which may be quantitative for some classes or subclasses of immunoglobulins and functional for some types of T lymphocytes, persists. This is especially true in high-risk patients who generally receive more aggressive treatment. However the question remains open[2].

The loss of immunological competence as a consequence of chemotherapy (and probably of the leukaemia itself) may compromise defense against vaccine-preventable diseases. Moreover, given the median age at disease onset, an insufficient vaccination program due to discontinuation of the schedule may occur.

Subjects whose levels of antibodies against specific vaccine antigens are below standard thresholds are considered to be without protection. Although there are some exceptions to this concept, the dosage of antibodies continues to be the most reliable method for the large-scale evaluation of protection in off-therapy ALL populations[2].

Several studies on residual vaccination titers have been published and very conflicting results have been shown. The differences in the sample sizes, timing of the titration of antibodies after chemotherapy, disparity in the antibody titration methods used as well as differences in the intensity and combination schedule of treatments over time that have been presented in various papers make comparison difficult[3,4].

As is observed for residual immunity to live vaccines, in particular against measles, after the end of therapy patients generally have lower levels of protection compared to the residual protection against the tetanus, polio and diphtheria vaccines[3,4]. The reported percentage of protection against measles is never greater than 75% among cohorts and the median values of protection are around 60%[3]. Some authors point out that the ability to respond to measles revaccination is seriously compromised due to the chemotherapy schedule that is adopted to treat leukaemia. One hypothesis, formulated by Nilsson et al.[5] is that depletion of antigen-specific B memory and plasma cells in the bone marrow compromises the ability to respond to the booster thus leading to a lack of specific antibody levels. Moreover, low responders to boosters seem to show both quantitative and qualitative defects in terms of low avidity of the antibodies to measles antigens[5]. Some authors sustain that the children who were not protected following chemotherapy were younger at the time of diagnosis than those who showed protective values[6,7].

As for residual immunity against hepatitis B, very few data have been published and data are quite conflicting even in two studies from the same country. In our cohort of leukemic children, protection against hepatitis B was found to be 80% and 82% respectively in patients 6 and 12 months after the completion of therapy for ALL[8], while in the other Italian study by Zignol et al.[9], of 73 patients with hematological malignancies (ALL and lymphoma), only 56% remained protected. Testing was carried out after a median of 15 months, and age at testing is not specified. A third study published on residual immunity against hepatitis B was carried out in the United States by Brodtman et al. and included 80 ALL patients who were titrated 2.2 years after the completion of chemotherapy; only 40% had protective titers[7].

The differences in protection titers might be due to age at titration, timing of antibody testing after the end of chemotherapy, and the different proportions of highly intensive treatments of the cohorts. Depending on the degree of loss of protection against vaccine-preventable disease, different strategies in revaccination should be applied. A selective policy could be to perform a blood test and only revaccinate non-protected subjects, chiefly those whose "protective" concentrations of antibodies are not comparable to what is seen in healthy children paired for age[8].

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Corresponding author:
Francesca Fioredda
Unit of Haematology
Giannina Gaslini Children's Hospital
Largo Gerolamo Gaslini 5
16147 Genova, Italy
francescafioredda@ospedale-gaslini.ge.it

www.rbhh.org or www.scielo.br/rbhh

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Universal revaccination is likely to be the easiest approach from a logistic point of view, mainly in countries with a weak "herd immunity" which is the "community barrier" against vaccine-preventable diseases.

In the light of this, protection after chemotherapy has to be conferred with high efficiency because of the possible diffusion of diseases such as measles which sometimes carry devastating consequences. In conclusion, revaccination policies have to be tailored very strictly to the local epidemiology of vaccine-preventable diseases.

In any case, when deciding whether or not to revaccinate children after chemotherapy, the risk /benefit and cost/ effectiveness ratios should be carefully evaluated in terms of sparing resources for the patient and health structures. Prospective multicentre studies will be able to provide clearer data on residual vaccination and will allow us to build the basis for more solid recommendations.

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