School of Pharmacy

A Retrospective Study to Evaluate Antibiotic Prescribing for Pediatric Appendectomy Procedures

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Declaration

This thesis titled “A Retrospective Study to Evaluate Antibiotic Prescribing for Pediatric Appendectomy Procedures” contain no material which has been accepted for the award of any other degree or diploma in an university

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made.

Signature

Date

Abstract

Objective: To retrospectively evaluate antibiotic use in pediatric appendectomy procedures following an educational intervention in December 2001.

Methodology: Demographic, clinical, and prescribing data was collected for all the patients <18 years old who have had undergone non-perforated appendectomy procedures at Princess Margaret Hospital for Children, WA. Data collection and analysis were divided into three groups. Group-I involved patients from May 2002 to April 2004 (which followed the post-intervention follow-up conducted from December 2001-April 2002 by Mallik et al.[1]). In May 2004, the Western Australian Therapeutic Advisory Group (WATAG) sent an advisory note which recommended a change from the use of cefotetan for surgical prophylaxis to cephazolin plus metronidazole. Group-II of the study involved patients between May 2004 (when the WATAG note was released) and June 2004; while Group-III involved patients from July 2004 to April 2005 (when the hospital issued the new guidelines and withdrawn cefotetan).Patient records were randomly selected for Group I & III and all the records were evaluated for Group III.

Results: Records for 408 patients were evaluated across the three groups of the study. There no significant difference ($p>0.05$) between gender and age across the three groups. An appropriate prophylactic drug regimen was prescribed in 68.5%, 66.7% and 39.8% of patients in Groups I, II and III respectively, with a significant difference in appropriate drug choice between Groups I and III ($p <0.05$). There was no significant difference between the groups with respect to appropriate prophylactic drug dose ($p>0.05$). Appropriateness rates for antibiotic choices for ward treatment were high at 91.0%, 92.0% and 92.7%, with no significant differences ($p>0.05$). There was a significant difference ($p<0.05$) between the three groups regarding the number of doses for ward treatment, with inappropriateness rates of 29.9%, 40% and 16.4%. The total appropriateness rates (drug choice plus dose in theatre and ward) across the study were 54.7%, 54.2% and 31.5%, with a significant difference ($p <0.05$) between Groups I and III.

Conclusion: This study has identified deficiencies related to the prescribing of antibiotics for prophylaxis. There was a varied level of prescribing appropriateness in terms of antibiotic choice for prophylaxis with an increasing trend for inappropriateness towards the end of the study period. This would indicate that issuing of changed guidelines and withdrawal of the drug being replaced did not positively influence appropriate prescribing. Further interventions are required to improve compliance with hospital prescribing guidelines.

1. Mallik A, Sunderland VB, Roberts MJ, Turner S, Lilley BJ. Impact of an Educational Program on Antibiotic Use in Paediatric Appendectomy Procedures. *Journal of Pharmacy Practice and Research* 2005;35(1):21-4.

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Abbreviations

CDC	-The Centre for Disease Control and Prevention
PAP	-Perioperative Antibiotic Prophylaxis
SAP	-Surgical Antimicrobial Prophylaxis
SSI	-Surgical Site Infection
PMH	- Princess Margaret Hospital for Children
WATAG	-Western Australian Therapeutic Advisory Group
TG-A	-Therapeutic Guidelines for Antibiotic
Timentin®	- Ticarcillin + Clavulanic acid

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1 Introduction

Appendicitis is the most common cause of acute abdominal pain that requires surgical intervention in the Western world[2] and is one of the most common surgical procedures performed in children. Antibiotic prophylaxis for abdominal procedures has been used since the 1940s.[1] In 1997, more than 260,000 new appendicitis cases occurred in the United States. The overall lifetime occurrence is approximately 12 percent in men and 25 percent in women.[3] An increase in the incidence of appendicitis was reported during the early part of the 20th century, but a decline has been evident since about 1930.[4-6] Patients with the disease may present with a wide variety of clinical manifestations, and the diagnosis may elude even the most experienced clinicians.[7] Prompt diagnosis is essential to minimize morbidity, which remains substantial if perforation occurs. The advent of antibiotics and effective surgical management has substantially reduced appendicitis-related mortality; however, deaths from appendicitis still occur, particularly in the elderly.

Appendicitis was rare in the past and remains so in underdeveloped countries. There appears to be no record of early physicians, from Moses to Hippocrates, recognizing this disease entity.[8] Although the anatomy of the appendix was well known by the 18th century, it was not until more recently that it was recognized that the appendix could become inflamed, with possibly fatal consequences.[9]

Confusion over this right-lower-quadrant entity existed until Reginald H. Fitz presented his landmark article in 1886, in which he coined the term ‘‘appendicitis’’ and correctly classified this disease by describing the appendix as the primary source of inflammation in acute typhlitis.[10] Fitz described the signs and symptoms of acute and perforated appendicitis, outlined the progression from acute right-lower-quadrant inflammation through peritonitis and iliac fossa abscess formation, and recommended early appendectomy if there were signs of spreading peritonitis or of clinical deterioration. Shortly thereafter, Charles McBurney and other pioneering surgeons began to intervene early in acute appendicitis.[11] These clinicians advocated prompt clinical diagnosis and surgical intervention. Their surgical aim was to operate in a timely fashion before appendiceal perforation and peritonitis developed.

The pathophysiology of appendicitis begins with obstruction of the narrow appendiceal lumen. Obstruction has many sources, including fecaliths, lymphoid

hyperplasia (related to viral illnesses such as upper respiratory infections, mononucleosis, or gastroenteritis), gastrointestinal parasites, foreign bodies, and Crohn's disease. Continued secretion of mucus from within the obstructed appendix results in elevated intraluminal pressure, leading to tissue ischemia, over-growth of bacteria, transmural inflammation, appendiceal infarction, and possible perforation. Inflammation may then quickly extend into the parietal peritoneum and adjacent structures.[3] The classic case is marked by (1) mild periumbilical discomfort, followed by (2) anorexia, nausea, and vomiting, soon associated with (3) right lower quadrant tenderness, which in the course of hours is transformed into (4) a deep constant ache or pain in the right lower quadrant. Fever and leukocytosis appear early in the course.[12]

1.1 Appendectomy in Western Australia

According to a study conducted by Donnelly et al[13], of the 59,749 appendectomies performed in WA during 1981-1997, 33,352 (58%) were performed on female patients and 26,397 (42%) on males. They found that a marked decline occurred in the rate of appendectomy during the study period; it was more marked in females than males which is consistent with trends reported from European countries.[5, 6, 13] Of the 30,934 appendectomies performed in WA during 1988-1997, 18,961 (61.3%) were acute emergency admissions, 3820 (12.3%) were other emergency admissions, 2192 (7.1%) were incidental procedures and 5961 (19.3%) were recorded as other appendectomy admissions.[13]

1.2 Antibiotics for surgical prophylaxis

Antibiotics have long been considered the "magic bullet" that would end infectious disease. Although they have improved the health of countless numbers of humans and animals, many antibiotics have also shown reduced effectiveness since the beginning of the antibiotic era. Bacteria have adapted defences against these antibiotics and continue to develop resistance, even as new antibiotics are developed. In recent years, much attention has been given to increased antibiotic resistance. As more microbial species and strains become resistant, many diseases have become difficult to treat, a phenomenon frequently ascribed to both indiscriminate and inappropriate use of antibiotics in human medicine. There is no doubt that the use of antibiotics provides selective pressure that result in antibiotic resistant bacteria and resistance genes.

Surgical antibiotic prophylaxis is defined as the use of antibiotics to prevent infections at the surgical site. It must be clearly distinguished from pre-emptive use of antibiotics to treat early infection. Wound infections are the common hospital-acquired infections in surgical patients.[14] They result in increased antibiotic usage, increased costs and prolonged hospitalisation.[15] The use of antibiotic prophylaxis before surgery has evolved greatly in the last 30 years. Improvements in the timing of initial administration, the appropriate choice of antibiotic agents, and shorter durations of administration have more clearly defined the value of this technique in reducing postoperative surgical site infections.[16] The pathologic state of the appendix is the most important determinant of postoperative infection. Wound infection after appendectomy for perforative or gangrenous appendicitis is four to five times higher than that for early disease.[16]

A prospective study of non-perforated appendicitis, using a logistic regression analysis of risk factors, showed that the risk for postoperative infection is related to lack of preoperative antibiotic prophylaxis and to the determination that the appendix was gangrenous.[17] Because the pathologic state of the appendix often cannot be determined before or during operation, a parenteral antibiotic agent is recommended as prophylaxis in all patients.[16]

1.3 Need for surgical prophylaxis

The economic consequences of hospital - acquired infections are well known and have changed little during the past few years. In the USA in 1995, hospital acquired infections account for approximately two million patients per year, with a mean hospital stay of four days and an associated cost of $ 2100 per patient. This equates to approximately US $ 4.5 billion of the health care budget. Many studies in other countries have yielded a similar cost per patient. In Turkey, an evaluation of health economics outcomes among patients with hospital acquired infections demonstrated a per-patient cost of $ 2280 and significant deterioration in a number of outcome measures compared with control patients.[18]

Several trials have shown that prophylactic antibiotics can significantly reduce the number of postoperative infective complications in non-perforated appendicitis compared with placebo.[17, 19-21] Each year, more than 18 million surgical procedures are performed in US hospitals. The Centre for Disease Control and Prevention (CDC) estimates that 2.7% of these are complicated by surgical-site infections (SSIs), accounting for at least 486,000 nosocomial infections each year. Such infections often lead to substantial morbidity and probably contribute to mortality in some patients. However, the extent of morbidity and mortality attributable to SSI is not known.

