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Risk of venous thromboembolism associated with peripherally inserted central catheters: a systemic review and meta-analysis

Chopra V, Anand S, Hickner A, Buist M, Rogers MAM, Saint S and Flanders SA. The Lancet 2013;382(9889):311-25.

The relative risk of the development of venous thromboembolism from peripherally inserted central catheters (PICC) and other central venous catheters (CVC) is unknown. More evidence should aid appropriate selection of the device and informed consent for a specific patient according to his or her need and preference. A systemic review and meta-analysis of the risk of venous thromboembolism associated with PICCs compared with CVCs has been undertaken. Several databases, including Medline, Embase, Biosis, Cochrane Central Register of Controlled Trials, Conference Papers Index and Scopus were searched. Other studies were identified through manual searches of bibliographies, the internet, and direct contacts (to obtain unpublished data). All human studies published in full text, abstract, or poster form were eligible for inclusion. These were of adult patients of 18+ years who had had a PICC inserted. They were assessed with the Newcastle-Ottawa risk of bias scale. Where there was no comparison group, the pooled frequency of venous thromboembolism was calculated for patients receiving PICCs. In studies comparing PICCs with other CVCs, summary odds ratios (ORs) were calculated with a random effects meta-analysis. Of the 533 identified citations, 64 (12 with a comparison group and 52 without) including 29 503 patients met the eligibility criteria. In the non-comparison studies, the weighted frequency of PICC-related deep vein thrombosis was highest in patients who were critically ill (13·9%, 95% CI 7·7-20·1) and those with cancer (6·7%, 4·7-8·6). Meta-analysis of 11 studies comparing the risk of deep vein thrombosis related to PICCs with that related to CVCs showed that PICCs had an increased risk of deep vein thrombosis (OR 2·55, 1·544·2, $p<0·0001$), but not pulmonary embolism. With the baseline PICC-related deep vein thrombosis rate of 2·7% and a pooled OR of 2·55, the number needed to harm relative to CVCs was 26 (95% CI 13-71). We conclude that PICCs are associated with a higher risk of deep vein thrombosis than CVCs, especially in patients who are critically ill or those with a malignancy. The decision to insert PICCs should be guided by weighing the risk of thrombosis against their benefit.

Reviewer's opinion: The meta-analysis results and comprehensive overview on the subject of "intravenous catheter use and the risk of associated complications" presented by the authors is plausible. Use of these devices has increased many folds in oncology over the last decade, particularly PICC, being easier to insert. After rigorous structured training, the procedure is mostly done by chemotherapy nurses and relatively junior medical staff. Identification of a higher incidence of PICC-associated deep vein thrombosis compared to central venous catheters identified in the meta-analysis could be due to these catheters being longer, increasing venous endothelial trauma, but the risk factors and safety measures need more assessment. Despite the inclusion of several unpublished data in this article, the authors should be congratulated because it is highly unlikely that a randomised controlled prospective study on the subject will be conducted. The evidence presented is compelling and consistent across all the studies included within their meta-analysis. Unfortunately, currently available pharmacological measures do not provide reasonable protection against thrombosis.

Risk assessment, fully informed consent and optimum precautions, like avoidance of misplacement of the tip of the catheter, must be undertaken when these devices have to be inserted. – SU

New England Journal of Medicine

Pazopanib versus Sunitinib in Metastatic Renal-Cell Carcinoma

Motzer R J, Hutson T E, Cella D et al. New England Journal of Medicine 2013;369(8):722-31.

Pazopanib and sunitinib provide a progression-free survival (PFS) benefit compared with placebo or interferon in patients with metastatic renal-cell carcinoma. This randomised trial compared head-to-head, the efficacy and safety of pazopanib and sunitinib as first-line therapy. In this multi-centre, phase III study, 1110 patients with clear-cell metastatic renal-cell carcinoma were randomised in a 1:1 ratio to receive a continuous dose of pazopanib (800 mg once daily; 557 patients) or sunitinib in 6-week cycles (50 mg once daily for 4 weeks, followed by 2 weeks without treatment; 553 patients). The primary end-point was PFS, the study being designed to show that pazopanib was not inferior to sunitinib. Secondary end-points included overall survival, safety and quality of life.

Pazopanib was not inferior to sunitinib with respect to PFS (HR for PFS or death from any cause, 1.05; 95% confidence interval [CI], 0.90 to 1.22), meeting the predefined non-inferiority margin. Overall survival was similar (HR for death with pazopanib, 0.91; 95% CI, 0.76 to 1.08). Patients treated with sunitinib were more (i) fatigue (63 vs. 55%), hand-foot syndrome (50 vs. 29%) and thrombocytopenia (78 vs. 41%); and those treated with pazopanib more often had increased ALT (60 vs. 43%), weight loss, alopecia and change of hair colour. The mean change from baseline in 11 of 14 health-related quality-of-life domains, particularly those related to fatigue or soreness in the mouth, throat, hands, or feet during the first 6 months of treatment, favoured pazopanib ($P<0.05$ for all 11 comparisons). Thus, pazopanib and sunitinib have similar efficacy, but the safety, quality-of-life and patient satisfaction with treatment profiles favoured pazopanib.

Reviewer's opinion: Side effects and its impact on quality of life (QOL) are important considerations for both patients and their clinicians in the management of advanced cancers. It (QOL) takes precedence when different therapies have similar efficacies (response rate, PFS and OS), but significant differences in their side effects for some of the patients. The results of a COMPARZ trial clearly establish the superiority of pazopanib over sunitinib, the reference standard on this front. Both drugs are multi-targeted TKI with similar efficacy, which is reassuring for patients and their clinicians. It allows them to choose the most appropriate agent. However, non-inferiority is not synonymous with equally efficacy. One of the most pertinent points is that pazopanib was superior on 11 out of 14 measures of QOL. Pazopanib has already been recommended by the NICE as first-line treatment for patients in the UK with advanced kidney cancer, since GSK officials had agreed to a 12.5% discount on the list price and possibly a second rebate following the outcome of COMPARZ. Lower medical resources need, e.g. fewer phone calls to clinics and visits to hospitals due to better tolerance, will favourably influence when cost-benefit issue have been reconsidered by the authorities. – SU