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Midline Catheters – a good alternative device?

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Safe and efficient administration of peripherally compatible intravenous (IV) therapy in hospitalised patients is a growing challenge and the need for reliable alternative vascular access device (VAD) options, particularly in those with difficult access, is increasing. Traditionally, peripheral intravenous catheters (PIVC) have been favoured, and are often the "default" VAD, without due consideration given to the planned type or duration of treatment [1]. Over 2 million PIVCs are purchased globally each year, with their popularity influenced by false perceptions of consistently “easy” insertion and few serious associated complications [2]. Nevertheless, there is increasing recognition of the high incidence of PIVC complications - occlusion, infiltration, phlebitis, dislodgement, infection – with all-cause failure now reported as high as 68% [3]. Such PIVC failure can interrupt ongoing medical treatment, extend hospital stay, increase patient anxiety (and needle phobia), and deplete patients’ vasculature for future treatment [4]. The resulting substantial financial burden of the endemically high PIVC failure rate is derived from additional resource consumption - the extra staff time and products needed to replace and treat the complications of failed PIVCs [4]. Hence there is currently an urgent necessity for the consideration of alternative VADs to optimally deliver peripherally compatible IV therapy, whilst preserving patient’s vasculature.

As highlighted by Queixalos et al. [5], the midline catheter (MC) has become an increasingly popular VAD choice for hospitalised patients. MCs offer an alternative to PIVCs and are considered appropriate to meet patients’ needs for short to moderate duration (up to 14 days) IV treatment [6]. MCs have been available since the 1950s; however, their popularity increased when remodelled with modern materials such as polyurethane and silicone [7, 8]. MCs for adults’ range in length from 7.5 to 25 centimetres, with the catheter tip terminating at the level of the axilla, thereby avoiding the central venous circulation and potentially reducing infection and thrombosis risks associated with central VADs. Despite the increased uptake of MCs as a VAD option in countries such as France, Australia and North America, their risk profile is still unclear, and a greater understanding is urgently needed to guide safe clinical practice.

Queixalos et al. [5] describe in this issue the infectious outcomes of 136 MCs from the University Hospital of Poitiers. The authors report both the European definition of *Catheter Related Clinical Sepsis* (CRCS; termed “catheter infection” in the study), as well as the *Catheter Related Bloodstream Infection* (CRBSI) definition more common in North America [9]. Both definitions require clinical manifestations of infection, with no other obvious source, but otherwise have quite different criteria. The CRCS diagnosis additionally requires both resolution of clinical manifestations within 48 hours of catheter removal and a positive catheter tip (≥ 10^3CFU/ml quantitative vortexing, ≥ 15 cfu/plate semiquantitative culture, or 10^2 cfu/ml quantitative sonication); no positive blood culture is required [9]. In contrast, CRBSI additionally requires one positive peripheral blood culture and (i) an organism matched positive tip culture, or (ii) matched blood cultures drawn from both the device and peripheral vein meeting a differential time to positivity of more than 120 minutes (catheter *versus* peripheral blood), or (iii) simultaneous quantitative blood cultures with a ratio of > 3:1 cfu/ml (catheter *vs.* peripheral blood) [9]. Queixalos’ study provides an interesting opportunity to compare the relative infection incidence obtained with the two definitions, and in this case, they produced similar results [5]. CRCS incidence was slightly higher at 9% compared with CRBSI 7%, suggesting that while the CRCS criteria are easier to apply, they do not drastically increase rates over microbiologically proven criteria. Presumably for the CRBSI outcome, patients met these criteria due to a positive matched tip rather than paired blood cultures, since blood sampling from peripheral devices is traditionally not recommended. However, MCs have a larger diameter than PIVCs; should blood be drawn through MCs in patients suspected of infection, and can the DTP or paired quantitative culture criteria be used to diagnose infection in these devices, as for central catheters? To our knowledge, no diagnostic accuracy studies have yet tackled these possibilities.

