The Journal of Arthroplasty xxx (2018) 1–6

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

AAHKS Award Paper

# The AAHKS Clinical Research Award: Intraosseous Regional Prophylaxis Provides Higher Tissue Concentrations in High BMI Patients in Total Knee Arthroplasty: A Randomized Trial

Seung Joon Chin, MBChB [a], Grant A. Moore, BSc (Hons) [b], Mei Zhang, PhD [c], Henry D. Clarke, MD [d], Mark J. Spangehl, MD [d], Simon W. Young, FRACS, MD [e, *]

[a] Department of Anaesthesia, Middlemore Hospital, Auckland, New Zealand
[b] Department of Toxicology, Canterbury Health Laboratories, Christchurch, New Zealand
[c] Clinical Pharmacology, University of Otago, Christchurch, New Zealand
[d] Department of Orthopedic Surgery, Mayo Clinic, Phoenix, United States
[e] Department of Orthopaedic Surgery, North Shore Hospital, Auckland, New Zealand

ARTICLE INFO

*Article history:*
Received 5 December 2017
Received in revised form
26 February 2018
Accepted 1 March 2018
Available online xxx

*Keywords:*
intraosseous regional antibiotic administration
vancomycin
total knee arthroplasty
obesity
morbid obesity

ABSTRACT

*Background:* Obesity is an established risk factor for periprosthetic joint infections after total knee arthroplasty (TKA). In obese patients, a larger dose of prophylactic vancomycin based on actual body weight is required to reach therapeutic concentrations. It is unclear how tissue concentrations are affected when intraosseous regional administration (IORA) is used in this population. This study compared tissue concentrations of low-dose vancomycin via IORA vs actual body weight–adjusted systemic intravenous (IV) dose in primary TKA.

*Methods:* Twenty-two patients with a body mass index (BMI) >35 undergoing TKA were randomized into 2 groups. The IV group received 15 mg/kg (maximum of 2 g) of systemic IV vancomycin and the IORA group received 500 mg vancomycin into the tibia. Subcutaneous fat and bone samples were taken at regular intervals. Tissue antibiotic concentrations were measured using liquid chromatography coupled with tandem mass spectrometry. A blood sample was taken 1 to 2 hours after tourniquet deflation to measure systemic concentration.

*Results:* The mean BMI was 41.1 in the IORA group and 40.1 in the IV systemic group. The overall mean tissue concentration in subcutaneous fat was 39.3 μg/g in the IORA group and 4.4 μg/g in the IV systemic group ($P < .01$). Mean tissue concentrations in bones were 34.4 μg/g in the IORA group and 6.1 μg/g in the IV systemic group ($P < .01$).

*Conclusion:* Low-dose IORA was effective in the high-BMI population group, providing tissue concentrations of vancomycin 5-9 times higher than systemic administration. IORA optimizes timing of vancomycin administration and provides high tissue antibiotic concentrations during TKA in this high-risk patient group.

© 2018 Elsevier Inc. All rights reserved.

Obesity is considered a global epidemic [1]. Through biomechanical and physiological mechanisms, it is a risk factor for both the incidence and progression of knee osteoarthritis [2–4]. As such, obese patients are over-represented in patients presenting for total knee arthroplasty (TKA) [5], and the obesity epidemic is a factor in the significant increase in the number of TKAs performed each year [6].

Obesity is also an important risk factor for periprosthetic joint infection (PJI) after TKA [7], a devastating complication for the patient [8] and the health-care system [9]. In a meta-analysis of 83,001 patients, obesity was associated with an odds ratio of 2.2 for superficial infections and 2.4 for deep infections [10]. Furthermore, registry data show a 7% increase in risk per unit of body mass index (BMI) above a threshold of 35 [11]. A number of potential mechanisms are implicated. Obese patients have disrupted microcirculation and macrocirculation [12], decreased wound healing [12], and impaired immune function [13]. Surgically, they are associated with

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to https://doi.org/10.1016/j.arth.2018.03.013.

* Reprint requests: Simon W. Young, MBChB, Department of Orthopaedic Surgery, North Shore Hospital, 124 Shakespeare Road, Takapuna, Auckland, New Zealand.

https://doi.org/10.1016/j.arth.2018.03.013
0883-5403/© 2018 Elsevier Inc. All rights reserved.

**Table 1**
Patient Demographics.

| Variable | Intraosseous Group | Systemic Group |
|---|---|---|
| Number of males | 7 | 6 |
| Number of females | 4 | 5 |
| Age (years) | 66 | 63 |
| BMI | 41 | 40 |
| Procedure length (minutes skin to skin) | 80 | 85 |
| Estimated glomerular filtration rate | 65 | 76 |
| ASA score | 3 | 3 |

ASA, American Society of Anaesthesiologists; BMI, body mass index.

greater difficulty [14] and a longer surgical time [15], prolonging exposure to microorganisms [16]. The higher risk of PJI has led some authors to suggest refusing TKA in patients above a certain BMI threshold [17]. However, obese patients benefit from TKA at least as much as patients with a normal BMI [5], and therefore, strategies to reduce PJI risk in high-BMI patients are needed.

In the nonobese TKA population, intraosseous regional administration (IORA) of prophylactic antibiotics provides tissue concentrations 5-8 times higher than systemic administration in TKA [18]. However, the physiology in the obese patient unpredictably alters pharmacokinetics for different drugs [19]. For vancomycin, there is a higher volume of distribution and a shorter elimination half-life in the morbidly obese to nonobese individuals [20]. Thus, vancomycin requires total body weight–based dosing to achieve ideal target steady-state concentrations when given systemically [21]. The importance of higher dose of vancomycin is emphasized with bony infections as it displays poor bone penetration in animal models [22]. We hypothesized that a non–weight-based low-dose of vancomycin via IORA could still achieve adequate tissue concentrations equal or superior to those of weight-based systemic administration of vancomycin before TKA. Hence, the purpose of this study was to compare tissue concentrations of intravenously and intraosseously administered vancomycin in the obese population undergoing TKA.

