Outpatient management in patients with neutropenia after intensive chemotherapy—is it safe?

Bone marrow involvement and intensive chemotherapy for remission induction and post-remission consolidation render the patient with acute leukemia (AL) highly vulnerable to fever and infection. Often, neutropenia lasts 3 weeks or longer, and the risk of developing fever approaches 100%. Patients with allogeneic and autologous bone marrow or peripheral blood stem cell transplantation (alloPBSCT and autoPBSCT) today often have shorter periods of neutropenia. In autoPBSCT patients, for example, the duration of neutropenia may be shorter than 10 days, depending on marrow reserves after more or less pretreatment with cytotoxic drugs, prior radiation and the number of reinfused CD34+ cells. If intensive antimicrobial prophylaxis is used the fever incidence in these patients can be reduced from >90% to <60% [1].

Outpatient management is the standard care for lymphoma patients receiving chemotherapy, who usually have a <50% risk of developing fever. Outpatient management with oral antibiotics is increasingly common for so-called low-risk febrile neutropenia [2]. Outpatient management has now also become a common mode of care for selected patients undergoing autoPBSCT [3–7] and even alloPBSCT [8], despite their increased risks of toxicity including infectious complications. There is published experience from several groups and different locations to suggest that carefully designed outpatient autoPBSCT programmes can be successful. What are the successes? Reduced inpatient care could reduce healthcare costs, prevent family disruption caused by prolonged hospitalisation and raise patients’ quality of life. In theory, less exposure to nosocomial pathogens might have additional favourable effects. However, this is not well documented, and exposure to certain pathogens such as respiratory viruses and moulds might rather be increased in the home environment compared with the hospital environment. Most centres have an early discharge and outpatient management programme, rather than a comprehensive outpatient management programme. Despite the need for readmission in a significant proportion of discharged patients (mostly due to fever, fatigue, mucositis/dehydration), the length of stay can be significantly reduced, and this reduces costs [9].

The article by van Tiel et al. [10] published in this issue of *Annals of Oncology* reviews a number of studies to examine the evidence for the safety of this modern approach. As van Tiel et al. point out, if the previously used protected environments (strict reverse isolation and filtered air) were highly effective, one would have to be extremely cautious about promoting home care without evidence from carefully designed prospective randomised controlled studies. Their review of these older studies (mostly published prior to 1980) on the value of protected environments, however, shows rather inconsistent effects that depend on the end point definition (major local infection/severe infection versus bacteraemia/septicemia), and which are significantly influenced by antimicrobial prophylaxis. These effects are not convincing in view of the missing impact on survival and the unmeasurable psychological burden of the isolation that was associated with ‘life islands’. In addition, the power of these studies was quite limited. The standard of care today is different from what it was prior to 1980.

I believe that improved antimicrobial prophylaxis (fluoroquinolones, aciclovir, fluconazole) together with much more effective supportive care algorithms on one hand, and professional risk assessment and appropriate infrastructure for follow-up on the other, are key in discussing the successes of early discharge and outpatient management programmes. But is it safe, or safe enough? Since there are no prospective randomised controlled trials, there is no ‘first class’ evidence for the safety of these programmes. As is reported by van Tiel and colleagues [10], there is no indication so far of increased infection rates in the home-care environment (rather, the opposite is the case) or of a reduced survival associated with outpatient management in selected patients. But numbers of patients are small, and this message is therefore uncertain. Randomised trials would be a solution. More likely and, I think, also adequate will be derivation, validation and constant refinement of risk prediction models, with clinical end points such as medical complications requiring readmission and survival. More microbial colonisation data, as proposed by van Tiel and colleagues, can only be a secondary end point.

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References