Queixalos et al.'s [5] results add to emerging evidence on the infection burden of MCs. Our exploration of MC literature found seven observational studies reporting MC infections in hospitalised patients - in Australia [10, 11], Europe [12, 13] and North America [14-16]. Four studies [10, 11, 13, 15] used the CRBSI criteria. Two of these reported zero CRBSI in 42 [10] and 231 MCs [11] in cystic fibrosis patients, a study of 80 MCs in a Cardiothoracic-Vascular Department reported one (1.25%) CRBSI [13], and a large study of 1161 MCs from the general medicine and intensive care units of twelve hospitals in Michigan, USA, reported 4 CRBSIs (0.3%). Despite MCs being peripheral and not central VADs, Mushtq et al. [14] defined MC infection using both CRBSI and central line associated bloodstream infection (CLABSI) definitions and reported one CRBSI (0.2%), but no CLABSI in 411 MCs. Two emergency department studies (total = 126 MCs) reported zero MC-associated infections, although the definition used was unclear [12, 17]. Thus, CRBSI rates for MCs appear low, but the lack of consensus in infection definitions makes benchmarking between studies problematic, and validation of existing definitions for MC use is urgently needed.

Queixalos et.al's [5] results suggest MC infection risk may be higher than previously reported, with the CRBSI incidence of 7% (10 of 136 patients) markedly higher than even those reported for central VADs. MCs are generally thought to have lower infection risk than central VADs, although a recent meta-analysis found CRBSI incidence in MCs not significantly different to that of peripherally inserted central catheters at 0.58% (40/6,900) *versus* 0.48% (127/26,422) respectively (RR = 0.77, 95% CI: 0.50-1.17, $p = .22$) [18]. Queixalos et al.'s sample may have been a high-risk group, since study inclusion required a catheter tip culture to have been performed. One could postulate that if the sample had included all MCs inserted in the institution over the period, also incorporating those without a tip culture undertaken, infection incidence would likely have been lower. Interestingly, despite all tip cultures in this study being ordered at the discretion of the treating physician, only one-third of MCs were removed for suspected infection. Guidelines do not recommend routine tip culture. [9] There remains variability in the proportion of MC tips sent for culture within studies, either they fail to outline the prompt for tip culture [15] or alternatively culture all tips. [10] The criteria used to order tip cultures "on suspicion of infection" remains unexplored and could be the focus of future work.

Although both PIVCs and MCs are registered as short-term (less than 30 days) devices, expert consensus from a multispecialty panel, and international guidelines, recommend MC use only up to 14 days, with consideration of a central VAD for longer therapy duration. [6, 19]. In the study of Queixalos et al. [5], participants had a median MC dwell of 18 days, potentially contributing to the higher observed infection incidence, since increased days of invasive device use equates to greater exposure to the possibility of infection. However, the CRBSI rate of 3.5 per 1000 days was also higher than previous MC studies (0.2 MC per 1000 days) [8], suggesting that the impact of dwell time was minimal. Nevertheless, caution should be exercised when considering MC use for the delivery of IV therapy that exceeds the recommended [6], or regulatory indicated time period. A key safety practice is for clinicians to undertake daily consideration of MC removal, in response to completion of therapy, conversion to oral or other routes of treatment, or MC complications.

MCs allow for a greater diversity of VAD options and the ability to tailor healthcare and IV treatment to patient need [8]. As they are inserted in the upper arm veins (typically cephalic, brachial or basilic), the catheter tip remains outside the central circulation and therefore radiographical confirmation of adequate placement is not required, expediting time to treatment [8]. In comparison to PIVCs, MCs allow greater catheter length to lie within the vein, which is strongly linked to superior device survival [20]. In addition, longer duration of complication-free dwell for MCs than for PIVCs avoids multiple PIVC insertions, preserving patients' vasculature for future IV treatment needs [1, 7]. The risk of device dislodgement is mitigated by optimal placement of MCs in the upper arm, thereby providing a stable platform with low mobility, in contrast to PIVCs, which are commonly placed over points of flexion such as the antecubital fossa, hand or wrist [4]. Moreover, as MCs are placed in larger diameter vessels than those in the hand or forearm, this facilitates adequate natural haemodilution of IV fluids and medications, reducing the likelihood of chemical phlebitis and infiltration [8, 19].

MCs are increasingly selected by clinicians for patient treatment; however, they are not risk-free alternatives to PIVCs, nor to central VADs. It is crucial that they are only used with due patient assessment and a clear treatment plan that is regularly revisited. High-quality prospective data and randomised controlled trials are urgently needed to not only quantify infection rates, but also to identify risk factors, and understand the optimal indications and contraindications for MCs.

Conflicts of Interest:

NM reports that Griffith University has received on her behalf, speaker fees from 3M, investigator-initiated research grants from Becton Dickinson, Cardinal Health, Eloquest Healthcare and a consultancy payment from Becton Dickinson for clinical feedback related to peripheral intravenous catheter placement and maintenance (unrelated to the current project).

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