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The quagmire of thromboprophylaxis

There isn't a surgeon or medical doctor among us who doesn't have, in some way or other, strong opinions on the topic of thromboprophylaxis. Unpicking the mess that this has all become is, to say the least, a challenge. There are so many issues to deal with: which patients require thromboprophylaxis, what type they require, and how long it is required for.

The easiest of these arguments to unpick is perhaps that of which medication should be given. There are powerful drug lobbies behind the use of extended thromboprophylaxis, particularly low-molecular-weight heparins and factor Xa inhibitors, their argument being that extended thromboprophylaxis is essential for patients with large joint arthroplasties, as the development of a thromboembolism continues well beyond the hospital stay. In a hugely important study published this month in the *New England Journal of Medicine*,[1] the use of thromboprophylaxis (and varieties thereof) has been tested in a large randomized controlled trial. The results of this are unequivocal: aspirin is "not inferior" to Xa inhibitors in extended thromboprophylaxis use for both hip and knee arthroplasty.[1] This won't be a surprise to many who have been keeping up to date with *The Bone & Joint Journal*.[2] However, the addition of a large, well-conducted, randomized controlled trial to this debate makes it likely that aspirin will become the standard medication of choice if extended thromboprophylaxis is required.

There have been several other landmark papers in recent years dealing with other potential questions surrounding thromboprophylaxis. The Prevention of Thrombosis after Knee Arthroscopy (POT-KAST) and the Prevention of Thrombosis after Lower Leg Plaster Cast (POT-CAST) trials published together last year,[3] again in the *New England Journal of Medicine*, give us evidence that patients undergoing arthroscopic surgery, and those in a lower limb cast, do not need to have thromboprophylaxis. This strengthens the findings of Selby et al,[4] who stopped their study evaluating the application for thromboprophylaxis in patients with isolated lower limb casts after 256 patients, due to an identical event rate in the two groups but a higher adverse event rate in the thromboprophylaxis group.

The question that we now find ourselves with is: how did we reach a point where trials are needed to withhold a medication that has no apparent benefit in many patients? The answer, of course, lies in the original studies and in the political lobbies.

This is not one of those cases where we are treating a problem that does not exist. The rates of significant thromboembolism without any prophylaxis are high. The original trials supporting the use of low-molecular-weight heparin were the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) studies, a group of three non-inferiority studies designed to establish if low-molecular-weight heparin had equivalent outcomes to aspirin. The eventual outcome of these studies was that it was indeed equivalent.

The trials we have now are no different to the ones we had then. The difference is that we don't have 'Big Pharma' pushing and lobbying for use of an expensive drug. The cost to the NHS alone of thromboprophylaxis is mind-boggling. In no small part, this is due to successful lobbying from the charity Thrombosis UK, the medical directors of which have conflicts of interest,[5] are supported by a number of pharmaceutical companies, and sit on the NICE thrombosis committee. Perhaps the most bizarre twist in this tale was the asking of questions in the House of Commons about what the government was planning to do to address the 32 000 preventable hospital deaths/year from thromboembolic disease. There are no scientific references I have been able to find to this number, which seems to have originated itself from the question put to the house and subsequently been recorded in Hansard.[6]

Remembering that the original studies showed non-inferiority of heparins to aspirin, the answer, strictly speaking, should have been to carry on recommending aspirin. It is an important reminder to us all that, through powerful lobbies and pressure groups – which are classically associated with, but by no means limited to, the United States – political and financial motivations pervade research and healthcare policy.

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