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Original Research

Intra-articular Vancomycin Reduces Prosthetic Infection in Primary Hip and Knee Arthroplasty

Alexander W.R. Burns, MBBS, FRACS, FAOrthA*,
Paul Smith, BMBS, FRACS, FAOrthA, HonDUniv, Joseph Lynch, BSc (Hons), MSc, PhD

Trauma and Orthopaedic Research Unit, Department of Orthopaedic Surgery, The Canberra Hospital, Canberra, ACT, Australia

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ABSTRACT

Background: Intravenous antibiotic infusion has been the standard prophylaxis for total joint arthroplasty surgery. However, infection rates still occur at 1%-2% in many series. Single-dose intra-articular antibiotics (IAAs) present a safe and potentially more effective prophylactic regime in total joint arthroplasty. This study aimed to assess the outcomes of a single-dose IAA injection on PJI rates in a single surgeon series of hip and knee arthroplasty.

Methods: We reviewed the data of all patients operated on for a primary hip or knee replacement from 2010 to 2021. From January 2018, 1 gm of vancomycin in 10 ml of saline was injected into every total joint replacement after fascial closure. A comparison was made with PJI referencing the Australian National Joint Replacement Registry data on revision for the 2 periods: 2010-2017 and 2018-2021.

Results: During the period without IAA (2010-2017) for TKR, 6 of 489 (1.2%), and for THR, 5 of 694 (0.7%) had PJI requiring revision surgery. In the period with IAA (2018-2021) for TKR, 0 of 214 (0%, $P = .11$), and for THR, 1 of 517 (0.2%, $P = .19$) PJI required revision surgery, but the overall incidence of PJI for TKR and THR was significantly reduced ($P = .03$).

Conclusions: A single dose of intra-articular vancomycin 1 gm injected into the total joint replacement following fascial closure reduced the incidence of deep PJI requiring a revision surgery in a single-surgeon series. These results demonstrate significant benefits to this technique which merit further larger trials.

Introduction

Total joint replacement (TJR; hip and knee replacement) surgeries have contributed to reduced pain and improved quality of life for millions of people worldwide. Improvements in bearing materials and advances in instrumentation have led to excellent prosthetic survivorships. However, prosthetic joint injection (PJI) continues to be a significant cause of morbidity, mortality, and economic cost in this patient group with mortality of up to 21% at 5 years [1]. Many strategies are being developed to reduce infection risk, including preoperative patient optimization, intraoperative washes, prosthetic surface coating, and different antibiotic regimes [2–4].

Intra-articular antibiotic (IAA) use has potential benefit of very high doses around the prosthesis when compared with intravenous (IV) administration. There is also the added benefit of reduced systemic effects and initial less renal excretion, ease of administration, and possible cost-effectiveness in prevention of PJI [5]. Direct application of antibiotic has been effectively used to reduce infections in spinal [6], anterior cruciate [7], trauma surgery [8], and in rat models [9]. Furthermore, there is a growing body of evidence for its use in TJR, with a number of reviews suggesting IAA importance [10–12]. A recent report by Lawrie et al. [13] examined a series of total knee replacements that had IA and found it reached therapeutic levels while not reaching sustained toxic level up to 24 hours after surgery. However, these studies were small and do not provide information on longer-term infection risk.

The aim of this study was to investigate the effect of adding IAA in reducing infection on a single-surgeon series of total hip and knee arthroplasty cases in Australia.

* Corresponding author. Orthopaedics ACT, 90 Corinna Street, Woden, ACT 2606, Australia. Tel.: +61 2 62219323.
E-mail address: aburns@orthoact.com.au

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Material and methods

A retrospective analysis of data from the Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) was undertaken with all TJR performed since the surgeon (A.W.R.B.) had been enrolled, comprising all TJRs at 4 hospitals in both public and private systems. The AOANJRR collects data with respect to prosthetic information, approach, diagnosis, and other patient demographics and has a capture rate of almost 100% of arthroplasty operations performed in Australia [14]. Individual surgeons have access to their data at any time, and it is accurate to within a month of recent cases. Revision for any reason is registered on dedicated forms that are sent to the NJRR weekly and continuously collated. If a patient is treated by another surgeon with exchange of any component in Australia, the AOANJRR receives notification of that case.