Kirkland et al. studied a diverse group of patients to quantitate the attributable costs of SSI. They showed a median attributable cost of US$ 3945 per SSI Vs matched uninfected control patients.[22] SSI clearly increased the cost of patient care. These costs are realized through increased hospital length of stay, ambulatory nursing visits for wound care, pharmacy costs for antibiotics, increased outpatient and emergency room visits, diagnostic laboratory studies, reoperation rate, and physician expenses.

A Spanish study by Rios et al. has shown that the surgical site infection increased the average length of stay between 7.7 days and 7.3 days in appendectomy with an average cost three times higher ($p<0.05$) than the ones not infected.[23]

1.4 Principles of prophylaxis

Infectious complications in surgical patients are responsible for prolonged wound healing, disability, deformity, prolonged hospitalization, increased overall cost of hospital care and even death, and since the patient's quality of life can be affected or even permanently altered by them, including very high human and economic costs, it is important to prevent them as far as possible. This is done by improving the patient's ability to overcome the microbial invasion, by improving the patient's general conditions (e.g. by improving the nutritional status, by normalizing plasma glucose levels, etc), by judicial surgical procedures and by using antibiotic prophylaxis. The objective of antibiotic prophylaxis in surgery is to prevent wound infection, in particular deep abscess, caused by intraoperative bacterial contamination. Success depends on the ability of the patient's local and systemic defence mechanisms to resist the microbial invasion.[24]

The principles of surgical prophylaxis have been defined over the years: administration just prior to surgery, maintenance of sufficient tissue drug levels for the duration of procedure and for not more than 24hr, and the antimicrobial agents given are active against those organisms most likely to be encountered in the particular surgical field.[25]

1.4.1 Timing of administration

The timing of antibiotic administration relative to the time of surgery is the most crucial factor in the success of surgical prophylaxis.[18] Timing of antimicrobial prophylaxis is considered to be optimal between 30 and 60 minutes before incision.[26] A prospective cohort study in a large teaching hospital in Utah found that 40% of patients who did not receive prophylactic antibiotics within the 2hr period prior to surgery accounted for nearly 80% of the wound infections.[27] In a subsequent study, the authors stated that improved timing of the use of prophylactic antibiotics, through changes in hospital systems, reduced the wound infection rate.[28]

A retrospective medical record review of 44 hospitals in New York State, USA, assessed 2,651 patients who underwent a procedure requiring surgical prophylaxis (abdominal aortic aneurysm repair, partial or total hip replacement, or large bowel resection). Investigators found that 86% of patients had documentation of receiving

antibiotics. However, only 46% of patients who underwent aneurysm repair, 60% of those who received hip replacements and 73% of those who underwent colon resection received antibiotic prophylaxis in a timely fashion (i.e. no more than 2 hr before the start of surgery). In total, 44 different antibiotics were used for surgical prophylaxis, far more than these included in published guidelines. Overall, although antibiotic prophylaxis was used in 81-94% of cases, the timing was incorrect in 27-54% of cases.[29]

Effective therapy depends on prompt treatment before culture results are available, based on the likely organisms and susceptibilities provided by local microbiological surveillance. Koleff[30] calls this 'getting it right from the start'. In the study of ventilator associated pneumonia by Iregui et al.[31], all patients eventually received appropriate antimicrobial therapy, but in one group the treatment was delayed with a mean time from diagnosis to starting appropriate therapy of ~ 29h compared with ~ 6 hr in the other. This delay was independently associated with mortality (adjusted OR 7.68, $p < 0.001$).

1.4.2 Optimum duration of administration

The incidence of postoperative infection for non-perforated appendicitis has been reported to range from 0 to 11.7%.[20, 32, 33] Such variation in the incidence of post operative infection might be accounted for differences in patient number, type of antibiotic used, follow-up duration and definition of wound infection between the studies. A single dose of antimicrobial agents is sufficient prophylaxis for most surgical procedures and, in rare circumstances, antibiotic therapy may be prolonged for 24 to 48 hours. However, some recommend that a second dose be administered intraoperatively for procedures lasting longer than 4 hours.[26] In a prospective randomized study by Mui at el.[34] for determining the optimum duration of prophylactic antibiotics in acute non-perforated appendicitis, 30 days postoperative infection rates were between 3.6 to 6.5%. The finding of this study revealed that a single dose of prophylactic antibiotics is adequate to prevent infective complications following open appendectomy for non-perforated appendicitis. Further they also showed that even in complicated appendicitis, prolonged use of antibiotics did not decrease the rate of post operative infective complications.

1.5 Misuse of antibiotics prophylaxis during surgery

Antibiotic use has soared in recent years. Furthermore, antibiotics appear to be used not only in excess but also inappropriately. The Center for Disease Control and Prevention in the USA has estimated that some 50 million of 150 million prescriptions for antibiotics written for outpatients every year were unnecessary.[18] An evaluation of antibiotic use at Hacettepe University hospital in Turkey in 1994 revealed that antibiotics were being used inappropriately in 23% of patients (6% in the field of general medicine, 28% in general surgery, 56% in urology and 44% in gynaecology).[35]

A retrospective study by Martelli and Mattioli[36] in patients undergoing appendectomy and cholecystectomy showed that a total of five antibiotics were used for prophylaxis in appendectomy and seven in cholecystectomy. Among the patients given antibiotics prophylactically, these drugs were used inappropriately in 63.6% of patients who underwent appendectomy and in 75% of those who underwent cholecystectomy. Reasons for inappropriateness were an excessive duration of treatment, incorrect timing of administration, inadequate antibacterial spectrum of the drugs used, and unnecessary combination of antibiotics.[36]

In a study of practice of perioperative antibiotic prophylaxis (PAP) in eight German hospitals, a total of 627 surgical procedures (appendectomies, other colorectal procedures, total prosthetic hip replacements) were assessed; 397 with PAP and 224 without PAP. Of the 397 PAP recorded, only 180 (45.3%) were performed correctly in accordance with international standards as a preoperative single dose; 19/59 (32.2%) PAP in appendectomies, 72/188 (38.3%) PAP in other colorectal procedures, 89/150 (59.3%) PAP in total prosthetic hip replacements. Of 397 PAP (appendectomies, colorectal procedures, total prosthetic hip replacements), only 180 (45.3%), were carried out correctly as a preoperative single dose. In 35.8% (142/397) of these procedures, PAP was given unnecessarily for more than 24 hr.[37]

A Belgian multicenter study conducted between 1992–1995 mentions the same problems: 11.4% of all procedures (genitourinary, abdominal and orthopaedic surgery) where PAP was indicated were in fact carried out without PAP while 40% of all PAP were administered incorrectly.[38] Two French studies[39, 40] also report differences between the recommendations given by a consensus-conference and daily

practice. Besides the widespread use of third generation cephalosporins for PAP, the point of time and duration of administration differed from the official recommendations, e.g. 9.5% of all PAP (digestive and ophthalmic surgery, orthopaedics, gynaecology) were given intraoperative and 2.5% even on the day before the intervention.[40]

A Canadian multicentric study by Zoutman et al. mentioned the same deficiencies; the wrong choice was made with respect to the point in time and in particular the duration of PAP (in this case referring to hip operations involving the implantation of foreign material), e.g. 78% of the PAP were continued postoperatively beyond 24 hr.[41] Harbarth et al.[42] documented a high rate of prolongation beyond 48 h, an ineffective practice that significantly increased antimicrobial resistance.

