Pharmacoeconomic Analysis of Peri-Surgical Antibiotics and Surgical Site Infections in Livingstone General Hospital, Zambia

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CLINICAL HIGHLIGHTS

- Multiple doses of peri-surgical antibiotics are employed prophylactically in Livingstone General Hospital, Zambia (LGH). This may reflect the practice of many third world hospitals
- The occurrence of Surgical Site Infections (SSI) in LGH is high (23%). Each SSI is associated with a considerable increase in patient stay and expenditure
- The use of prophylaxis beyond the duration of surgery is without benefit to the patient and there is evidence that doing so increases the risk of SSI
- The lack of rationale behind this strategy leads to significantly increased expenditure without proven clinical benefit in an environment of extremely limited resources
- Significant and measurable savings can be made through the development and optimisation of a prophylactic antibiotic protocol

ABSTRACT

Background: There is significant evidence to support the use of single dose surgical antibiotic prophylaxis in prevention of surgical site infections (SSI). Multiple peri-operative antibiotic doses have been observed in African hospitals by students on elective placements with unknown clinical and financial consequences. **Objective:** To investigate the use of prophylactic surgical antibiotics in Livingstone General Hospital, Zambia, in the areas of suitability, combinations, duration, cost and incidence of SSI. Furthermore, to compare these findings with evidence from the literature and current best-practice at St James's Hospital (SJH) in order to determine any possible benefits from the pharmacoeconomic optimisation of current regimes. **Methods:** A retrospective analysis of all surgical patient files from January to July, 2006. **Results:** The data gathered demonstrates a lack of prophylactic protocols and resultant ad-hoc antibiotic administration that sometimes lacked pharmacological rationale. In spite of evidence in the literature to the contrary, dosing was continued in all cases for several days. The absence of a prophylactic protocol results in increased expenditure on antibiotics without proven patient benefit and may contribute to surgical site infections with resistant organisms. The occurrence of surgical site infections was 23% and is associated with a significant cost of €133.84 per infection. In the context of limited health budgets in developing countries, this result is likely highly significant. **Conclusions:** The implementation of single dose prophylactic protocols can be expected to result in significant financial savings and may reduce the cost of treating surgical site infections. Investigation into financially feasible modifiable factors contributing to SSI would lead to significant savings and improved patient outcome.

INTRODUCTION

Livingstone General Hospital Zambia (LGH) is a 250 bed regional hospital in southwest Zambia, providing health services to 800,000 people in the area. It also trains nursing students in The Livingstone School of Nursing. Services covered include surgery, general adult medicine, paediatrics and obstetrics and gynaecology. It is staffed at any point in time by 7 to 10 doctors, three of whom are Zambian trained – of which two are qualified to consultant level – the remaining doctors come from The Ukraine (4), Egypt (1), and neighbouring African countries. The hospital also receives residents from Yale Medical School on 6-8 week tropical medicine training placements. The shortfall of qualified doctors is compensated for by 15-20 clinical officers who train for 3 years in medicine, surgery or anaesthetics and enjoy a freedom to practice which compares with that of senior house officer status, in Europe.

Financial restraints within the public health system of Zambia are severe with annual spending on essential equipment and supplies for Livingstone General Hospital at less than €12,000[1]. In this environment, rationalisation of all equipment and drugs used is essential to maximise the services that can be provided to the region.

Surgical Site Infections (SSI) are associated with significant patient morbidity and mortality as well as prolonged hospital stay and a resulting increased cost of care[2]. Rates of SSI, in African hospitals, have been found to range from 16% to 37.8%[3]. This differs from the range of reported incidences in Europe and the U.S. of between 1.5 – 20%[3,4].

This study examined the areas of SSI and peri-operative antibiotics, in LGH, from a pharmacological and economic viewpoint. The aim was to assess the pharmacological rationale of antibiotic regimes used and their economic consequences for the hospital.