From 2010, every total hip replacement and total knee replacement patient had an IV infusion of 2 gm of cefazolin and 1 gm of vancomycin 30 minutes prior to surgery. All TJRs were performed with alcoholic chlorhexidine skin preparation and occlusive Ioban (3M, St. Paul, MN) draping, using a pneumatic tourniquet for total knee replacement, inflated immediately before skin incision and released once the final compressive dressings were applied. From January 2018 onward, IA injection of 1 gm of vancomycin in 10 ml of normal saline was performed at the end of the procedure after closure of the fascia with an 18-gauge spinal needle. Two grams of tranexamic acid was also injected into the joint using the same needle. Betadine wash was not used in this period although it is now our preference to do so, rather saline with pulsatile lavage was used. The delivery of vancomycin mixed in saline rather than as powder, which is the more common technique referred to in the literature, is simpler and allows injection immediately after capsular closure at the same time as the tranexamic acid. Fat and skin layer closure was completed as routine. While implant make and design was not uniform, all hip and knee components were cemented using antibiotic-enriched Simplex bone cement (tobramycin) (Stryker, Kalamazoo, MI). Our wound dressings have remained the same Post-op Opsite (Smith & Nephew, Memphis, TN) for this study period. The approach for both procedures was standardized with a medial parapatellar approach and posterior approach for TKR and THR, respectively. Where reported by the AOANJRR, data were collected for revision, BMI, American Society of Anaesthesiologists score, sex, and age. Continuous data were summarized using means and standard deviation or confidence intervals while categorical data were summarized with percentages. Statistics were performed using SPSS (Version 26, IBM, Armonk, NY). Independent samples *t*-tests were used to compare continuous variables, and chi-squared exact tests were used to compare categorical variables. Ethical approval was gained from our institutional ethics and research committee.

Results

NJRR data from January 2010 to December 2021 were accessed via the AOANJRR Surgeon Portal. A total of 1211 primary total hips and 703 primary total knees were performed during the time period. The addition of IA vancomycin began from January 2018. There were no differences between either of the pre-intraarticular antibiotic (pre-IAA) and intraarticular (IAA) groups in terms of age, BMI, or ASA grade for both hip and knee replacements (Table 1).

There was a greater proportion of females in the IA group. AOANJRR data showed that for the pre-IAA period of January 2010 and December 2017, 489 TKRs were performed with 6 revisions for infection (1.2%), and 694 THRs were performed with 5 revisions for infection (0.7%). In the period from January 2018 to December 2021,

Table 1
Breakdown of demographics in total hip and knee replacement patients prior to and after introduction of intraarticular antibiotics.