1.6 Economic impact of inappropriate antibiotic usage

Inappropriate antibiotic use has been shown to have implications for cost-effectiveness of patient care. A study based in Naples, Italy, examined surgeons' compliance with published international guidelines for surgical prophylaxis during the period January-March 1996, and evaluated the cost of the surgical prophylaxis compared with what it would have been had the guidelines been followed.[43] The first observation to emerge was that the duration of prophylaxis used was longer than recommended. Two hundred and twenty patients who underwent clean surgical procedures, for which prophylaxis was not generally recommended, received prophylaxis lasting from 1.1 ± 0.3 days to 4.6 ± 2.8 days. Similarly, 440 patients who underwent clean-contaminated surgical procedures, for which single-dose prophylaxis is indicated, received prophylaxis lasting from 3.6 ± 2.4 days to 5.2 ± 3.7 days. Patient records showed that 84% and 90.5% of patients who underwent clean and clean-contaminated surgical procedures, respectively, received non-standard antibiotics. Third-generation cephalosporins were the most popular prophylactic agents for both clean (74.1% of cases) and clean-contaminated (73%) surgery, even though these agents were not recommended in any published guidelines. The cost of antibiotic prophylaxis in monitored departments over the study period was calculated to be US $ 31,113. Astonishingly, if the recommendations regarding choice of antibiotic and timing of prophylaxis had been followed, the approximate cost of prophylaxis would have been US $ 3556 - approximately 10% of the actual cost.[43]

A study from Cornell University, New York, USA, tells a similar story.[44] Antibiotic use (therapy or prophylaxis) was considered inappropriate for 156/211 (74%) patients who underwent common surgical procedures. Reasons that antibiotic use was considered inappropriate included excessive duration of administration, incorrect timing, incorrect antimicrobial spectrum and premature switch from intravenous to oral dosing. A total of 17 antibiotics were used for prophylaxis and 21 for therapy, and the average duration of antibiotic administration after elective and emergency operations was 3.3 and 5.7 days, respectively. The total cost of excessive duration of antibiotic administration alone was estimated to be US $ 18,533. Perhaps most disturbingly, these data suggest that many surgeons were familiar with the

antimicrobial spectra of antibiotics and did not distinguish between prophylactic and therapeutic administration.[44]

Schmidt-Matthiesen et al. drew attention to the enormous costs incurred by non-rational use of antibiotics on surgical wards. In their prospective study they estimated that costs could be cut by up to 60% if the use of antibiotics was guided by rational considerations. PAP, which was frequently continued unnecessarily, offered enormous potential for cost cutting.[45] On the basis of a Belgian study[38], Sasse et al.[46] calculated the possibility of cutting costs by 6.1 million USD per year if the use of PAP was optimized in the 72 Belgian hospitals covered in the study.

1.7 Antibiotic resistance

Growing resistance means that once good - and cheap - treatments for infections have been lost, including penicillin and, in hospitals, oxacillins for use against staphylococcal infections; sulphonamides and ampicillin against urinary tract infections; and penicillin and – increasingly - fluoroquinolones for gonorrhoea.[47] Mortality is increased among intensive care patients whose infections are resistant to first-line empirical therapy,[48, 49] and the presence of bacteria resistant to antibiotics has been associated with increased rates of re-operation, surgical-site infection, and abscess formation in intra-abdominal infection.[50] The evidence that antimicrobial prescribing was the main driver of resistance is overwhelming. Since around 1998, concern about resistance has spread from specialist professionals to health-care bureaucrats, politicians, and the public, with numerous agency and governmental reports. These reports vary in emphasis, but can be summarised as advocating less antibiotic use, better use, improved infection control and - less prominently - continued antimicrobial innovation.[51]

1.7.1 Economic burden of resistance

Antimicrobial resistance is an economic as well as a medical problem. Resistant organisms cause infections that are more difficult to treat, requiring drugs that are often less readily available, more expensive and more toxic.[52] Costs associated with antimicrobial resistance among outpatients in the USA have been estimated to lie between US $ 400 million and US $ 18.6 billion, and corresponding inpatient costs are likely to be several times higher.[53] Abramson and Sexton demonstrated that the

attributable financial cost and time to cure were trebled in cases of methicillin-resistant *S aureus* infections compared with infections caused by susceptible strains.[54] Hensher[55] reports that the cost of a full course of drug treatment for multidrug-resistant tuberculosis in the northwest province of South Africa was Rand 26,354 (approximately US $ 4300) compared with Rand 215 for susceptible tuberculosis (approximately US $ 35). Data from Peru support the hypothesis that multi-drug-resistant tuberculosis is much more expensive to treat than susceptible tuberculosis strains that are resistant only to one or two drugs—costs were estimated at US $ 8000 and US $ 267, respectively.[53]

1.7.2 Abuse of the use of antibiotics in clinical practice results in selective pressure

The use of antibiotics in humans results in "selective pressure" in the host receiving the antibiotic. The broader the spectrum of activity, the higher the chance for bacteria to develop resistance. Third-generation cephalosporins, fluoroquinolones and more recently azithromycin have been linked to these problems.[56] The net result is that after administration of the antibiotic, most susceptible bacteria in the host, the majority of which are part of the normal saprophytic bacteria colonizing that individual, are eliminated thus selecting only those resistant bacteria capable of surviving despite the presence of the antibiotic. The natural consequence of this selection process is that there is excessive growth of one or more resistant strains. In this way, the host becomes a reservoir of resistant bacteria that can cause an infection in this individual or they can easily spread to other hosts causing serious infections in the most debilitated ones. It is for these reasons that antibiotics should be used cautiously and should be prescribed only to those individuals in whom their use is clearly justified and when it clearly outweighs the potential risks, including the risk of the development of resistance. Unfortunately, in today's healthcare system where physicians have only a few minutes to fully evaluate a patient, make a diagnosis and prescribe a treatment, and given the increasingly litigious nature of society, physicians frequently find themselves under tremendous pressured to prescribe an antibiotic even when this may not be appropriate.[57]Appropriate use of antibiotics may delay or prevent the emergence and spread of resistant pathogens. Maintaining the useful life of antibiotics is relevant in all countries and for all people.[58]

1.8 Drug utilization evaluation in children

Drug use review is the process by which the quality of drug prescribing is measured by organizing important predetermined criteria.[59] The rising costs in health care, lack of uniformity in prescribing, attitudes of prescribers and the emergence of antibiotic resistance is of growing concern.[60] Drug utilization review is a quality assurance approach for the facility per se, and involves the setting of criteria and standards, an assessment phase using a set of screening criteria and a follow-up correctional phase with the prescriber, to the final outcome of the therapy.[61] It also evaluates medical care in retrospect through analysis of clinical records. The study of prescribing patterns is a component of medical audit, which seeks monitoring, evaluation, and necessary modification in the prescribing patterns of prescribers to achieve rational and cost-effective medical care.[62] Several studies have evaluated antibiotic usage evaluation in children[60, 63-65] and in appendicitis in children.[66-68]

In a study by Lesar et al.[61] the most common type of medication prescribing errors detected among the 696 dosing errors, were overdoses 291 (41.8%) and underdoses 115 (16.5%); prescribing medication to which the patient was allergic occurred on 90 (11.6%); and errors involving prescribing of inappropriate dosage forms on 81 (11.6%) occasions. The most common medications involved were antimicrobial 276 (17.5%), gastrointestinal agents 122 (7.3%) and non-narcotic analgesics and antipyretics 46 (6.6%). Many of these were clinically significant 557 (80%), fatal 43 (6.2%) and 96 (13.8%) were rated as serious.

Medication errors and adverse drug events are serious problems in pediatrics. The relatively higher rates of potentially harmful errors in hospital for children compared with adults probably occurs primarily because dosing is more complex in pediatrics and underscores the need for safer systems in this setting. However, until recently, the incidence of pediatric medication errors has received relatively little scrutiny compared with adults, and even less has been done to assess their preventability.[69]

Pharmacist's today frequently provide the important service of drug usage review/evaluation. The outcomes of these assessments often lead to improvement in cost effective prescribing and better utilization of limited resources.[70]

1.9 Guidelines for improved quality of surgical prophylaxis

Surgical antimicrobial prophylaxis (SAP) is an essential, fundamental tool for lowering the risk of infection. SAP corresponds to more than one-third of overall in-hospital consumption of anti-infective agents. Although validated guidelines for the practical use of SAP have been available for many years, numerous errors in their application persist, as confirmed by the author's in-hospital audit. Indeed, improvements in appropriate prescription and compliance with guidelines are the main objectives in terms of the local bacterial micro-ecological risk and for economic reasons.[71]