METHODS

A retrospective analysis of all available surgical patient charts from January to July, 2006, was performed. Data was collected in all relevant areas including type of surgery, peri-surgical antibiotic use, the incidence of SSI, the duration of patient stay, both pre- and post-operatively, the cost of antibiotics and the cost of hospital stay, per patient, per night. A total of 63 surgeries occurred during this period, for which only 43 charts were available for analysis.

The data collected was analysed from a number of different perspectives. The combinations of antibiotics used for each type surgery (both with and without SSI), the frequency and duration of use of each combination and a comparison with SJH were summarised (Table 1). A comparison of antibiotic costs per dose between Zambia and Ireland (Table 2) was performed. Furthermore, the different expenditure on prophylactic antibiotics in LGH and St. James's Hospital (SJH) and the saving in LGH from switching to a single dose regimen were estimated (Table 3). Finally, the total overall cost associated with SSI for each type of surgery in terms of prolonged hospital stay and increased antibiotic expenditure (Table 4) was highlighted.

RESULTS AND DISCUSSION

Analysis of the results clearly demonstrates the lack of any coherent prophylactic antibiotic protocol in LGH. Across all surgical groups, both when SSI was or was not present, there was no consistency in antibiotic combinations prescribed or the duration of prophylaxis

Table 1. *Comparison of prophylactic antibiotics and number of doses used per type of surgery where no SSI is recorded and where an SSI is recorded in LGH and comparison with SJH surgical protocol.*

Surgery Type (number of surgeries with given SSI status/total number of surgeries)	Antibiotics Used in LGH (number of times combination was used) All I.V. unless otherwise indicated.	Mean number of days of prophylaxis in LGH	Antibiotic prophylaxis in St James' Hospital Prescribers Guide[5]	Number of prophylactic doses per surgery in SJH
Gastrointestinal [without SSI] (14/17)	Benzylpenicillin [QDS] (3)	3.66	Ulcer resection/Gastrectomy, Appendecomy Co-amoxiclav 1.2g IV	1
	Benzylpenicillin [QDS] + Gentamycin [TID] (5)	5.2		
	æBenzylpenicillin [QDS] + Gentamycin [TID] + Metronidazole [TID] + Other (4)*	5.5	Large Bowel Resection Co-amoxiclav 1.2g IV + Gentamycin 4mg/kg IV +Metronidazole 500mg IV	
	Other(2)†	5		
Gastrointestinal [with SSI] (3/17)	Doxycyclin po [OD] (1)	7		
	Benzylpenicillin [QDS] + Metronidazole [TID] (1)	7		
	Benzylpenicillin [QDS] + Gentamycin [TID] + Metronidazole [BD] (1)	5		
Orthopaedic [without SSI] (4/8)	æBenzylpenicillin [QDS] + Metronidazole [TID] (2)#	7	Cefuroxime 1.5g IV + Metronidazole 500mg IV	Up to 2 to 3 doses may be required
	Benzylpenicillin [QDS] + Metronidazole [TID] + Cloxacillin (1)	7		
	No antibiotic use recorded (1)	-		
Orthopaedic [with SSI] (4/8)	Benzylpenicillin [QID] + Metronidazole [TID] (3)	7.7		
	Benzylpenicillin [QID] + Metronidazole [TID] + Cloxacillin (1)	7		
Gynaecological [without SSI] (4/4)	æBenzylpenicillin [QDS] + Gentamycin [TID] (2)	3.5	Co-amoxiclav 1.2g IV	1
	Gentamycin [TID] + Metronidazole [TID] (1)	3		
	Benzylpenicillin [QDS] + Gentamycin [TID] + Metronidazole [TID] (1)	5		
Urological [without SSI] (4/7)	Benzylpenicillin [QDS] (2)	3.5	None if pre-op urine clear. If culture positive Gentamycin 120mg IV or Cefuroxime 1.5g IV	1
	Benzylpenicillin [QDS] + Metronidazole [TID]	2.5		
Urological [with SSI] (3/7)	Cefotaxime [BD] (1)	3		
	Gentamycin [TID] (1)	6		
	No antibiotic used(1)	-		

