The incidence and impact of thrombocytopenia in myelodysplastic syndrome

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Origin of Study USA

Type of Study LITERATURE AND CHART REVIEW

Objectives Perform a systematic review of the myelodysplastic syndrome (MDS) literature published between 1980–2005.

Compare the findings of this literature review with results from a retrospective chart review of MDS patients referred to The University of Texas M. D. Anderson Cancer Center (MDACC) since 1980.

Study Design The MEDLINE, EMBASE, and Cochrane databases were searched using specific keywords to identify literature concerning MDS that was published between January 1980 and November 2005; in addition, searches of Web sites from societies (eg, the American Society of Hematology, the American Society of Clinical Oncology) and the Internet were performed.

Different search strategies using specific keywords and inclusion criteria were followed for each topic of interest (ie, clinical consequences of thrombocytopenia in MDS, efficacy and safety of treatments for the condition, treatment guidelines).

Articles were reviewed independently by two reviewers; agreement concerning inclusion in the literature review was excellent, and disagreements were resolved by consensus.

Patients In all, 85 publications were included in the literature review—16 on the clinical consequences of thrombocytopenia, 60 on the efficacy of MDS treatments, and 9 on treatment guidelines. In all, 2,410 patients were referred to MDACC over the prescribed study period.

Observations The prevalence of thrombocytopenia in MDS patients ranged from 40%–65% in the literature review; the median frequency of thrombocytopenia before therapy was 65% (range, 23%–93%).

The MDACC database review identified 1,605 (67%) patients with thrombocytopenia at referral; severe thrombocytopenia was found in 425 (18%) patients.

Of the total number of patients, 1,756 were categorized according to the International Prognostic Scoring System (IPSS); 896 patients (51%) had intermediate-2 or high-risk disease, and 77% and 20% of these patients had platelet counts $< 100 \times 10^9$/L and $< 20 \times 10^9$/L, respectively. Corresponding event frequencies decreased to 51% and 12% in patients with low- or intermediate-risk disease, respectively.

The reported incidence of thrombocytopenia related to MDS treatment was > 50% in studies involving lenalidomide (Revlimid), azacitidine (Vidaza), or combined use of idarubicin, cytarabine, and topotecan (Hycamtin). Treatment-related thrombocytopenia was also seen in studies involving tipifarnib (Zarnestra), linomide (Roquinimex), decitabine (Dacogen), all-trans retinoic acid, and sirolimus (Rapamune).

The reported incidence of hemorrhagic complications was 3%–53%, and the frequency of hemorrhagic deaths ranged from 14%–24%. Finally, at MDACC, 460 patients had a coded cause of death (hemorrhage as a cause, 20%; hemorrhage as the only cause, 10%).

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Conclusions

The incidence of severe bleeding in MDS was higher than that reported in current guidelines or reviews.

Discussion

Thrombocytopenia and platelet dysfunction contribute to the hemorrhagic complications observed in MDS. Reliable data regarding the frequency and clinical consequences of thrombocytopenia in patients with MDS are lacking, and there is little consensus regarding its optimal treatment. This study was performed to provide this information through a systematic review of the MDS literature published between 1980 and 2005. The findings from the literature review of 85 publications were compared with results from a retrospective chart review of 2,410 MDS patients at MDACC (79% with primary and 21% with secondary MDS).

The literature and chart review confirmed that thrombocytopenia is common in MDS, especially in patients in higher risk categories of IPSS, and that bleeding risk is not inconsequential.

In the literature review, thrombocytopenia in MDS ranged from 40%–65%, with a median frequency before therapy of 65%. In the chart review, 67% of patients had thrombocytopenia at the time of referral to MDACC, with 17% exhibiting severe thrombocytopenia (platelet count $< 20 \times 10^9$/L). By IPSS group, 82% of patients at high risk developed thrombocytopenia, 25% of it severe, whereas low-risk IPSS patients had only a 20% incidence.

Thrombocytopenia was just as common among patients with secondary MDS (75% incidence, 21% severe) and in patients who underwent primary chemotherapy (73% and 22%, respectively).

The analysis also confirmed that many MDS therapies cause or exacerbate pre existing thrombocytopenia. In studies involving lenalidomide, azacitidine, or a combination of idarubicin, cytarabine, and topotecan, the reported incidence of MDS treatment-related thrombocytopenia was > 50%. Treatment-related thrombocytopenia was also observed in studies involving tipifarnib, linomide, decitabine, all-trans retinoic acid, and sirolimus.

In some cases, thrombocytopenia led to serious clinical consequences. Although none of the studies examined the risk of bleeding based on platelet counts exclusively in an MDS population, the chart review from MDACC (in the 460 patients with a coded cause of death) cited hemorrhage as a contributory cause of death in 20% of patients and as the only cause of death in 10%.

Nine sets of guidelines were identified in the publications, but they were not clear or in agreement regarding the treatment of thrombocytopenia. Some guidelines for platelet transfusions concluded that MDS patients may have minimal or no serious hemorrhage; however, the literature review and the MDACC experience showed that bleeding complications in MDS patients may be more common than current opinion would suggest. The investigators concluded that development of novel agents that specifically treat thrombocytopenia is clearly warranted.

Key Points

- Thrombocytopenia is more common in MDS patients than previously reported and is more prevalent in patients in higher risk IPSS categories.
- Many approved and investigational MDS treatments cause or exacerbate preexisting thrombocytopenia.

Reference

Kantarjian HM, Giles F, List AF, et al. The incidence and impact of thrombocytopenia in myelodysplastic syndrome. Presented at the 48th Annual Meeting of the American Society of Hematology; December 9–12, 2006; Orlando, Florida. Abstract 2617.