There are at least three reasons to promote the rational use of antibiotics: to improve the quality of patient care, to delay the development of antibiotic resistance, and to increase the cost-effective use of antibiotics. With regard to the quality of care, inappropriate hospitalization, medical treatments and/or surgical intervention clearly represent poor quality medical care. In addition, large variations in practice patterns have implications for quality of care, as does variation in the way a treatment is applied. Variation in practice can be overcome by a combination of outcomes management, the effective application of practice guidelines, and traditional clinical research that supports an evidence-based approach. In particular, the development of guidelines and their incorporation into a target-oriented clinical practice may serve to diminish clinical uncertainty and lead to overall improvement in the practice of medicine. Whether practice guidelines achieve the goals of guiding good prescription and the rational, cost-effective use of antibiotics, limiting emergence of resistance, conserving new antibacterial agents, and educating physicians depends on the manner in which they are applied.[18] It is important to remember that antibiotics are 'societal' drugs, in that the way in which an antibiotic is used to manage infection in one patient has implications not just for the response of that patient but also for the response of future patients. The appropriate implementation of practice guidelines is capable of achieving significant improvements in antibiotic use.[18]

1.10 Study Objectives

Pediatrics presents, additional challenges in adhering to prescribing guidelines due to the wide range of doses used.[1] Therefore, we set out to evaluate the appropriateness of prescribed antibiotics for non-perforated appendectomy procedures in pediatric patients. This will be achieved by

- Evaluating the effect of hospital based interventions on four aspects of antibiotic prescribing:
  - ❖ Decision to prescribe antibiotics (ward treatment only).
  - ❖ Antibiotic regimen (drug, dosage, dosing interval, route).
  - ❖ Duration of prophylaxis and ward treatment.
  - ❖ Timing of prophylaxis and ward treatment.
- Evaluate the effectiveness of various sequential interventions over the period of three years.

2 Methodology

2.1 Setting and patient population

The retrospective analysis was a post-intervention follow-up from a study[1] which was conducted at Princess Margaret Hospital for Children (PMH), Subiaco, Western Australia a 250-bed pediatric hospital for a period of three years. Samples of pediatric patients of age <18 years who underwent an appendectomy procedure which were diagnosed as non-perforated were evaluated in the study. The study was divided into three parts; the first group involved the collection and analysis of data for a sample of patients from May 2002 to April 2004 (the post intervention follow up period of an intervention which was carried out by Mallik at el.[1] in December 2001 and follow-up continued till April 2002). The second group involved collection of data between May-June 2004. In May 2004 the Western Australian Therapeutic Advisory Group (WATAG) released new guidelines recommending cephazolin with metronidazole to be used for antibiotic prophylaxis instead of cefotetan for non-perforated appendectomies. These guidelines were issued but not enforced until July 2004 as the hospital was using the remaining stock of cefotetan. Therefore it was unlikely that cefotetan usage would have disappeared from the hospital usage. For this group the collection and analysis of data was from May 2004 to June 2004, the period following the release of Western Australian Therapeutic Advisory Group (WATAG) advisory note in May 2004. The third group describes the data between July 2004 till April 2005, when the guidelines were reinforced in the hospital. This includes the usage of cephazolin plus metronidazole to be used for antibiotic prophylaxis and withdrawal of cefotetan.

2.2 Data collected

The data that related to antibiotic prescribing were entered from the medical records into a coded prepared form. Patient details included age, weight, sex, date of admission, date of discharge, clinical details such as principle diagnosis and principle procedure, medication details including drug name, dose, frequency, route and number of doses administered. There were almost 1000 cases of appendectomies available in the hospital over the time period of study. These cases were entered in Microsoft excel sheets and were randomized for selection.

2.3 Inclusion criteria

All pediatric patients undergoing non-perforated appendectomies at PMH and under 18 years of age were eligible to be included in the study. Non-perforated appendix was defined as being stated in the medical record in histopathology reports post surgically.

2.4 Sample size

The sample size calculation was based on running repeated simulations (5000 for each sample size estimate) with different sample sizes (we started at n=300 and worked up to n=400). The observed power was based on the percentage of studies for which that sample size would show a significant linear trend at a Type 1 error rate of 5% i.e. alpha=0.05 and a Type 2 error rate of 80%. In other words, 80% of the 5000 samples using n=380 produced a p-value for the trend of <0.05. Therefore we needed a sample size n=380 from May 2002 to April 2005. There were an additional 28 patients identified who underwent simple appendectomy procedures during the period between May-June 2004. Therefore, 408 patients were included in the study.

2.5 Ethical approval

The study involved the collection and analysis of patient's recorded data, therefore ethical approval was obtained from Curtin University of Technology Human Research Ethics committee. As this study involved the analysis of patient records, ethical issues arise in relation to confidentiality and release of data. A unique non-patient identifiable code was allocated to each record to enable re-identification of the record if necessary. The key to the code was held at all times by the Chief Pharmacist of PMH. Any coded data to leave the hospital was kept secure in accord with National Health and Medical Research Council guidelines and only group data will be released from the research. The data will be stored in the School of Pharmacy for a period of seven years in a locked cabinet.

2.6 Interventions

There were three interventions carried out between December 2001 and April 2005.

- The intervention which was carried out by Mallik et al.[1] on 5th December 2001 at PMH involved:
  - ❖ Releasing a newsletter to the relevant key prescribing medical and other appropriate staff, detailing current recommendations for the prophylaxis and treatment of appendectomy
  - ❖ Chief Pharmacist and the surgical ward pharmacist held personal discussions with the appropriate staff.
  - ❖ A senior pharmacist gave a presentation to surgeons and subsequent regular follow-up occurred by clinical pharmacists regarding the choice of antibiotic treatments.
  - ❖ The guidelines posters were displayed in the operating theatres and wards.
- The second intervention involved the sending of WATAG advisory note to all the hospitals, with no formal action taken in the hospital (PMH) for another two months.
- The third intervention was the change in prescribing guidelines after the release of WATAG note it involved:
  - ❖ Releasing a newsletter to the relevant key prescribing medical and other appropriate staff, detailing the change in recommendations for the prophylaxis and treatment of appendectomy
  - ❖ The changed guidelines were also conveyed to the prescribing doctors via e-mail.
  - ❖ The new changed guidelines posters were displayed in the operating theatres and wards
  - ❖ Cefotetan was withdrawn from use in the operating theatre.

2.7 Definitions

The definitions and criteria's used to evaluate the data collected were the same as were used by Mallik et al.[1] which are detailed in Table 2.1

Table 2.1 Definitions of terms used in the study

Term	***Definition***
Appropriate choice	Drug/drug combination prescribed as recommended in TG-A or in-hospital guidelines
Appropriate dose	Dose prescribed within ± 25% (variability allowed in dosage form and bioequivalency studies) of the recommended dosage
Theatre antibiotics	Prophylactic antibiotics prescribed in theatre
Theatre dosage	Dosage of theatre antibiotic given
Ward antibiotic	Post-operative antibiotic prescribed in the ward
Ward dosage	Dosage of ward antibiotics given
Appropriate Timing	One hour deviation from the exact time recorded on the medical chart was allowed and considered appropriate
Total theatre appropriateness	Appropriateness of a combination of the choice and dosage of antibiotics prescribed in the theatre in accordance with the TG-A or in-hospital guidelines
Total ward appropriateness	Appropriateness of a combination of the choice and dosage of antibiotics prescribed in the ward in accordance with the TG-A or in-hospital guidelines
Total antibiotic choice	Choice of drug/drug combination prescribed in the theatre and ward
Total antibiotic dosage	Choice of combined dosage of antibiotics prescribed in the theatre and ward
Total appropriateness	Appropriateness of a combination of the choice and dosage of antibiotics prescribed in the theatre and the ward in accordance with the TG-A or in-hospital guidelines
Non-recommended antibiotics	Antibiotic not recommended by the TG-A or in-hospital guidelines

TG-A[72] **-** Therapeutic guidelines :antibiotic.

2.8 Statistical analysis

The study was a retrospective; statistical analysis of the data was performed using the SPSS version 13 for windows. One-way Analysis of Variance was used to compare the scale variables of age, weight, length of stay across the three groups. The Bonferroni Post Hoc test was performed for multiple comparisons between the groups. Chi-square (χ^2) analysis was used to show any significant difference between the three groups on the appropriate/inappropriate choice of drug, dose, route and timing of administration. P value less than 0.05 was considered statistically significant, except where multiple comparisons occurred.

2.9 Data analysis

The data was evaluated against hospital in-house guidelines for appendectomy procedures, which was written in detail according to TG-A.[72] Antibiotic guidelines for group-I are summarized in the Table 2.2. The guidelines for group - II were the same as group - I as the guidelines were unclear as conflicting events occurred. A letter was issued by an authoritative group (WATAG) but no response was seen to be made by the hospital. The guidelines for group - III were the same as that for group I, except that the cefotetan was replaced with combination of cephazolin with metronidazole. The guidelines for group III are summarized in Table 2.3.

