(Acta Anaesth. Belg., 2003, 54, 301)

New antithrombotic agents : unsolved issues

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Venous thromboembolism (VTE) is known as a common complication of surgery, with some procedures, such as orthopaedic and abdominal surgery for cancer, carrying a particularly high risk. However recent studies have shown that in patients undergoing a prolonged prophylaxis after total hip replacement, the clinical venous thromboembolic (VTE) risk was almost controlled, and limited to only 2% of the patients after 6 weeks of low molecular heparin LMWH) prophylaxis.

Nevertheless, limitations of currently available prophylactic options, particularly in high-risk settings such as orthopaedic surgery, include prophylaxis failure and bleeding complications. The ongoing need for improved prophylaxis has led to the development of several novel drugs, including recombinant hirudin, pentasaccharides, and oral thrombin inhibitors. The emergence of new, and potentially more expensive, antithrombotics highlights the need for accurate identification of high-risk patients for whom conventional prophylaxis may be ineffective (the remaining 2%). The pentasaccharide (Arixtra® - fondaparinux) and the new oral antithrombin agent (Exanta® - Ximelagatran) are now almost available on the market. Thousands of patients have been included in the pivotal studies. These treatments have shown to be effective in decreasing the global deep vein thrombosis (DVT) rate, based on a *venographic* standpoint. However no clinical difference in VTE has ever been observed. Furthermore the treatment safety when started before surgery (Exanta®) or less than 6 hrs after surgery (Arixtra®) was not optimal, leading to reconsider the benefit of these new agents in orthopaedic surgery based on a *clinical* standpoint. The development of validated risk assessment models will allow rational use of these molecules. Fondaparinux, for instance, could be interesting in obese patients or high risk patients with a normal renal function. Only studies with clinical endpoints will lead the anaesthesiologists to switch from a well know group of molecules (LMWH) to these new promising agents.

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