Demographic	Total knee replacement			Total hip replacement			Combined hip and knee arthroplasty		
	Pre-intra-articular antibiotics	Intra-articular antibiotics	*P* value	Pre-intra-articular antibiotics	Intra-articular antibiotics	*P* value	Pre-intra-articular antibiotics	Intra-articular antibiotics	*P* value
Age									
Mean ± SD	66 ± 9.6	66.1 ± 9.4	.898	61.4 ± 13.9	61 ± 13.1	.611	63.7 + 11.3	63.6 + 11.3	.851
Age group									
<55	64 (13.9%)	16 (8.9%)	.369	196 (29.7%)	154 (31%)	.739	260 (23.2)	170 (25.2)	.507
55-64	148 (32%)	64 (35.8%)		172 (26.1%)	134 (27%)		320 (28.5)	198 (29.3)	
65-74	145 (31.4%)	59 (33%)		174 (26.4%)	132 (26.6%)		319 (28.5)	191 (28.3)	
≥75	105 (22.7%)	40 (22.3%)		117 (17.8%)	76 (15.3%)		222 (19.8)	116 (17.2)	
Gender									
Male	203 (43.9%)	71 (39.7%)	.326	295 (44.8%)	193 (38.9%)	.053	498 (44.4)	264 (39.1)	.031
Female	259 (56.1%)	108 (60.3%)		364 (55.2%)	303 (61.1%)		623 (55.6)	411 (60.9)	
American Society of Anaesthesiologists class [1]									
1	21 (8.4%)	6 (3.4%)	.176	88 (20.7%)	81 (16.4%)	.416	109 (16.1)	87 (12.9)	.196
2	120 (48%)	102 (57%)		218 (51.3%)	268 (54.4%)		338 (50.1)	370 (55.1)	
3	107 (42.8%)	71 (39.7%)		116 (27.3%)	141 (28.6%)		223 (33.0)	212 (31.5)	
4	2 (0.8%)	0		3 (0.7%)	3 (0.6%)		5 (0.7)	3 (0.4)	
5	0	0		0	0		0 (0)	0 (0)	
Body mass index [2]									
Underweight (<18.50)	0	1 (0.6%)	.102	3 (1.1%)	1 (0.2%)	.127	3 (0.7)	2 (0.4)	.778
Normal (18.50-24.99)	22 (13.3%)	17 (9.5%)		57 (21.5%)	106 (22.4%)		79 (18.3)	123 (18.9)	
Pre-obese (25.00-29.99)	44 (26.5%)	47 (26.3%)		90 (34%)	183 (38.7%)		134 (31.1)	230 (35.3)	
Obese class 1 (30.00-34.99)	48 (28.9%)	51 (28.5%)		66 (24.9%)	115 (24.3%)		114 (26.5)	166 (25.5)	
Obese class 2 (35.00-39.99)	25 (15.1%)	34 (19%)		31 (11.7%)	40 (8.5%)		56 (13.0)	74 (11.3)	
Obese class 3 (≥40.00)	27 (16.3%)	29 (16.2%)		18 (6.8%)	28 (5.9%)		45 (10.4)	57 (8.7)	

the post-IAA period, there were no infections in 214 TKRs and 1 infection in 517 THRs (0.2%). While the incidence of PJI was significantly reduced for all joints that underwent a procedure in the IA group ($P = .03$), separate analyses for TKR ($P = .11$) and THR (0.19) approached but did not reach significance (Table 2). Based on our data, the number needed to treat (NNT) in order to prevent 1 PJI was 111.1.

In addition, the single infected joint in the IAA group was infected following surgery for removal of wires from the greater trochanter 13 months after the primary surgery and grew *Staphylococcus aureus* sensitive to penicillin and cephalosporin (not resistant to vancomycin).

Discussion

Hip and knee arthroplasty continue to improve pain and quality of life for patients with degenerative joint disease. Improvements in bearing materials and advances in instrumentation have led to improved survivorships, with the percentage of revision hip procedures declining from a peak of 12.9% in 2003 to 8.4% in 2019, equating to 2283 fewer hip revisions and similar declines in revision knee surgeries equating to 515 fewer knee revisions for Australia in 2019 [14]. Despite this improvement, infection of TJR continues to be a major cause of failure, with significant morbidity, mortality, and economic cost [1,15]. Clearly any reduction in the incidence of PJI will have substantial benefits for the individual and the health system alike.

IAA use originated in veterinary medicine but has initially been used successfully in spinal surgery [16]. In TJR, IAAs have been used as both prophylaxis in primary surgery [5,17] and also in the more complex scenario of infected total joints with success by several authors [18–21] The rationale for use of IAA is that IV antibiotics, even at maximal tolerable doses, may be subtherapeutic in synovial fluid for part of the day, whereas IAA have peak synovial levels orders of magnitude greater than those achievable with IV administration, at safe systemic levels which are above minimum inhibitory concentration for the entire day [22].

