

Drug-Induced Thrombocytopenia

An Updated Systematic Review, 2006

Using our established methodology,^[1] we have regularly and systematically reviewed all English-language reports on drug-induced thrombocytopenia. Our goal for this continuing update is to provide an accessible resource for all reports of drug-induced thrombocytopenia, describing the level of evidence for a causal role of each drug as well as clinical outcomes. We have previously reported the results of our continuing systematic reviews through 14 August 2004;^[1-4] this letter describes our systematic review up to 20 October 2006.

Using our previously described MEDLINE literature search strategy,^[1] we retrieved 55 articles; we identified four additional articles by searching the bibliographies of the retrieved articles. Using our previously published evaluation criteria,^[1] each patient case report was reviewed independently by three of the authors to assess the level of evidence for a causal role of the drug for the thrombocytopenia; disagreements were resolved by consensus. Forty-seven articles contained 74 case reports of individual patient data, of which 18 were excluded because they did not meet previously defined criteria.^[1] The remaining 56 patient case reports involved 21 drugs: seven drugs had level I (definite) evidence and eight other drugs had level II (probable) evidence. Of these 15 drugs with definite or probable evidence for causing thrombocytopenia, six had not been documented in our previous reviews^[1-4] as causing thrombocytopenia, defined by at least one report with level I (definite) evidence or two reports with level II (probable) evidence (table I).

For individual patient data, definite evidence (level I) required re-exposure to the drug that result-

Table I. Drugs causing thrombocytopenia that had not been documented in previous reviews^[1-4] as causing thrombocytopenia

Drug	Number of reports	
	level I evidence	level II evidence
Individual patient data		
Adefovir dipivoxil	1	0
Lopinavir/ritonavir	1	0
Teicoplanin	1	0
Efalizumab	0	5
Etretinate	0	2
Oxaliplatin ^a	0	2
Group data		
Famotidine	0	2 ^b

- a Chemotherapeutic agents have been excluded from our previous evaluations because of their predictable potential for causing thrombocytopenia due to dose-dependent marrow suppression. For this review, an exception was made for oxaliplatin because of multiple reports of the sudden occurrence of isolated thrombocytopenia immediately following an oxaliplatin infusion, without accompanying neutropenia or other evidence of marrow suppression and with demonstration of oxaliplatin-dependent anti-platelet antibodies.
- b One of the reports was the description of an individual patient.

ed in recurrent thrombocytopenia or validation of the causal relation to thrombocytopenia by at least two patient case reports with probable evidence (level II), requiring all criteria except re-exposure to the drug. For group patient data, definite evidence (level I) was defined as a significantly increased rate of thrombocytopenia associated with the drug compared with a control group in a randomised clinical trial; probable evidence (level II) was defined as a significantly increased rate of thrombocytopenia associated with the drug compared with a control group in a nonrandomised study. Twelve articles reported group patient data on 16 studies, of which four were excluded because they did not meet previously defined criteria.^[1] Among the remaining 12 studies, one additional drug was identified as having definite evidence for causing thrombocytopenia that had not been documented in our previous review^[1-4] as causing thrombocytopenia (table I).

The complete database of all articles from this report plus our previous reviews, including the defi-

nitions of levels of evidence and exclusion criteria, complete citations and demographics and clinical outcomes of the individual patients is available at <http://moon.ouhsc.edu/jgeorge>.

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