*A fourth antibiotic was added to this combination of three on two occasions. Cloxacillin QID for 4 days, Ciproflxacin BD for 6 days
† Two combinations used only once each were: Gentamycin and Metronidazole for 5 days and Amoxycillin, Metronidazole and Cirpofloxacin for 6 days.
# Cloxacillin was given to both patients who received this prophylaxis commencing 7 days post surgery for 7 and 10 day courses. There was however no SSI recorded.
æ These antibiotic combinations are used in calculations of the cost of switching to a single dose prophylactic regimen (table 3).

(Table 1). In all surgeries, patients were commenced on their prophylactic regime in the hours before surgery and continued for the number of days indicated.
Combinations of prophylactic antibiotics usually demonstrated pharmacological rationale. Occasionally, inappropriate antibiotics were used, notably, in gastrointestinal surgery where cloxacillin and doxycyclin were each used once. Furthermore, within each category of surgery the difference in prophylactic combination employed did not reflect a difference in infection risk and was without rationale (Table 1). While regular stock shortages were a significant issue for the hospital, they did not correspond with the variability from surgery to surgery and no protocols were in place for such circumstances. It is also of note that there were no culture and sensitivity facilities in LGH, and all antibiotic prescribing in the hospital was on the basis of clinical acumen.

The duration for which the prophylaxis was employed varied greatly both within and between each surgical category. In each case, prophylaxis was continued for a number of days with most patients receiving either 5 or 7 day courses (Table 1). As discussed below, this is entirely without evidence.

In comparison, current practice in SJH employs a policy of specific antibiotic prescribing of single dose duration according to surgical category, with the exception of orthopaedics which may need up to 3 doses[5].

Comparison of the cost per dose of antibiotics used peri-surgically, in LGH and SJH, reveals a large variability (Table 2). All antibiotics in LGH were less expensive, except for gentamycin, which for unknown reasons is 154% the cost in SJH. However, analysis of the total expenditure in surgical prophylaxis shows that gastrointestinal and gynaecological surgery have a 3.7-4.7 fold greater expenditure in absolute terms in LGH than SJH. Likewise, orthopaedic and urological surgery were of similar magnitude (Table 3). The increased cost of gentamycin in LGH does contribute to this difference, however, comparison of the cost of a single dose regimen in SJH with a single dose in LGH (Table 3, column 3,4) demonstrates the predominant discrepancy is the practice of using several days of surgical prophylaxis. Conversely, on a single dose basis, the costs of antibiotic prophylaxis for gastrointestinal and gynaecological surgery at SJH are 2.9 and 2.4 fold greater than in LGH. In addition, orthopaedic and urological surgery are 11.4 and 10.2 fold more expensive per dose in SJH.

Switching to a dosing regime equivalent to SJH (Table 1, column 5) would result in significant financial savings per surgery where no SSI occurs. A total savings of between €416.71 to €427.19 is estimated for the period under investigation (Table 3). This variability in savings is accounted for by the requirement of between 1 and 3 doses of antibiotics in orthopaedic surgery in SJH.

The overall incidence of SSI in LGH was 23% and varied

Table 2. *Comparison of Antibiotic cost per dose in LGH and SJH*

Antibiotic	Antibiotic Cost per dose in Zambia (1)	Antibiotic Cost per dose in Ireland (6)	Cost of drug per dose in Zambia as a % of that in Ireland
Benzylpenicillin (1megaunit)	€0.37	€0.60	62%
Gentamycin (80mg/2ml)	€0.86	€0.56	154%
Metronidazole (500mg/100ml IV)	€0.57	€06.16	9%
Amoxycillin (125mg/ml)	€01.43	€2.29	62%
Cloxacillin (500mg/50ml)	€0.02	- †	- †
Ciprofloxacin (2mg/ml.50ml vial)	€1.26	€16.37	7.7%
Cefotaxime (500mg IV)	€02.86	€3.34	8.6%
Doxycyclin po (course of 8 tabs)	€0.11	€4.69	2.3%

This table compares the cost of all antibiotics recorded in the study regardless of the pharmacological rationale for their use.
† Other anti-staphylococcal penicillins are used in Ireland. No price was available for cloxacillin and thus no price comparison made.

