Reducing the Incidence of Acute Kidney Injury in Elective Total Hip Replacements

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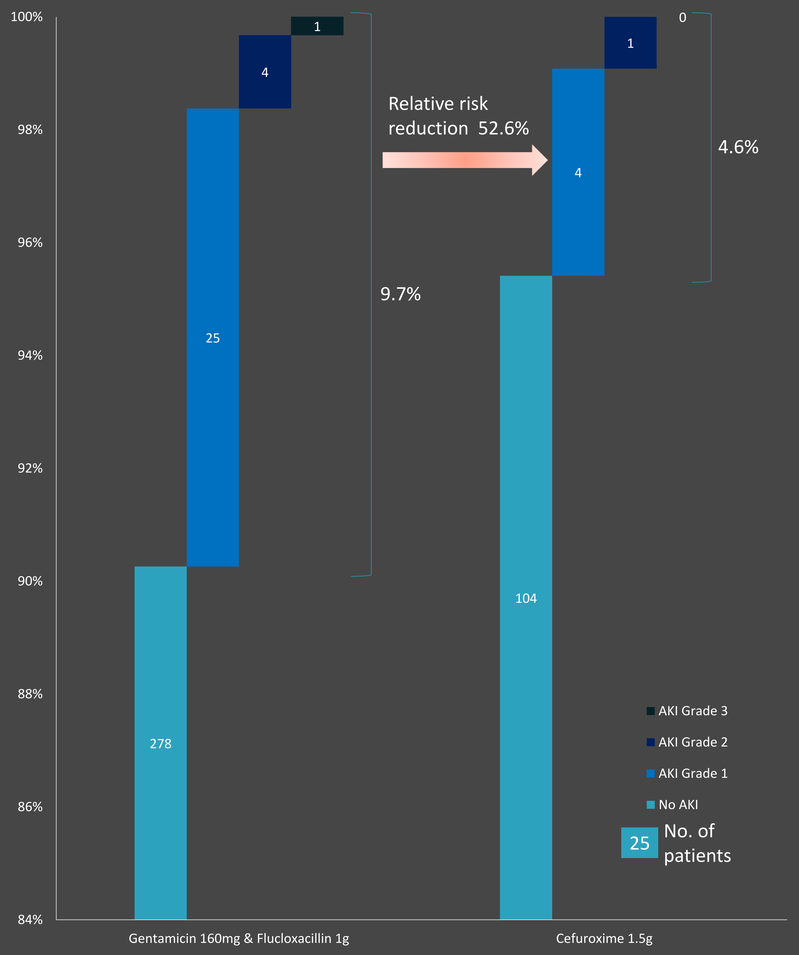
Introduction and Aims

Acute kidney injury (AKI) occurs in 1 in 5 hospital inpatients globally[1] and is a leading cause of morbidity and mortality[2].
A recent multi-centre study in the UK found that 7-11% of patients undergoing orthopaedic surgery will experience AKI, and that even mild (Grade 1) AKIs are associated with a 46% increase in overall mortality at 5 years post-operatively[3].

This project aimed to identify the incidence of AKI in patients undergoing elective total hip replacement (THR) at a district general hospital, and to assess whether this could be reduced by changing the antibiotic regime used for routine prophylaxis. For those patients who developed AKI, compliance with local guidelines for management was reviewed.
A secondary aim was to validate a set of criteria previously shown to identify patients at increased risk of developing AKI and use these to aid management of high-risk patients in future.

Fig 1: AKI Incidence more than halves from 9.7% to 4.6% by using cefuroxime instead of gentamicin and flucloxacillin as pre-op prophylaxis



Method

Records for all adults admitted to Dorset County Hospital for an elective THR over a twelve month period were reviewed for evidence of AKI of at least Grade 1 based on the KDIGO criteria[4], defined as an absolute rise in serum creatinine of >26.4µmol/L, or a relative increase of >50% above baseline. Urine output was not used to identify AKI as this was not reliably recorded in all patients. Presence of known risk factors (increased age, male gender, low pre-operative eGFR and use of nephrotoxic drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and angiotensin receptor blockers (ARBs)), was assessed, as was compliance with Trust guidelines for recognition and management of AKI in those patients who developed it. Patients with missing pre-operative (within 3 months of operation date) or post-operative (within 7 days after the operation) creatinine measurements were excluded, as were those with chronic kidney disease on renal replacement therapy. All patients were prescribed gentamicin 160mg and flucloxacillin 1g IV 1 hour before their procedure as per department protocol.

Closing the loop: The department changed antibiotic protocol 6 months after conclusion of the original audit. According to the revised protocol, elective THR recipients received one dose of cefuroxime 1.5g IV an hour before their operation. Rates of post-operative AKI were then assessed for patients over the next 4 month period.

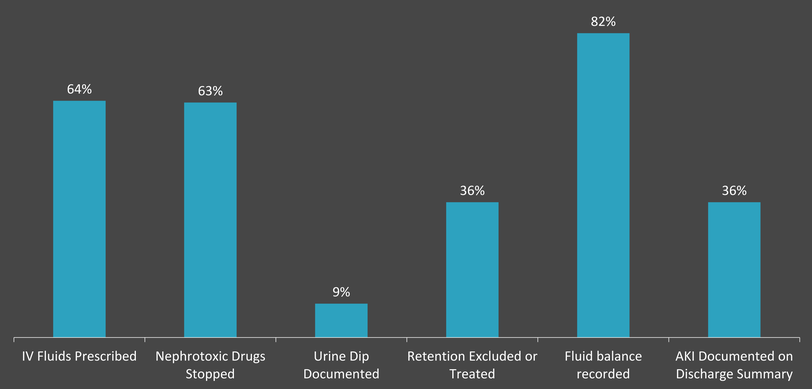
Results

AKI incidence: 308 patients met the initial inclusion criteria, of whom 30 were found to have developed an AKI within a week of their operations. After changing antibiotic protocol, a further 105 records were audited. 5 patients developed an AKI, a relative risk reduction of 52.5% (Fig. 1). At 30 day follow up there were no reported cases of *C. difficile* infection in either group, and no significant difference in joint infection rates between groups (0.6% in the original cohort, 0% in the cefuroxime cohort, p>0.99)

Compliance with management guidelines: Compliance was less than 100% for all trust guidelines (Fig. 2), though reassuringly those with the most clinical impact (prescribing IV fluids, stopping nephrotoxic drugs and monitoring fluid balance) were best adhered to.