The determination of pathology was based on histopathology report following the operation. For administration of antibiotic prophylaxis the decision has to be based on surgeon's diagnosis prior to surgery, where a surgeon commented, that they considered the procedure to be for a perforated appendicitis, then the prophylaxis for that procedure was counted appropriate even the appendix was classified as normal or inflamed in the histopathology report.

Table 2.2 Antibiotic guidelines for appendectomy procedure for group - I

Category	**Prophylaxis (at the time of induction)**	**Post-operative treatment**	
		Inflamed appendix	**Peritoneal soiling / peritonitis detected**
Normal patient	Cefotetan 50mg/kg single dose (maximum dose 1g)	Ticarcillin / Clavulanic acid (Timentin®) 50mg/kg (maximum dose 3g) 2doses 6 hours apart	Ticarcillin / Clavulanic acid (Timentin®) 50mg/kg (maximum dose 3g) four times daily for up to 5 days
Non – anaphylactic penicillin allergy patients	Cefotetan 50mg/kg single dose (maximum dose 1g)	Ceftriaxone 50mg/kg)maximum dose 1g) as a single dose with Metronidazole 12.5mg/kg IV (maximum dose 500mg) as single dose given 6 hours post-operatively	Ceftriaxone 50mg/kg (maximum dose 1g) once daily with Metronidazole 12.5mg/kg IV (maximum dose 500mg) twice daily for 5 days
Anaphylactic penicillin allergy patients	Clindamycin 10mg/kg (maximum dose 600mg) with Gentamicin 7mg/kg IV single dose	Clindamycin 10mg/kg (maximum dose 600mg) 2 doses given 6 hours apart starting 6 hours post – operative with Gentamicin 7mg/kg IV single dose (if Gentamicin has been given as prophylaxis at the induction then no further dose is required)	Clindamycin 10mg/kg (maximum dose 600mg) four times daily with Gentamicin 7 mg/Kg once daily for 5days

Table 2.3 Antibiotic guidelines for appendectomy procedure for group - III

Category	**Prophylaxis (at the time of induction)**	**Post-operative treatment**	
		Inflamed appendix	**Peritoneal soiling / peritonitis detected**
Normal patient	Cephazolin 25mg/kg (maximum dose 1g) plus Metronidazole 12.5mg/kg (maximum dose 500mg)	Ticarcillin / Clavulanic acid (Timentin®) 50mg/kg (maximum dose 3g) 2doses 6 hours apart	Ticarcillin / Clavulanic acid (Timentin®) 50mg/kg (maximum dose 3g) four times daily for up to 5 days
Non – anaphylactic penicillin allergy patients	Cephazolin 25mg/kg (maximum dose 1g) plus Metronidazole 12.5mg/kg (maximum dose 500mg)	Ceftriaxone 50mg/kg)maximum dose 1g) as a single dose with Metronidazole 12.5mg/kg IV (maximum dose 500mg) as single dose given 6 hours post-operatively	Ceftriaxone 50mg/kg (maximum dose 1g) once daily with Metronidazole 12.5mg/kg IV (maximum dose 500mg) twice daily for 5 days
Anaphylactic penicillin allergy patients	Clindamycin 10mg/kg (maximum dose 600mg) with Gentamicin 7mg/kg IV single dose	Clindamycin 10mg/kg (maximum dose 600mg) 2 doses given 6 hours apart starting 6 hours post – operative with Gentamicin 7mg/kg IV single dose (if Gentamicin has been given as prophylaxis at the induction then no further dose is required)	Clindamycin 10mg/kg (maximum dose 600mg) four times daily with Gentamicin 7 mg/Kg once daily for 5days

3 Results

3.1 Demographic data

3.1.1 Patient group comparison

A total of 408 patients where included in the study, with 250 patients in Group-I, 28 in Group-II and 130 in Group-III. There was no significant difference found between the mean ages or gender between the groups ($p > 0.05$).

3.1.2 Mean age comparison

Table 3.1 Mean age of patient in each group

	Group	Number	Mean (years)	P value
Age in years	I	250	10.75	0.733
	II	28	10.42	
	III	130	10.89	

3.1.3 Gender comparison

Table 3.2 Patient gender statistics in all three groups

Group	Male	Female	P value
I	138(55%)	112(44.8%)	0.983
II	15(53.6%)	13(46.4%)	
III	71(54.6%)	59(45.4%)	

3.2 Diagnosis

Patients were included in the study on the basis of a diagnosis reported in histopathology report prepared post-surgery. The various forms of appendix reported were classified in the four categories as show in the Table 3.3. Acute appendicitis was diagnosed in 56.8% of patients in Group-I, 60.7% in Group-II, and 68.5% in Group-III and acute suppurative appendicitis in 34.4% of patients in Group-I, 3.6% in Group-II and 16.9% in Group-III. There were 5.6% of patients in Group-I, 3.6% of Group-II and 12.3% of Group-III with normal appendix removed (Table 3.4).

3.2.1 Classification of diagnosis

Table 3.3 Classification of various types of appendices

Types	Description
Normal Appendix	▪ Vermiform Appendix ▪ Appendix within normal limits ▪ Normal Appendix ▪ Early Appendix ▪ Appendix minor changes ▪ Appendix unremarkable
Acute Appendix	▪ Appendicitis ▪ Acute Appendicitis ▪ Early Acute Appendicitis ▪ Appendicitis - Acute Inflammation ▪ Focal Appendicitis ▪ Mild Acute Appendicitis ▪ Severe Acute Appendicitis ▪ Vermiform – Acute Inflammation ▪ Appendicitis Mildly Inflamed

	▪ Appendix - Enterobius Vermicularis ▪ Acute Appendicitis with Ent Ver. ▪ Sub Acute Appendicitis ▪ Vermiform Appendix with Necrosis ▪ Appendicitis with Hyperplastic polyp ▪ Appendix – early mucosal appendicitis ▪ Appendix Mildly congested
Acute Suppurative Appendix	▪ Acute Suppurative Appendix ▪ Vermiform with Acute Suppurative Appendix
Complicated Appendix	▪ Acute Suppurative Appendix with Peritonitis ▪ Acute Gangrenous Appendix ▪ Acute Appendicitis with Peritonitis ▪ Appendicitis plus Pus ▪ Acute Gangrenous Appendix with Peritonitis ▪ Gangrenous Appendix

Table 3.4 Comparison of principal diagnosis of appendectomy in patients in all the three groups

Type	Group		
	I*	II*	III*
Normal Appendicitis	14(5.6)	1(3.6)	16(12.3)
Acute Appendicitis	142(56.8)	17(60.7)	89(68.5)
Acute Suppurative Appendicitis	86(34.4)	4(3.6)	22(16.9)
Complicated Appendicitis	8(3.2)	6(21.4)	3(2.3)

*Number of patients (percentage)

3.3 Theatre antibiotics

3.3.1 Theatre antibiotic choice

There were nine different antibiotic regimen prescribed for prophylaxis in group-I, as shown in the Table 3.5. Six of the nine prescribed regimen were inappropriate, as they were not the recommended regimens according to the in-hospital guidelines. There were three different antibiotic regimen prescribed for prophylaxis in group-II, as shown in the Table 3.6. Two were inappropriate. There were ten different antibiotic regimens prescribed for prophylaxis in group-III, eight out of ten antibiotic regimes prescribed were inappropriate (Table 3.7).

Table 3.5 Prophylactic antibiotics administration to Group - I

Drug/s prescribed	**Group-I*(%)**
Amoxicillin + Gentamicin + Metronidazole	2 (0.8)
Cefotetan†	141 (58.5)
Cefotetan + Metronidazole	3 (1.2)
Cefotetan + Timentin	15 (6.2)
Ceftriaxone†	1 (0.4)
Gentamicin	1 (0.4)
Metronidazole	1 (0.4)
Timentin‡	76 (31.5)
Clindamycin + Gentamicin†	1 (0.4)

*Number of patients (percentage)

† Appropriate

‡ Appropriate only when peritoneal soiling suspected

Table 3.6 Prophylactic antibiotics administration to Group – II

Drug/s prescribed	**Group-II*(%)**
Cefotetan†	8 (29.6)
Timentin‡	18 (66.7)
Amoxicillin + Gentamicin	1 (3.70)

*Number of patients

† Appropriate

‡ Appropriate only when peritoneal soiling suspected

Table 3.7 Prophylactic antibiotic administration to Group – III

Drug/s prescribed	**Group-III*(%)**
Cefotetan	3(2.3)
Cefotetan + Timentin	1(0.8)
Ceftriaxone†	2(1.5)
Gentamicin	1(.8)
Cephazolin	8(6.25)
Cephazolin + Metronidazole†	32(25.0)
Timentin‡	78(60.9)
Timentin + Metronidazole	1(.8)
Cephazoline + Timentin	1(.8)
Flucloxicillin + Gentamicin	1(.8)

*Number of patients (Percentage)

† Appropriate

‡ Appropriate only when peritoneal soiling suspected

3.3.2 Theatre antibiotic choice comparison

Of the patients in Group-I 165 (68.5%) received an appropriate choice of antibiotic regimen for prophylaxis according to the prescribing protocol for abdominal surgery in hospital. In the case of Group-II, 18 (66.7%) were on appropriate antibiotic regimens, with no significant difference between Groups I and II ($p>0.05$). In case of the Group-III, there were 51 (39.8%) of patients on appropriate antibiotic regimens for prophylaxis, with significant reduction ($p<0.05$) between Groups I and III. No prophylaxis given was deemed to be in appropriate, as prophylaxis was recommended for all the appendectomy procedures performed in PMH. There were nine in Group-I, one in Group-II and two in Group-III patients with no prophylaxis given as shown in Table 3.8. There was no patient on unnecessary prophylaxis doses i.e. none of the patient's received more than one dose of antibiotics for prophylaxis across the three groups.

