

173. Thrombocytosis Induced by Low-Molecular-Weight Heparins' Therapy

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Introduction: The prophylaxis and therapy of deep venous thrombosis by low-molecular-weight heparins (LMWHs) can be associated with the occurring of thrombocytosis. This uncommon side effect is now mentioned for all LMWHs in the French summary of product characteristics as a "possibility of asymptomatic and reversible increased of platelet's count".

Objective: Following a report of a man who developed serious thrombocytosis during enoxaparin therapy after an aortic surgery, we analyzed all cases of thrombocytosis with LMWH's therapy reported in the French Pharmacovigilance database.

The objective of our study is to test the significance of the association between reports of thrombocytosis in the French Pharmacovigilance database and LMWH's therapy.

Methods: All cases reported in the French Pharmacovigilance database since 1985 until March 2006 were analyzed. We selected the reports mentioning the LMWHs (enoxaparin, nadroparin, tinzaparin, dalteparin and reviparin) as a "suspected drug" with the following adverse drug reaction key words according to the WHOART terminology: thrombocytosis, thrombocytemia, increased platelet count. The analysis relied on the case/non-case method and the association was measured by an odds ratio (OR) with a 95% CI ($p < 0.0001$). Cases correspond to reports of thrombocytosis identified with the chosen key-words and non-cases are defined as all other reports of adverse reactions reported in the database.

Results: There were 366 cases of thrombocytosis among the 283 563 reports of drug-induced adverse effects in the database, with 178 of 8544 involving LMWHs. For the analysis, we retained only cases with a laboratory platelet count test ($n=150$).

The number of non-exposed cases is 188. The total number of non-cases is 283 197 of which 8366 patients were exposed to an LMWH (exposed controls).

The calculated OR were: OR enoxaparin = 32.67, 95% CI: 26.13-40.85, OR nadroparin = 9.89, 95% CI: 6.79-14.41, OR tinzaparin = 21.32, 95% CI: 12.83-35.41, OR dalteparin = 7.67, 95% CI: 4.30-13.68 and OR reviparin = 41.39, 95% CI: 18.09-94.69.

Conclusion: This analysis confirms that LMWH's therapy is clearly associated with a higher risk of thrombocytosis. This event remains rare but can be associated with clinic symptom (thrombotic accident), particularly for cases with a platelet count $> 1\ 000\ 000$ cells/mm³ and when thrombosis risk factors coexist. A risk of thrombotic accident is not insignificant although no evident clinic sign was observed in the reported cases of thrombocytosis. All the more since the physiopathologic mechanism is not still precisely defined.