Surgeons may reduce the number of doses of systemic antibiotic prophylaxis to one preoperative when they use antibiotic-loaded bone cement in primary total knee arthroplasty A register-based meta-analysis (2010-2020)

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INTRODUCTION:

Systemic antibiotic prophylaxis (SAP) is the accepted standard practice to reduce the risk of periprosthetic joint infection (PJI) in primary knee arthroplasty (TKA). Whilst some form of SAP in combination with antibiotic-loaded bone cement (ALBC) has been used in many countries, the practice varies internationally and current evidence for using ALBC is subject to debate. Furthermore, the World Health Organization and the US Center for Disease Control and Prevention recommended against the usage of repeated doses of postoperative SAP and advocate for a preoperative single dose. In a recent meta-analysis including 10 national and regional registries we showed no difference in 1-year revision risk for PJI between ALBC and plain bone cement.

The purposes of this study therefore were (1) to assess the prophylactic effectiveness of use of ALBC+SAP vs. plain bone cement (PBC)+SAP in primary total knee arthroplasty (TKA) on risk of revision for PJI at 3-months, 1-, 5-, and 10-years of follow-up; and (2) to assess whether the number of SAP doses was associated with the risk of revision for PJI following primary TKAs.

METHODS: International register-based meta-analysis using regional/national registery data from Denmark, New Zealand, Norway, Romania, and USA. The study includes 289,926 primary TKAs for osteoarthritis enrolled from January 1, 2010 to December 31, 2020. Primary TKA with ALBC+SAP vs. PBC+SAP as well as number of SAP doses were the exposures. The primary outcome was risk of revision for PJI at 1-year and secondary outcomes were revision for PJI at 3-months,5-, and 10-years follow-up. We computed cumulative percent revision (1 minus Kaplan-Meier) using distributed analysis method and adjusted Hazard Rate Ratios (HRR), as an expression for risk, using Cox regression analyses within each registry. Advanced distributed meta-analysis was performed to summarize HRRs from all countries. Finally, sensitivity analysis was performed to assess the influence of individual registry results on the meta-analysis results.

RESULTS: Among primary TKAs included, 64.4% were performed with ALBC+SAP. Each participating registry reported a 1-year cumulative percent revision for PJI of <1.00% for both primary TKAs with ALBC+SAP (ranging from 0.34% to 0.80%) and with PBC+SAP (ranging from 0.54% to 0.69%). Higher crude revision rate for PJI was observed in primary TKAs with 4 doses of SAP both among the ALBC+SAP (1.21%) and the PBC+SAP (2.06%) groups. The distributed meta-analysis showed similar risk of PJI revision when comparing primary TKAs with ALBC+SAP vs. PBC+SAP at 3-months (HRR=1.21; 95%CI, 0.63-2.72); 1-year (HRR=1.21; 95% CI: 0.79-1.87); 5-years (HRR=1.11; 95%CI, 0.85-1.45); and 10-years (HRR=1.11; 95%CI, 0.85-1.48). Similar risk of PJI revision was observed between TKAs with ALBC +single vs. multiple doses of SAP: 2-doses (HRR=0.95; 95%CI, 0.68-1.33), 3-doses (HRR=1.09; 95%CI, 0.64-1.87); and 4-doses (HRR=1.23; 95%CI, 0.69-2.21). Similar results were found for the PBC+ SAP group except for higher risk of PJI revision with 4-doses of SAP (HRR=2.74; 95%CI, 1.11-6.75).

DISCUSSION AND CONCLUSION: We found no evidence for effectiveness of ALBC+ SAP use in primary TKAs on reducing the risk of PJI revision compared to PBC+SAP regardless of number of SAP doses. Furthermore, there was a similar risk of PJI revision between single and multiple doses of SAP in primary TKAs with ALBC or PBC. However, the risk of PJI revision was about 3 times higher among TKAs with PBC+ 4-doses of SAP compared to single dose SAP. Thus, it seems that if ALBC is used in combination with SAP in primary TKAs one single preoperative dose of SAP may be sufficient without compromising patient safety. The possibility of reducing the use of postoperative SAP in primary TKAs with ALBC or PBC without compromising patient safety will pose many advantages; including reduction of potential adverse events such as acute kidney injury, multidrug-resistant bacteria, opportunistic infections, as well as a reduction in the overall use of antibiotics and subsequently cost burden in the healthcare system. Further prospective, multicenter pragmatic randomized controlled trials investigating if the number of SAP doses can be reduced when used in combination with ALBC or PBC in primary TKAs are warranted.