Table 3.8 Comparison of theatre prophylaxis between the three groups

Group	**Appropriate Prophylaxis***	**Inappropriate Prophylaxis***	**No Prophylaxis***	**Total***
I	165(68.5)	76(31.5)	9(3.6)	250
II	18(66.7)	9(33.3)	1(3.5)	28
III	51(39.8)	77(60.2)	2(1.5)	130
P value	0.000			

*Number of patients (percentage)

Table 3.9 Comparison of Timentin® as theatre prophylaxis between the three groups

Groups	Appropriate *	Inappropriate *	Total*	P value
I	17 (22.4)	59(77.6)	76	I & II - 0.018
II	9(50.0)	9(50.0)	18	II & III - 0.031
III	19(24.4)	59(75.6)	78	I & III - 0.770
P value	0.049			

*Number of patients (Percentage)

3.3.3 Theatre antibiotic dose comparison

The theatre drug dose appropriateness was high with 216 (89.6%) in Group-I, 26(96.3%) in Group-II and 114 (89.1%) of patients in Group-III as shown in the Table 3.10. No significant difference ($p>0.05$) was observed between the groups.

Table 3.10 Comparison of theatre prophylaxis drug dose between all the three groups

Group	Appropriate Prophylaxis drug dose*	Inappropriate Prophylaxis drug dose*	No Prophylaxis*	Total*
I	216(89.6)	25(10.4)	9	250
II	26(96.3)	1(3.7)	1	28
III	114(89.1)	14(10.9)	2	130
P value	0.513			

*Number of patients (percentage)

3.3.4 Theatre antibiotic route and timing of administration.

None of the patients in Group I and II received an inappropriate route of administration. There was only one patient identified in Group-III with an inappropriate route of administration (Table 3.11) with no significant difference ($p>0.05$) between the groups. The appropriateness of timing of prophylaxis administration was also high with 230(95.4%), 27(100%), and 125(97.7%) patients in group I, II and III (Table 3.12) with no significant difference across the groups ($p>0.05$).

Table 3.11 Comparison of theatre prophylaxis route of administration between the groups

Group	**Appropriate route of administration***	**Inappropriate route of administration***	**No Prophylaxis***	**Total***
I	241(100.0)	-	9	250
II	27(100.0)	-	1	28
III	127(99.2)	1(.8)	2	130
P value	0.350			

*Number of patients (percentage)

Table 3.12 Comparison of theatre prophylaxis timing of administration between the three groups

Group	**Appropriate timing of administration***	**Inappropriate timing of administration***	**No Prophylaxis***	**Total***
I	230(95.4)	11(4.6)	9	250
II	27(100.0)	-	1	28
III	125(97.7)	3(2.3)	2	130
P value	0.321			

*Number of patients (percentage)

3.4 Ward antibiotics

3.4.1 Ward antibiotic choice

According to the in-house protocol for prophylaxis for abdominal surgery, two doses of Timentin® were recommended for patients with inflamed appendix in case of non-perforated appendix. Therefore, it was the surgeon's decision to prescribe ward treatment. Table 3.13 shows the number of patients that were on ward treatment post surgically. Nine different antibiotic regimes were prescribed for ward treatment in Group-I, with 210 (95%) of patients on Timentin®. There were two and seven different antibiotic regimes prescribed respectively in Groups-II and III with 24 (96%), 102 (92.7%) of patients on Timentin® in both the groups (Table 3.14). The ward antibiotic for treatment post surgically were appropriate in 201 (91%), 23 (92%), and 102 (92.7%) patients in group I, II and III (Table 3.15). There was no significant difference observed ($p>0.05$) between the groups in term of antibiotic choice for ward treatment.

Table 3.13 Comparison of ward antibiotic administration between the three groups

Groups	**Ward Treatment given***	**No ward treatment given***	**Total***
I	221(88.4)	29(11.6)	250
II	25(89.3)	3(10.7)	28
III	110(84.6)	20(15.4)	130

*Number of patients (percentage)

Table 3.14 Ward antibiotics prescribed in the three groups

Drug/s prescribed	Group-I*	Group-II*	Group-III*
Amoxicillin + Gentamicin	1 (0.5)	-	-
Amoxicillin + Gentamicin + Metronidazole	1 (0.5)	-	-
Cefotetan	1 (0.5)	-	-
Ceftriaxone	1 (0.5)	-	2 (1.8)
Cephalothin	-	1 (4.0)	-
Cephazolin	-	-	1(0.9)
Timentin	210 (95.0)	24 (96.0)	102 (92.7)
Clindamycin + Gentamicin	1 (0.5)	-	-
Cefotetan + Ceftriaxone	1 (0.5)	-	-
Ceftriaxone + Metronidazole	3 (1.4)	-	1(0.9)
Cephalothin + Metronidazole	-	-	1 (0.9)
Gentamicin + Timentin	2 (0.9)	-	2 (1.8)
Timentin + Benzylpenicillin	-	-	1 (0.9)

*Number of patients (percentage)

Table 3.15 Comparison of appropriateness of ward antibiotic choice between the three groups

Group	Appropriate Ward Treatment*	Inappropriate Ward Treatment*	No Treatment*	Total*
I	201(91.0)	20(9.0)	29(11.6)	250
II	23(92.0)	2(8.0)	3(10.7)	28
III	102(92.7)	8(7.3)	20(15.4)	130
P value	0.858			

*Number of patients (percentage)

3.4.2 Ward antibiotic dose and number of doses comparisons.

Appropriateness in terms of dose for antibiotic administered for ward treatment appears to be high and well maintained. There was no significant difference ($p>0.05$) between the three groups (Table 3.16). The number of patients on unnecessary doses for ward treatment which were inappropriate, shows a downward trend, with a significant difference ($p<0.05$) between Groups I and III (Table 3.17).

Table 3.16 Comparison of appropriateness of ward antibiotic dose between the three groups

Group	**Appropriate Dose***	**Inappropriate Dose***	**No Treatment***	**Total***
I	196(88.68)	25(11.32)	29	250
II	23(92.0)	2(8.0)	3	28
III	105(95.45)	5(4.55)	20	130
P value	0.126			

*Number of patients (percentage)

Table 3.17 Comparison of patients on ward antibiotic doses between the three groups

Groups	**Unnecessary ward antibiotic doses administered***	**P value**
I	66(29.9)	0.009
II	10(40.0)	
II	18(16.4)	

*Number of patients (percentage)

3.4.3 Ward antibiotic timing of administration.

The timing of administration for antibiotic administration post-surgically was high with appropriateness in 187 (84.6%), 22 (88%), and 102 (92.7) patients in Groups I, II and III respectively, as shown in Table 3.18. No significant difference ($p>0.05$) was observed within the groups.

Table 3.18 Comparison of ward antibiotic timing of administration between the three groups

Groups	**Appropriate timing of administration***	**Inappropriate timing of administration***	**No Treatment***	**Total***
I	187(84.6)	34(15.4)	29	250
II	22(88.0)	3(12.0)	3	28
III	102(92.7)	8(7.3)	20	130
P value	0.112			

*Number of patients (percentage)

3.5 Total theatre and ward comparisons

Total theatre appropriateness is the appropriateness of combination of choice and dose of antibiotic prescribed in theatre. The total theatre appropriateness was 61.6%, 60.7%, 34.6% respectively in the three groups (Table 3.19) with a significant difference ($p<0.05$) between Group I and III & II and III. No antibiotic prophylaxis given was considered inappropriate. Total ward appropriateness is the appropriateness of combination of choice and dose of antibiotic prescribed in ward. The total ward appropriateness was 88.0%, 89.2%, 93.0% respectively in the three groups (Table 3.20) with no significant difference ($p>0.05$) between groups. No antibiotic given for ward treatment was considered appropriate, as it was surgeon's decision to prescribe antibiotic post surgically based on the pathology of the patient.

