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Summary

According to current guidelines, patients with thrombocytopenia due to myelosuppression are supported with platelet concentrates in order to prevent and treat bleeding complications using algorithms which include the level of thrombocytopenia as well as varying clinical parameters, e.g. concomitant infection, the use of anticoagulant drugs, specific interventions. In the last three decades, mainly driven by safety issues, several platelet product changes were made with leukoreduction in the eighties of the previous century, plasma reduction and the use of additive solution in the nineties and the use of pathogen reduction in the first decade of this century (chapter 1). Pre-transfusion in-vitro quality testing, considered essential by the FDA draft guidance, shows several significant differences during storage, however the used tests do not predict clinical efficacy. It is hypothesized that a combination of tests using a rating score could be a better alternative for the prediction of clinical efficacy (chapter 2). This thesis is mainly based on two randomised controlled trials testing the clinical efficacy of the use of additive solutions and pathogen reduction, essentially showing a decreased clinical efficacy as well as a decrease in adverse transfusion events (chapter 3-5). Platelet transfusion refractoriness occurred very frequent, but more importantly it was mainly if not solely caused by clinical factors (chapter 3) and associated with bleeding and a decreased patient survival (chapter 6). The second trial emphasising the difficulty of measuring and grading bleeding complications, nowadays considered as an essential endpoint in platelet transfusion trials, resulted in the performance of a pilot study showing that despite platelet transfusion support bleeding occurred in the vast majority (87%!) of patients (chapter 7). Similar studies from other investigators as well as these observations are leading to an era of "rethinking" the pathophysiology of bleeding and the role of platelet transfusion support: endothelial damage as a common pathway (chapter 8). As the development of novel platelet products continues recently a randomised controlled trial started, comparing conventional plasma stored platelets with riboflavin-UVB treated platelets using bleeding as primary outcome. In addition, this trial allows for several side studies, including HLA-immunisation as well as testing patient and product parameters in relation to clinical efficacy and the occurrence of bleeding (chapter 9). A better understanding of the pathophysiology of bleeding, thrombocytopenia and platelet transfusion refractoriness will lead to improvements in supportive care as well as patient survival, the common goal of all physicians.