Table 3. *Expenditure on antibiotic prophylaxis per surgery in LGH compared with SJH where no SSI occurs. Column 4 shows savings per surgery from switching to a dosing regimen equivalent to SJH*

Surgery Type	Mean prophylactic antibiotic expenditure per surgery in LGH	Mean prophylactic antibiotic expenditure per surgery in SJH	Predicted cost per surgery of switching to a single dosing regime as per SJH‡	Predicted saving per surgery from switching to a single dosing regime as per SJH‡
Gastrointestinal	€23.17	€6.23*	€2.17	€21.00
Orthopaedic	€12.89	€14.89 - €47.67	€1.31 - €3.93	€8.96 - €11.58
Gynaecological	€17.89	€3.84	€1.60	€16.29
Urological	€6.29	€8.73	€0.86	€5.43

*Prophylaxis in GI surgery in SJH varies according to the extent of the surgery. This figure is the mean expenditure per surgery that would have occurred had SJH encountered the same GI procedures as LGH.
‡Dosing regimen in SJH is single dose except for orthopaedic where 2-3 doses may be required. Agents used in calculations were chosen to maintain the spectrum of activity in SJH presrcribers guide (see Table 1 marked æ).Gentamycin is used for urological procedures.

from 0% for gynaecological to 50% for orthopaedic. This figure lies within the range found in other African studies[3].

The occurrence of SSI were associated with an average increase in pre- and post-operative hospital stay of 6.8 and 10.5 days respectively, and also increased antibiotic usage. A wide range and standard deviation for both pre- and post-operative hospital stay was found (Table 4).

The average increase in cost per SSI was €131.84 (Table 4). This figure takes into account the increased post-operative hospital stay and increased cost of antibiotic usage as a result of infection. It does not account for the any increased pre-operative stay, as this is not incurred as a result of the infection. The total cost of all SSIs during the period examined was €1318.40, a significant sum in the context of the extremely limited hospital budget.

The availability of patient charts was limited to 43 of the 63 surgeries in the period under investigation. This was attributed to general administrative problems and issues of inadequate record keeping in an environment of limited resources. However, it is notable that no deaths were recorded in any of the files available. Data on the incidence of death from SSI in Africa is unpublished [7] and it is therefore impossible to make any inferences or conclusions about the significance of unavailable files.
It is of further note that the comparison made with SJH is based entirely on protocols outlined in SJH Prescriber's Guide rather than an actual comparison with prophylactic antibiotics used in practice. A future study on the level of compliance with SJH guidelines is needed to make a realistic comparison between SJH and LGH, along with the appropriateness of calculating cost savings on the basis of these prescribing practices.

An investigation into prophylactic surgical antibiotic use by Harbrath et al.[8] concluded that only one dosage of antibiotic pre-operatively is of benefit to the patient, unless the surgery is longer than three hours. For surgeries longer than 3 hours, a second dose is the most effective way to maintain antibiotic levels in the desired range. Twenty minutes pre-incision is the optimal time for administration of the antibiotic. Alternatively, in long surgeries, single preoperative doses of extended half-life antibiotics were as effective as a two-dose regimen in preventing wound infection and have been shown to be more cost effective than multiple-dose regimens[9].

There is no evidence of benefits in extending antibiotic administration beyond the completion of surgery. Furthermore, the practice of multiple post-operative doses has been found to increase the incidence of antibiotic resistant bacteria in SSIs that do occur and, therefore, increases the risks to the patient[8,10,11].

