Burden of costs associated with heparin-induced thrombocytopenia: is time to remove unfractionated heparin from the drug formularies in medical institutions?

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Heparin-induced thrombocytopenia (HIT) represents a serious complication of heparin therapy. Despite generally safe, heparin use can trigger a transient and life-threatening immune-mediated response in which immunoglobulin G antibodies set off immunological complexes against platelet factor 4 (PF4) (1). This determines a highly pro-thrombotic state through different pathways: intensive platelet aggregation, augmented thrombin generation and intravascular platelet aggregation. It has already been established that the risk for HIT is approximately 5- to 10-fold with the use of low-molecular weight heparin (LMWH) than with unfractionated heparin (UFH) (2,3). This finding seems enough intuitive that using less UFH would reduce the incidence of HIT. However, demonstrate this theory is very far to be simple. Generally, the previous medical literature has focused on early recognition and treatment of HIT but its prevention has been neglected. Recently, McGowan et coll. have published their results about their 10-year quality-improvement study, performed in a tertiary-care Canadian hospital, in which they tested whether substituting LMWH for UHF would reduce the risk and global costs for HIT (4). More precisely, UFH was replaced with LMWH for all prophylactic and therapeutic indications except during haemodialysis, cardiac surgery and in selected patient with acute coronary syndrome (ACS). Furthermore, all heparin flushes for central and arterial venous lines were replaced with saline. To notice that most care providers of the enrolling center were unware that heparin was being replaced with by LMWH and none were aware that this practice change was under evaluation. The protocol of the study divided the research into two phases: a pre-intervention phase (from 2003 to 2005) and an "Avoid-Heparin phase" (from 2007 to 2012). As result, the annual rate of suspected HIT decreased from 85.5 per 10.000 admissions, in the pre-intervention phase, to 49.0 per 10.000 admissions in the "Avoid- Heparin phase" (42%, P<0.001). The annual rate of patients with a positive HIT assay drastically decreased from 16.5 to 6.1 per 10.000 admissions (P<0.001). Also adjudicated HIT and HIT with thrombosis dropped from 10.7 to 2.2 and from 4.6 to 0.4 per 10.000 admissions, respectively (relative risk reduction were 79% and 91%, P<0.001, respectively). Furthermore, avoiding the use of UFH reduced the average estimated costs of HIT care per year by 83% (4). Similar results were obtained in a recent sub-study obtained from the PROTECT Trial, in which deltaparin was found to be more cost-effective than UFH (5). Nowadays, it is well-established that LMWH has several advantages over UFH, not only compared to the lower risk of HIT. Indeed, LMWH required a once daily dosing for prophylaxis, is administered subcutaneously and no laboratory monitoring is needed. However, in terms of costs, a unit of LMWH is 6- to 8-fold higher than of UFH (6). It could seem paradoxical that despite LMWH is more expensive than UFH, the reduction of HIT obtained with the avoid of this latter results in a substantial decrease of global costs. However, in a period like this, where healthcare system must be parsimonious, is the replacement of UFH with LMWH sustainable? If LMWH is able to reduce both the clinician and financial burdens oh HIT, is it indicated to remove UFH from medical institutions?

We are in accordance with the answer given by Linkins in a commentary accompanying McGowan's report (6). The answer is obviously no, because UFH remains the best option in some clinical scenarios as cardiac surgery, renal failure and in those patients at high risk of bleeding. In last years, we are seeing that LMWH and novel oral's anticoagulant (NOACs) are gradually replacing, in some diseases, the treatment with UFH. For example, NOACs have been recently analysed as a cost-effective alternative to LMWH/warfarin in venous thromboembolism (VTE) (7). Indeed, current data about the avoidance of HIT have some limitations; in fact, they are obtained in a monocentric study and the number of patients enrolled is relative low. The avoidance of UFH represents a possible valid and relative simple strategy to obtain reduction in morbidity, mortality and costs for HIT; however, further studies are needed to confirm and optimize this kind of program. Apart from that, the study of McGowan *et al*. represents an important progress in the prevention, treatment and costs management of HIT.

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Footnote

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