Table 3.19 Comparison of total theatre appropriateness across the groups

Groups	**Appropriateness***	**Inappropriate***	**Total***
I	154(61.6)	96(38.4)	250
II	17(60.7)	11(39.3)	28
III	45(34.6)	85(65.4)	130
P value	0.000		

*Number of patients (percentage)

Table 3.20 Comparison of total Ward appropriateness across the groups

Groups	**Appropriateness***	**Inappropriate***	**Total***
I	220(88.0)	30(12.0)	250
II	25(89.3)	3(10.7)	28
III	121(93.0)	9(7.0)	130
P value	0.302		

*Number of patients (percentage)

3.6 Total antibiotic choice comparisons

Total antibiotic choice comprises the combination of antibiotic choice in theatre and ward. The total antibiotic choice appropriateness across the three groups was 60.8%, 62.5%, 35.2% respectively (Table 3.21). There was a significant difference ($p<0.05$) between Groups II and III & I and III.

Table 3.21 Comparison of total antibiotic choice appropriateness across the groups

Group	**Appropriateness***	**Inappropriate***	**Total***
I	129(60.8)	83(39.2)	250
II	15(62.5)	9(37.5)	28
III	38(35.2)	70(64.8)	130
P value	0.000		

*Number of patients (percentage)

3.7 Total antibiotic dosage comparisons

Total antibiotic dosage comprises the combined dosage of antibiotic in theatre and ward. The total antibiotic dosage appropriateness across the three groups was 80.7%, 87.5%, 86.1% respectively (Table 3.22) with no significant difference ($p>0.05$).

Table 3.22 Comparison of total antibiotic dosage appropriateness across the groups

Group	**Appropriateness***	**Inappropriate***	**Total***
I	171(80.7)	41(19.3)	250
II	21(87.5)	3(12.5)	28
III	93(86.1)	15(13.9)	130
P value	0.389		

*Number of patients (percentage)

3.8 Total appropriateness

The total appropriateness has been declined over the study period (Table 3.23). There was no statistical significant difference between Group I & II ($p>0.05$). But there was a significant difference in total appropriateness between Groups I & III ($p<0.05$)

Table 3.23 Comparison of total appropriateness across the three groups

Groups	**Appropriateness***	**Inappropriate***	**Total***
I	116(54.7)	96(45.3)	250
II	13(54.2)	11(45.8)	28
III	34(31.5)	74(68.5)	130
P value	0.000		

*Number of patients (percentage)

3.9 Trend over time for total appropriateness

The trend over time for Group I is shown in the bar graph (Figure 3.1). This shows a tendency for more inappropriate prescribing well after the intervention occurred. Linear regression gave a slope of 0.164 (± 0.55) for inappropriate prescribing over the two year period following the initial intervention plus five months follow-up period . There is a sampling factor to consider since the sampling was for the whole period and not defined at monthly intervals. Hence lower levels of sampling occurred for each month which is included on the bar graph. Figure 3.2 shows the data similarly collected for 10months past the last intervention. Linear expression gave a slope of 2.65 (±1.66). An increasing trend in appropriate prescribing is evident in this period.

Figure 3.1 Prescribing pattern in terms of total appropriateness for Group-I

There was reduction in appropriate prescribing after ceasing the follow by Mallik[1] as show in the bar diagram below. The bar diagram below show the inconsistency in appropriate prescribing for the period.

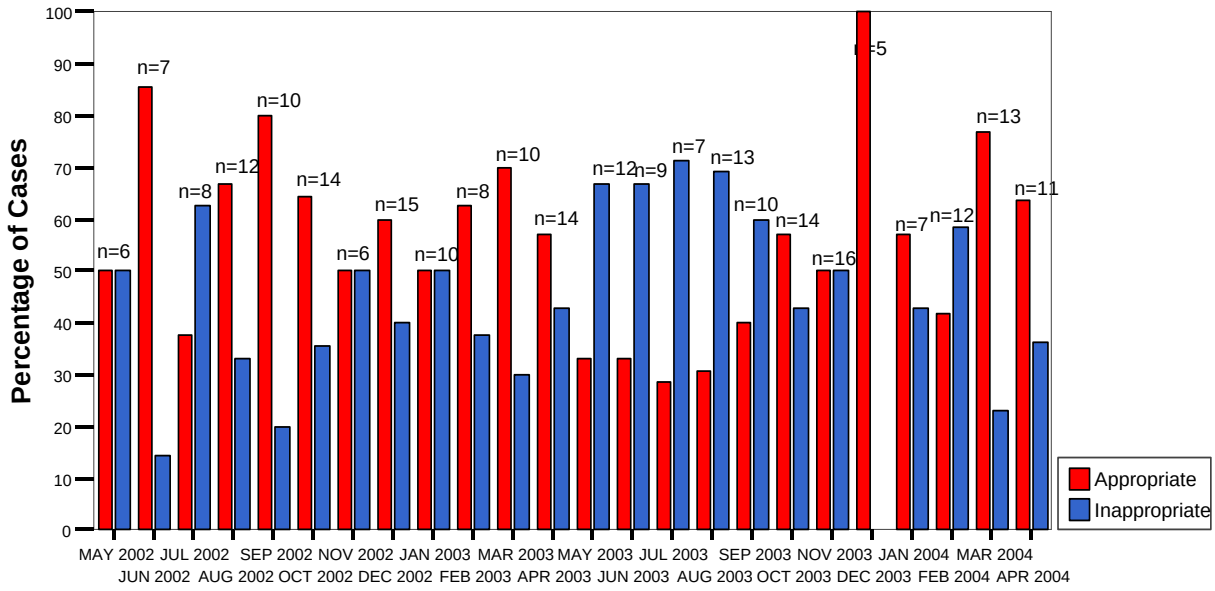
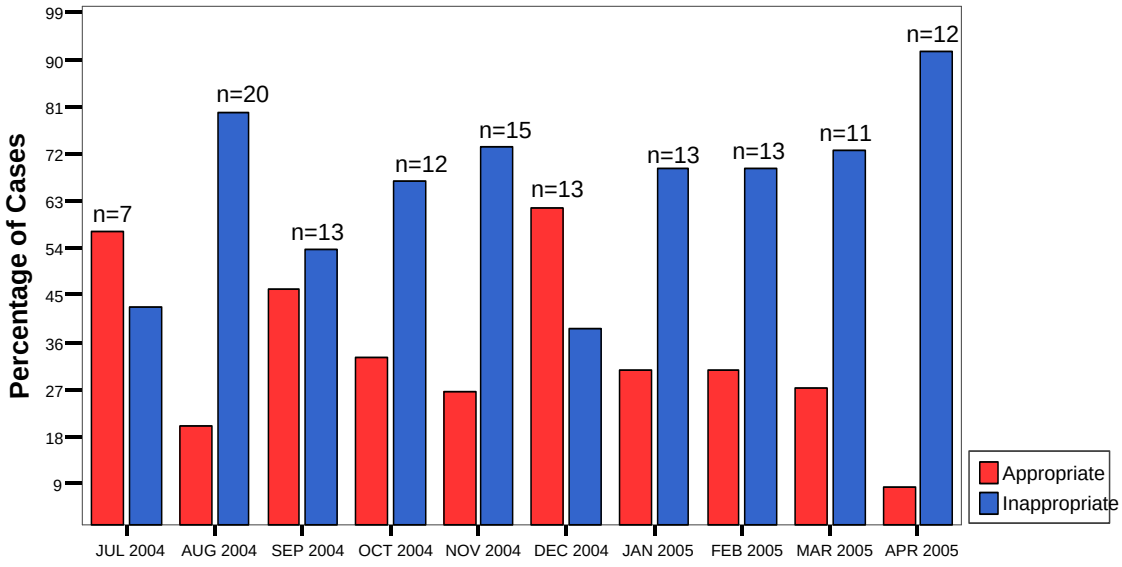


Figure 3.2 Prescribing pattern in terms of total appropriateness for Group-III

The bar diagram below illustrate the prescribing trend in group - III. It shows a trend with increasing inappropriateness from December 2004 till the end of the study period.