Risk factor analysis: Of a set of four independent risk factors previously shown to increase the change of developing AKI[3] all were validated except for gender, where the balance between those who developed AKI and those who did not mirrored that of the overall cohort (Table 1). Our results also suggest that whilst pre-operative use of both classes of nephrotoxic drug significantly increases the risk of AKI, and avoiding both significantly decreases it, using one or other class independently does not significantly increase risk, contrary to previous findings (Fig. 3c). These results should be interpreted with caution however, as they may be due to our relatively small sample size.

Fig. 2: Trust guidelines for management of AKI are not uniformly followed



Conclusion and next steps

Cefuroxime was traditionally used as antibiotic prophylaxis for joint replacement until global concerns about the link with the antibiotic and *Clostridium difficile* infection precipitated a change of protocol. Anecdotal and published evidence suggests that, whilst this and other infection control improvements have succeeded in reducing *C. diff.* infections, the incidence of AKI in hip arthroplasty patients has increased.
Results presented here show that reverting to cefuroxime from gentamicin and flucloxacillin halves the incidence of AKI without any increase in complication rates such as *C. diff.* infection or joint/wound infections, a finding supported by published data from other centres[5]. Moreover, the use of gentamicin appears to raise the risk threshold for AKI development in terms of age and pre-operative eGFR, with no patients in the gentamicin cohort with a normal eGFR (>90) developing AKI.

Results presented here will be used to design pre-operative assessments to identify those at greatest risk and take steps to mitigate AKI development, and further data will be collected over the remainder of 2018 to ensure that initial progress in reducing AKI rates is maintained and built upon.

Fig. 3a: Age distribution

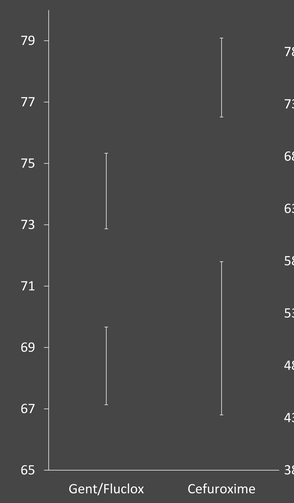


Fig. 3b: Baseline eGFR

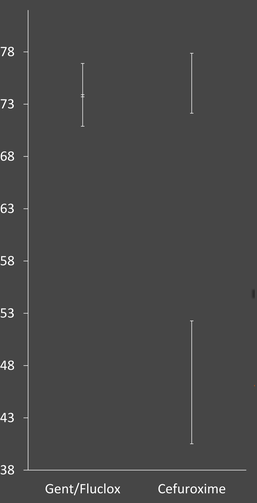


Fig. 3c: Nephrotoxic drug use

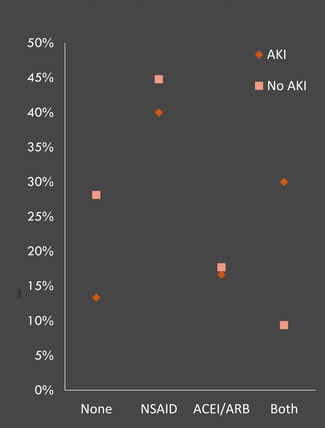


Table 1: Risk Factor Analysis

		Gentamicin/Flucloxacillin			Cefuroxime		
Characteristic		**AKI**	**No AKI**	**Overall**	**AKI**	**No AKI**	**Overall**
Mean age (SD)		74.1 (10.8)	68.4 (11.1)	68.9 (11.2)	77.8 (6.6)	69.3 (12.8)	69.7 (12.7)
Men		11 (37%)	109 (39%)	120 (39%)	2 (40%)	40 (40%)	42 (40%)
Women		19 (63%)	169 (61%)	188 (61%)	3 (60%)	60 (60%)	63 (60%)
Baseline eGFR (SD)		72.4 (13.3)	75.3 (14.0)	75.0 (14.1)	46.4 (30.1)	75 (14.7)	73.6 (16.7)
No. eGFR >90		4 (13%)	64 (23%)	68 (22%)	0 (0%)	26 (26%)	26 (25%)
Nephrotoxic drugs	**None**	4 (13%)	78 (28%)	82 (25%)	N/A*		
	NSAID	12 (40%)	125 (45%)	137 (44%)			
	ACEI / ARB	5 (17%)	49 (18%)	54 (17%)			
	Both	9 (30%)	26 (9%)	35 (14%)			

*: Risk factors not yet assessed for this cohort

References
1) World incidence of AKI: a meta-analysis, Susantitaphong et al. 2013; 2) Acute kidney injury: what's the prognosis?, Murugan et al. 2011; 3) Risk of postoperative acute kidney injury in patients undergoing orthopaedic surgery, Bell et al. 2015; 4) Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group Clinical Practice Guideline for Acute Kidney Injury, 2012; 5) A retrospective study of acute kidney injury in hip arthroplasty patients receiving gentamicin and dicloxacillin, Johansson et al. 2016