More recently, Wang et al. [23], in a meta-analysis of intrawound vancomycin powder (VP) in orthopedic surgery, showed a significant reduction in overall surgical site wound infections (SSWIs) ($P < .001$), deep SSWIs ($P = .02$), and superficial SSWIs ($P = .04$). Another meta-analysis of intra-articular VP and povidone iodine lavage again showed a significant reduction of periprosthetic joint infection in primary and revision total joint arthroplasty [24].

Further meta-analyses by Heckmann et al. [25] and Xu et al. [12] on the use of VP showed very significant PJI reduction in primary TKA and THR, although the latter authors reported an increase in aseptic wound complications. There is a growing volume of literature supporting the safety and efficacy of this technique.

In a similar study to our own, Tahmasebi et al. used IA VP in 1710 TKR patients and reported reduced PJI rates against historical controls from 1.91% to 0.41% [26]. Patel et al. demonstrate a similar reduction in PJI rate (2.7% vs 0.29%) vs historical controls [5]. Those authors calculated that the NNT to prevent 1 infection was 47.5 [5]. Their cost to prevent 1 infection with the addition of intrawound vancomycin was US$816, in a system where the cost of a revision TJR can reach US$100K [10]. In our series, the NNT was 111.1, and in our institution, a vial of 1 g of vancomycin costs $6.60, meaning such prevention would cost $732, clearly cost-effective.

Our study illustrates that for a single surgeon, an injection of 1 g of vancomycin at the end of fascial closure is a simple, low-risk, and efficacious intervention. There was a slightly greater portion of females in the IA group, which may have influenced infection rates. Our study has limitations as it is retrospective and as such could be biased by incremental changes in perioperative risk management. We have however used preoperative methicillin resistant Staphylococcus aureus screening and treatment, antibacterial body wash, and IV cefazolin and IV vancomycin for the whole period of the study; used the same skin preparation and iodine-impregnated drapes; have not used drains but have used the same dressings; and have used topical tranexamic acid from 2012 onwards. We no longer use IV vancomycin after publication of the results of the Australian Surgical Antibiotic Prophylaxis trial [27]. In addition, while our surgical numbers are not very high, they represent the practice of a generalist arthroplasty surgeon in Australia. It is also possible that an infected TJR could not be recorded if it were treated with debridement by another surgeon without component exchange, as this procedure without revision of any component would not be notified to the AOANJRR. While possible, such a standard of care would be very uncommon in our country now.

IAA represent a low-cost, effective, and safe intervention for the prevention of PJI in primary hip and knee arthroplasty. Larger prospective randomized studies are needed to confirm the overall effectiveness and generalizability prior to widespread adoption of this technique, but there are now multiple studies that are supportive of such trials being performed.

Table 2
Incidence of prosthetic joint infection in hip and knee arthroplasty.

Joint	Pre-intraarticular vancomycin	Intraarticular vancomycin	*P* value
Total knee replacement	6/489 (1.2%)	0/214 (0%)	.11
Total hip replacement	5/694 (0.7%)	1/517 (0.2%)	.19
Total	11/1183 (0.9%)	1/731 (0.1%)	.03[a]

[a] Denotes statistical significance ($P < .05$).

Conclusions

A single dose of intra-articular vancomycin, injected into the joint of a total joint arthroplasty, provides a significant reduction in prosthetic joint infection rates in our single surgeon series. It is simple, safe, efficacious, and highly cost-effective and warrants further study in future prospective trials.

Conflicts of interest

The authors declare there are no conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2024.101333.

CRediT authorship contribution statement

Alexander W.R. Burns: Writing – original draft. **Paul Smith:** Writing – review & editing. **Joseph Lynch:** Data curation, Methodology, Writing – review & editing.

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