The most significant factor influencing the healing of surgical wounds and subsequent development of SSI is the level of bacterial burden at the incision site[12,13,14]. The primary source of this contamination has been found to be the skin[15]. Preoperative skin preparation with chlorhexidine has been found to reduce the bacterial count on skin by 80%-90%, though it has not been possible to correlate this directly with a corresponding reduction in SSI incidence[16]. Prolonged skin preparation may release organisms from deeper layers[16].

The risk of SSI infection has been found to increase with the length of time between shaving the site for surgery and commencement of surgery[13]. In a study of clean wound

Table 4. *Incidence of SSI, associated increase in hospital stay, antibiotics usage and overall expenditure*

Types of Surgery	Total Number	Number of SSI	Mean pre-op stay per SSI (days) (range)	Mean post-op stay per SSI (days) (range)	Mean increase in cost of antibiotic treatment per SSI*	Total additional cost incurred per SSI#
Gastrointestinal	17	3	17.3 (7-24)	14.3 (7-28)	€26.84	€126.58
Orthopaedic	8	4	8.25 (0-15)	14 (5-27)	€12.78	€109.23
Gynaecological	4	0	-	-	-	-
Urological	7	3	10.3 (1-24)	19.3 (11-26)	€12.00	€166.53
Otheræ	7	0	-	-	-	-
Total SSI	43	10	11.6 (0-24) SD = 9.25	15.7 (5-28) SD = 8.89	€16.76	€131.84
Total for no SSI§	43	33§	4.8 (0-20) SD = 4.82	5.2 (0-16) SD = 4.01	-	-

The average pre-op stay with no SSI was 4.8 days, The average post-op stay with no SSI was 5.2 days. *This figure is the average expenditure on antibiotics including prophylaxis per SSI minus the average expenditure on antibiotic prophylaxis in those who do not get an SSI. #Total additional cost = Cost of increased post-op stay compared with no SSI + Increased expenditure on antibiotics due to SSI. The cost per patient per night in LGH was €10.96. æSurgeries in the 'other' category were due to trauma(4), thyroid cyst(1), cleft palate(1) and lumpectomy(1). §This row is for comparison with Total SSI row. Data fits in the same columns as with SSI columns except for entry number 3 which is the number of surgeries without SSI (33).

SSIs, shaving more than two hours prior to the surgery was found to be associated with an SSI rate of 2.3%, in comparison to trimming of body hair which was associated with an SSI rate of 1.7%[14].

The abrasive action of shaving on the skin is the most likely reason for this and essential shaving should be carried out as close to the time of surgery as possible[14].

It is important to note that good infection control is multi-factorial and dependant on suitable infrastructure, equipment, clean rooms and appropriate training for staff. In developing countries, many of these factors cannot currently be altered without massive investment and thus key areas of intervention are limited.

CONCLUSION

Surgical antibiotic prophylaxis in LGH was highly variable and reflected the lack of protocols in this area. As a result, the prophylaxis used varied greatly between patients and sometimes lost rationale. Without exception, prophylaxis continued for several days, contrary to clinical evidence. The continuation of antibiotic dosing beyond the end of surgery is associated with increased expenditure on antibiotics of over €400 for the period in question. There is also strong evidence in the literature to suggest that this may be a contributory factor to SSIs with resistant organisms. The combined increase in antibiotic expenditures for the files available was €1730. Extrapolation of this figure to the entire year for all patients undergoing surgery would result in an annual cost of over €4,300, though it should be noted that the reason for limited chart availability is unknown and the real cost could be higher.

The implementation of an evidence-based prophylactic antibiotic protocol at LGH would likely result in significant savings on antibiotic expenditure without increasing risk to patients. Such a protocol might also reduce the cost associated with treating those SSI that occur due to resistant organisms. It should be noted that without culture and sensitivity screening at LGH, such a protocol would be impossible to develop. However, switching to a single prophylactic pre-operative dosage strategy should be given serious consideration. This straightforward change in practice would results in significant cost reduction and may reduce the development of resistant pathogens.

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