Letters to the Editor

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Occult Cancer and Venous Thromboembolism

Dear Sir,

Recently in this journal, Rajan and colleagues (1) found no increased risk of subsequent cancer in patients presenting with idiopathic venous thromboembolism (VTE) compared with patients with secondary VTE (8.6% of prevalence vs. 7.1%, respectively; odds ratio, 1.2) and claim that the effects of compounds such as sodium salicylate may vary under different conditions.

However, in support of our findings, aspirin enhanced LPS-induced pro-coagulant and pro-inflammatory activity in HWB (4, 5). Thus, the potentiation of LPS-induced TF expression in HWB appears to be a consistent finding, but it is not clear why sodium salicylate or aspirin inhibited the inducible expression of TF in isolated monocytes (2, 3).

The possible role of cyclo-oxygenase (COX) inhibition in these effects of NaSal was explored in subsequent experiments. Indomethacin (10 μM), a COX inhibitor, produced a much less marked potentiation of the LPS response but completely inhibited LPS-stimulated PGE₂ release in HWB (data not shown). Moreover, NaSal had no effect on PGE₂ production, suggesting that this pathway is not involved in the NaSal-induced potentiation of TF expression.

Our findings are discordant with those in which NaSal or aspirin inhibited the inducible expression of TF in isolated monocytes (2, 3). However, in support of our findings, aspirin enhanced LPS-induced pro-coagulant and pro-inflammatory activity in HWB (4, 5). Thus, the potentiation of LPS-induced TF expression in HWB appears to be a consistent finding, but it is not clear why sodium salicylate or aspirin are inhibitory in some studies involving isolated monocyte/mononuclear cells (2, 3), but not others (present study) using isolated monocytes/mononuclear cells. Differences in culture conditions or the use of cells in different states of differentiation may result in some signalling pathways becoming more or less prominent and it is therefore possible that the effects of compounds such as sodium salicylate may vary under different conditions.

Table Prevalence of newly diagnosed cancer in patient with idiopathic or secondary VTE at the end of follow-up period after VTE

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biopsies), it should be demonstrated that the results of testing are really useful to improve life expectancy. Some authors suggest the usefulness of extensive screening including abdominal and pelvic CT scan, with or without additional gastro-intestinal endoscopy (5, 9, 12). Others, such as Cornuz et al. (13) propose a simplified approach which includes history, physical examination, routine laboratory tests and chest x-ray (i.e. the standard clinical evaluation performed at admission in the hospital), with more extensive screening procedures in few selected patients only. Unfortunately, the sample size of the published studies is generally too small to draw any conclusion and to suggest reliable guidelines. In a recent paper Barosi et al. (14) showed that the only cost-effective strategy in patients with idiopathic VTE includes the search of colon and breast cancer in females and colon cancer in males.

A large, prospective clinical trial on the effect on survival of an extensive screening for occult cancer in patients with idiopathic VTE is ongoing (15), and it should give us the definitive answer. However, the starting point (i.e. the increased risk of subsequent cancer in these patients) seems to be solidly demonstrated.

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References


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Successful Calibration of a Reagent from Human Placenta against rTF/95, the WHO International Reference Preparation for Thromboplastin, Human Recombinant, Plain

Dear Sir,

The World Health Organization (WHO) recommends to express results of the prothrombin time (PT) test for patients on oral anticoagulants by the scale named International Normalized Ratio (INR). To this end WHO established a system of calibration that requires different steps. In the first step, International Reference Preparations (IRPs) for thromboplastin are established and distributed to national control laboratories and reagent manufacturers. In the second step the IRPs are used to calibrate national or manufacturers house standards.

These are in turn used in the third step to calibrate working reagents (1). Until recently, there were three different IRPs characterized by the species from which they have been derived and by their composition with respect to whether or not fibrinogen and factor V have been added (combined, or plain reagent): rabbit, plain (coded RBT/90); bovine, combined (OBT/79) and BCT/253, human, plain. The latter was very recently replaced by a new preparation (coded rTF/95) made of relipidated human recombinant tissue factor (2). According to the guidelines issued by the WHO, national and working reference preparations must be calibrated against the appropriate IRP (1). It is recommended that plain reagents from rabbit origin be calibrated against RBT/90; combined bovine and combined rabbit reagents against OBT/79 and human reagents against rTF/95. The idea behind this recommendation is to perform like-to-like calibration in order to...