

Drug-Induced Thrombocytopenia An Updated Systematic Review, 2010

Using methodology initially established 12 years ago,^[1] we have systematically reviewed all English-language reports on drug-induced thrombocytopenia and published updates every 2 years; our most recent previous update was 6 October 2008.^[2] Our goal for these continuing updates is to provide an accessible website resource for standardized analysis of all published reports of drug-induced thrombocytopenia, describing the level of evidence for a causal role of the drug, patient demographics, clinical outcomes and link to the publication for each report (www.ouhsc.edu/platelets). This letter presents the results of our current literature search.

Using our previously described MEDLINE literature search strategy^[1] on 20 October 2010, we identified articles published since October 2008. Reviewing the bibliographies of the selected articles, additional articles published prior to October 2008 were also identified that had not been previously identified. We retrieved 76 articles for review. Using our evaluation criteria,^[1] each article was reviewed independently by the authors to assess the level of evidence for a causal role of the drug for the thrombocytopenia; disagreements were resolved by consensus. Twelve articles were excluded from further analysis because they were review articles or experimental studies with no primary patient data, or they reported heparin-associated thrombocytopenia, a topic excluded from our reviews.^[1] Fifty-five articles reported data on 67 individual patients who had thrombocytopenia associated with 28 different drugs. Eight patient reports were excluded because they met one or more of our six exclusion criteria.^[1] The remaining 59 patient reports described thrombocytopenia associated with 27 drugs: 10 reported level 1 (definite) evidence, 17 reported level 2 (probable) evidence, 26 reported level 3 (possible) evidence and 6 reported level 4 (unlikely)

evidence. Nine articles reported group data; in five articles a causal role for the drug could not be assessed because the study met one or more of our six exclusion criteria.^[1] The remaining four articles reported data on three drugs: one had level 1 (definite) evidence, one had level 2 (probable) evidence and two had level 3 (possible) evidence. From the reports of both group and individual patient data, two drugs were identified as having evidence supporting a causal relation to thrombocytopenia, defined by at least one report with level 1 (definite) evidence or two reports with level 2 (probable) evidence, which had not been documented in our previous systematic literature reviews (table I). The complete database of all articles from this literature search, together with our previous literature searches, including the definitions of levels of evidence, exclusion criteria, complete citations with links to the published articles, and demographics and clinical outcomes of the individual patients is available at www.ouhsc.edu/platelets. In addition, this website also contains databases for drugs that were confirmed as causes of drug-induced thrombocytopenia by demonstration of drug-dependent, platelet-reactive antibodies by the Blood Center of Wisconsin and drugs demonstrating a statistically distinct reporting association with thrombocytopenia in the Adverse Event Reporting System database of the US FDA. These three methods of

Table I. Drugs identified as causing thrombocytopenia in the 2010 literature search that had not been documented in previous reviews

Drug ^a	Reports (n)	
	level 1 evidence	level 2 evidence
Methylprednisolone	1	0
Filgrastim (G-CSF)	0	2

a These two drugs were not reported in our previous systematic reviews (www.ouhsc.edu/platelets) as having evidence supporting a causal relation to thrombocytopenia, defined by at least one report with level 1 (definite) evidence or two reports with level 2 (probable) evidence. These reports are both individual patient data. For individual patient data, definite evidence (level 1) required re-exposure to the drug, causing a repeat episode of thrombocytopenia. Probable evidence requires all criteria except re-exposure to the drug; therefore, two reports with probable evidence are accepted as establishing a causal relation to thrombocytopenia.

G-CSF = granulocyte colony-stimulating factor.

identifying drugs that can cause thrombocytopenia have been compared in a recent publication.^[3]

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