HK85: Is there a role for intraosseous administration of prophylactic antibiotics?

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Response/Recommendation:

Yes. Low dose (500 mg) intraosseous (IO) administered vancomycin distal to an inflated tourniquet results in tissue concentrations 6 to 10 times greater than intravenously administered vancomycin. The use of IO administration of vancomycin, when combined with a first line intravenously administered prophylactic antibiotic (eg cefazolin) results in a lower post-operative infection rate compared to systemic administration alone.

Strength of recommendation: Moderate

Delegate Vote:

Rationale:

Certain antibiotics such as vancomycin, when used as a perioperative prophylactic antibiotic can be difficult to administer prior to skin incision and can lead to adverse effects such 'Red Man Syndrome'. Underdosing or incomplete infusion prior to incision results in suboptimal tissue concentrations and leads to an increased risk of periprosthetic joint infection (PJI).[1-3]

Intraosseous (IO) administration of prophylactic antibiotics is easy, rapid to administer and provides high tissue concentrations. The technique involves a needle inserted into the proximal medial tibia between the tibial tubercle and joint line, distal to an inflated torniquet, through which antibiotics can be administered.[4-6] IO administration provides consistently higher tissue concentrations compared to intravenously administered antibiotics. Young et al, reported on comparing IO administration of cefazolin (1 gram) to intravenous administration (also 1 gram) in patients undergoing primary total knee arthroplasty.[7] The IO administered group had tissue concentrations over 10 times greater than the intravenous group. Subsequently, multiple studies comparing tissue concentration of low dose vancomycin (500 mg) have shown 6 – 10 times higher concentrations with IO infusion compared to ideally timed and fixed or weight based vancomycin intravenous infusion.[8-11] This high tissue concentration of vancomycin is maintained even with shortened tourniquet duration (10 min)[9], in high BMI patients[8], and in revision TKA[11].

When infused without tourniquet restriction, IO administration results in antibiotic tissue levels similar to intravenous infusion.[12,13] However, IO administration avoids the difficulties of incomplete systemic administration prior to skin incision and results in lower systemic levels, potentially reducing systemic side effects.

The majority of earlier studies using IO vancomycin are underpowered to detect differences in PJI and were undertaken to measure tissue concentrations of IO versus intravenous administration in various clinical scenarios. However, there is growing evidence of the clinical benefit for PJI reduction when IO vancomycin is used prophylactically in conjunction with a first

line intravenously administered antibiotic in aseptic primary and revision arthroplasty surgery, as well as for the treatment of acute PJI.

In a multi-centered retrospective study on patients undergoing primary TKA, Parkinson et al, noted a reduced rate of post-operative PJI at one year in patients receiving IO prophylaxis (0.1% IO group vs 1.4% IV group (p=0.03).[14] It should be noted that the IO group was a mix of either cefazolin or vancomycin. Similar results were reported by Park et al, in a single institution retrospective study of 488 patients receiving IO administered low dose (500gm) vancomycin compared to 572 patients receiving IV weight-based (15 mg/kg) vancomycin, both combined with IV cefazolin.[15] The incidence of PJI at 90 days was 0.22% in the IO group and 1.4% in the IV group (p=0.047). No increased adverse events were noted in the IO group. Lastly, Klasen et al 2021 reported on the safely of IO administration in 631 primary TKA's and found the PJI rate at 90 days and 1 year were 0% and 0.2% respectively.[16]

While there are no prospective studies comparing dual intravenous antibiotics to IO administration of vancomycin combined with intravenous first line antibiotic with the outcome of PJI rates in aseptic arthroplasty surgery or for the treatment of PJI, there are studies comparing IO to retrospective IV cohorts.

In a retrospective-cohort study of 117 aseptic revision knee arthroplasties, the use of prophylactic IO vancomycin, when combined with a first line (eg Cefazolin) intravenously administered antibiotic (dual antibiotic prophylaxis) resulted in substantially lower PJI rates when compared to historical controls; 0% at 3 months and remained at 0% for the 113 patients followed to 1 year.[17] A similar study by McNamara et al, compared 386 cases of intravenously administered Vancomycin to 333 IO administered vancomycin. Both groups received weight-based cefazolin perioperatively. At 30 days, 90 days and 1 year follow-up the IO administered group had a significantly lower rate of PJI than the intravenous cohort (0.3 vs 2.1% (p=0.03), 0.9 vs 3.1% (p=0.04) and 1.6 vs 4.9% (p=0.04) respectively).[18]

There is limited data on the use of IO administration for the management of PJI. Kildow et al, 2021 reported on a retrospective series of 26 acute and 9 chronic PJI patients treated with debridement, irrigation and implant retention in conjunction with IO administration of vancomycin and noted infection control in 92.3% of the acute PJI cases, but only 44.4 % of the chronic PJI cases.[19]

Additionally, the safety of IO vancomycin administration has been specially studied by Klasen et al who reported on 631 primary TKA cases with no cases of Redman syndrome, or neutropenia, nor increased risk of acute kidney injury.[16] Similarly, Harper et al. 2020 reported on a mixed group of primary and revision total knee arthroplasties and noted no differences in complication between the groups and no specific complications related to IO administration.[20] Parkinson et al. also noted no adverse reaction on a group of 725 IO injections.[14]

In summary, IO administration of antibiotics results in tissue concentration on average a magnitude greater than levels achieved with intravenous administration. IO vancomycin combined with a first line intravenous prophylactic antibiotic (eg first generation cephalosporin - cefazolin) results in lower PJI rates compared to intravenous administration alone in primary and

revision knee arthroplasty. There is some evidence for treatment benefit using IO vancomycin in acute PJI treated with debridement irrigation and implant retention. No increase adverse events are reported with the use of IO administration.

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