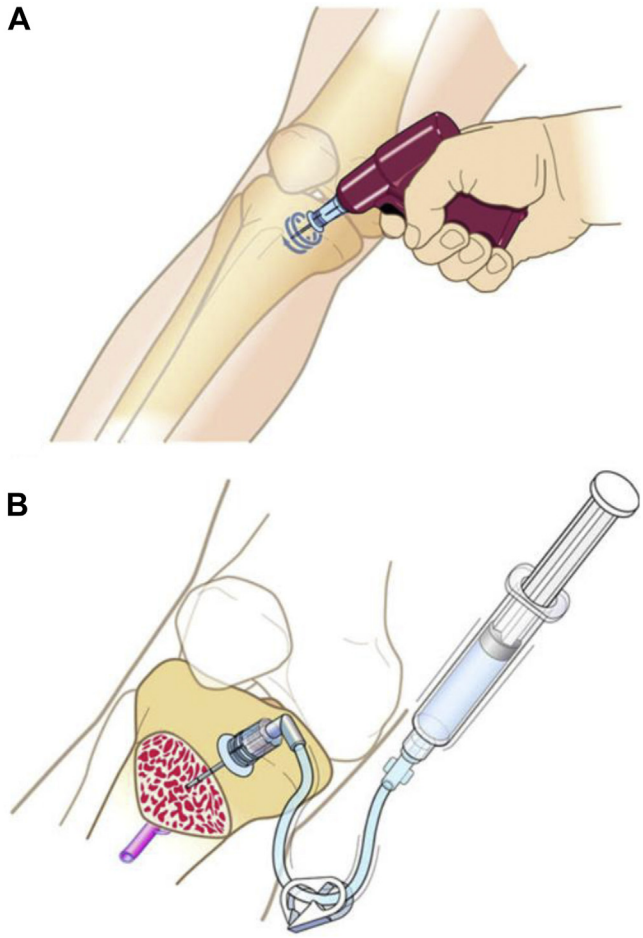


**Fig. 1.** Images show (A) insertion of the intraosseous needle using a sterilized driver and (B) the needle in situ allowing injection of the antibiotic, occurring after tourniquet inflation and before skin incision.
Reprinted with permission of Teleflex Corp (www.teleflex.com).

## Patients and Methods

Patients undergoing primary TKA at a single institution were eligible for enrolment into this prospective, randomized controlled trial. Ethical approval was obtained from the national ethical review board, and the trial and protocol were registered with ClinicalTrials.gov (Identifier: NCT02527148). Inclusion criteria were patients with a BMI ≥35, age 55-85 years, and undergoing primary TKA for a diagnosis of osteoarthritis. Exclusion criteria were allergy to an antibiotic used in the study or abnormal cardiac or renal function or concurrent nephrotoxic medications or previous compartment syndrome. From May 2015 to May 2016, 22 patients were enrolled and randomized into 2 groups using computer-generated random allocations placed in numbered, opaque, sealed envelopes (Table 1). Patients were randomized in the preoperative area to allow time for systemic vancomycin infusion and appropriate setup in the operative room. Patients were followed up for 6 months for potential complications.

All patients received standard prophylaxis of systemic intravenous (IV) cefazolin 15 minutes before tourniquet inflation regardless of randomization—either 2 g for patients between 80 kg and 120 kg or 3 g for patients over 120 kg. All patients underwent limb exsanguination and inflation of an above-knee tourniquet to 300 mmHg before routine preparation and draping. The tourniquet remained inflated for the entire procedure.

The intervention group (500-mg IORA) received 500 mg of vancomycin in 150 mL of normal saline via IORA using an EZ-IO (Teleflex Corp, San Antonio, TX; Food and Drug Administration approved) intraosseous cannula, placed into the medial aspect of the proximal tibia approximately at the level of the tibial tubercle after draping and before skin incision (Fig. 1). The injection was administered as a bolus immediately after tourniquet inflation, and surgical incision occurred immediately (<1 minute) after this. The control group (systemic) was given 15 mg/kg vancomycin based on actual body weight (maximum of 2g) through a forearm vein over a 1-2 hour infusion (1g per hour), beginning 60 to 120 minutes before surgery.

Samples of subcutaneous fat and femoral cancellous bone (approximately 0.5 $cm^3$) were taken at 4 points during the procedure. The first subcutaneous fat sample was taken immediately after skin incision, and subsequently, both bone and fat samples were taken at the time of the distal femoral cut, at the time of trialling components, and immediately before closure. Bone samples were taken from the distal femur using a curette. Collection times were recorded for each sample (Table 2). In addition, systemic blood samples were taken 1-2 hours after tourniquet deflation. In our previous study of IORA vancomycin, peak systemic concentration in the intraosseous group occurred 60 to 70 minutes after tourniquet deflation [18].

Tissue samples were rinsed in saline to remove excess blood and stored at −80°C until analyzed. Vancomycin concentrations were analyzed using our previously published liquid chromatography coupled with tandem mass spectrometry method [18,23]. All

Download English Version:

https://daneshyari.com/en/article/8799157

Download Persian Version:

https://daneshyari.com/article/8799157

Daneshyari.com