4 Discussion

The increasing prevalence of antibiotic-resistant bacteria poses a major threat to the health of hospitalized patients. The relationship between emergence of resistance and antibiotic use and misuse is well recognized. It is evident that antibiotics affect not only the microorganism and the individual patient, but also the population as a whole.[73] The inappropriate usage of antibiotics, the most commonly used treatment in the hospital practice plagues all the medical specialities across the world.[64] In an attempt to promote appropriate usage of antibiotics in surgical practice, guidelines for prophylaxis and treatment were developed for abdominal procedures at PMH and an intervention was carried by Mallik[1] in December 2001 with the aim to improve prescribing based upon adherence to the protocol. Mallik[1] followed up for five months post-intervention and reported an increase in appropriateness of theatre antibiotics from 0 to 65% and appropriateness of ward antibiotics from 48% to 84.7%. Our aim of the study was to evaluate the prescribing from there onwards and to evaluate the adherence to prescribing protocols for a three years time period (May 2002 until April 2005).

4.1 Patient demographics

There was no significant difference between patient demographics within each group. The only concern was a small group of patients in group – II which was a census of the whole population over the period. This period provided an opportunity to identify the impact of an external intervention lacking local support.

4.2 Diagnosis

Overall, the general population has a 7% risk of appendicitis. The risk is higher in males (8.6%) than females (6.7%). The incidence of appendicitis peaks between the ages of 10 and 30 years.[74] In our study the removal of the appendix was found to be slightly more prevalent in males (53.6 - 55%) than in females (44.8 – 46.4%), which was consistent with Reynolds[74] findings and other studies.[75] Appendicitis is the most common surgical emergency in children, yet its diagnosis continues to challenge clinicians. The diagnosis of appendicitis subsequently found to be normal in this study was 5.6 - 12.3% across the three groups (Table 3.4), which is similar to rates reported in other studies of 5 - 25%.[76]

Misdiagnosing acute appendicitis as gastroenteritis is particularly apparent. In a child with vomiting and diarrhoea, acute appendicitis should always be considered if lower abdominal pain is severe, predates the diarrhoea, and/or is accompanied by abdominal tenderness. In the United Kingdom, delay in diagnosis is the most common reason for complications of appendicitis resulting in litigation. The diagnosis of acute appendicitis in children still remains heavily reliant on clinical acumen. The temptation with modern technology is to bypass the detailed clinical assessment of the child with acute abdominal pain. The importance of "active observation" in which the child with abdominal pain is deliberately and regularly reassessed by the surgeon for signs of acute appendicitis cannot be overstated. This approach was championed by Peter Jones in Aberdeen, and its validity is underlined by a recent report of a 6-year prospective study from this same centre, which documented a normal appendectomy rate of 2.6%, no mortality and an overall surgical morbidity rate of 6%. Regular and experienced clinical assessment is even more important in the diagnosis of acute appendicitis in small children.[77]

The preschool child is especially prone to complicated appendicitis and is much more likely to present with appendiceal perforation or an appendix mass. Non-specific symptoms, poorly localised signs, and prior antibiotic treatment for presumed infection elsewhere explain some of the difficulties in diagnosis in this age group.[77] The perforation rate in children less than 8 years old is twice that in children over the age of 8. The perforation rate in pre-school children can be as high as 83%.[74] Delays in operative intervention have classically been felt to increase complications. The mortality and morbidity of removing a normal appendix are 0.14% and 4.6%. These rise to 0.24% and 6.1% for acute appendicitis and to 1.7% and 19% for perforated cases. Delayed appendectomies of greater than 72 hours from presentation can have serious effects with a reported perforation rate of 90% and major complication rate of 60%.[78]

4.3 Theatre antibiotics

Nine different antibiotics regimen were prescribed for prophylaxis pre-surgically in Group-I (Table 3.5), followed by three in Group-II (Table 3.6) and ten in Group-III (Table 3.7). There were 6/9 antibiotic regimens in Group-I which were deemed inappropriate as they were not recommended by the guidelines for surgical prophylaxis. In Group-II 2/3 and 8/10 antibiotics regimens in Group-III were deemed inappropriate on the same basis (Table 3.5, 3.6, & 3.7). Some 59/76, 9/18 and 59/78 patients were prescribed Timentin® inappropriately since it is a broad spectrum antibiotic and not the agent of choice for prophylaxis for non-perforated appendicectomies according to hospital guidelines (Table 3.9). Unlike the study by Mallik[1] where 59/102 (57.8%) patients were prescribed third generation cephalosporins as prophylactic antibiotics in the test-1 group, one patient in Group-I and only two patients in Group - III were prescribed inappropriate third generation prophylactic antibiotics. This is a clear improvement over pre-2002 prescribing previously reported.

According to the hospital guidelines all patients undergoing non-perforated appendectomies should be given a single dose of prophylactic antibiotic/s. There were nine, one and two patients in the three groups not given prophylaxis and these were deemed inappropriate (Table 3.8). The number has decreased over the course of study period, probably with increased awareness. Hence underutilization of antimicrobial prophylaxis in these procedures occurred at a low level. The literature supports the American Academy of Pediatrics' recommendation for surgical prophylaxis in these procedures. In one study, there was 64% less morbidity in children who received perioperative antibiotics for otolaryngology procedures compared with those who did not, as judged by the amount of time to resumption of normal diet and pain analog scores.[79] Several trials have shown that prophylactic antibiotics can significantly reduce the number of postoperative infective complication in non-perforated appendicitis compared with placebo.[17, 19-21]

None of the patients was identified in any of the three groups to be on more that one prophylactic dose of antibiotic/s, which was consistent with Mallik's[1] findings. This is in contrast to a study in an Italian hospital where the average duration of antibiotic administration was 3.9 days in 42.2% of the patients undergoing

appendectomy.[36] Continuation of antimicrobials used for surgical prophylaxis is commonplace among many surgical specialities. Sixty-two percent of pediatric patients who underwent orthopaedic surgery continued to receive antibiotics postoperatively for longer than 48 hours without documentation of infections.[80] Despite numerous adult studies that have indicated that 24 hours of antibiotic prophylaxis for cardiothoracic surgery is effective in preventing postoperative infections,[81, 82] a survey of US pediatric cardiothoracic surgery programs reported administration of prophylaxis for at least 2 days in 68% of the centres with no indication of any benefit associated with the longer duration of surgical prophylaxis.[79]

A study by Mui et al. was done to determine the optimum duration of prophylactic antibiotics in acute non-perforated appendicitis. Out of 269 patients, 92 patients received a single dose of preoperative antibiotics (group A), 94 patients received three doses (group B) and 83 patients received a five day perioperative antibiotic regime (group C). Six patients in group A, six patients in group B and three patients in group C had wound infections within the 30-day postoperative follow-up period, which were not significantly different. Therefore it was concluded that a single dose of prophylactic antibiotics was adequate for prevention of wound infection in patients with non-perforated appendicitis.[34]

The theatre drug dose accuracy was also high in this study ranging from 89.1 - 96.3% (Table 3.10) between the three groups with no significant difference ($p>0.05$) and was consistent with Mallik's findings.[1] In a cross-sectional retrospective study, of 54 cases of colorectal surgical procedures for which antibiotics were administered for prophylaxis, 44 (81.5%) cases were considered to have inappropriate dosing exceeding the stipulated duration of 24 hours. In the same study patients undergoing cholecystectomy and inguinal hernia repair, 50 (51.6%) and 83 (31.1%) cases, respectively, had inappropriately prolonged antibiotic prophylaxis exceeding a single dose. The direct cost attributed to inappropriate administration for the time period was calculated to be US $ 12,057.[83]

There was only one patient identified in Group-III on an inappropriate route of administration (Table 3.11), giving almost 100% accuracy in terms of route of administration with no significant difference ($p>0.05$) between the three groups. The stated timing of administration for prophylactic antibiotic/s administration were

appropriate ranging between 95.4 - 100% (Table 3.12) with no significant difference ($p>0.05$). Hence the timing of administration was well managed.

There was a significant reduction between Groups I and III ($p<0.05$) in the number of patients on an appropriate choice of antibiotics for prophylaxis (Table 3.8) following the change in guidelines in July 2004. This clearly shows that the intervention did not have a full impact on the prescribing. The level of pre-operative non-recommended antibiotic/s combinations prescribed has been increasing after the change in prescribing guidelines in July 2004 (Fig 3.2). The administration of appropriate antibiotic regimes was significantly increased after a multifaceted intervention by Mallik in December 2001.[1] The prescribing appropriateness has been gradually falling after the follow-up period evaluated by Mallik which occurred for five months.[1]

A retrospective study by Martelli and Mattioli[36] showed the antibiotic prophylaxis given for appendectomies was appropriate in 5(15.2%) of the 33 patients who received antibiotics. These five patients were treated with a single dose of antibiotic at the induction of anaesthesia. In the remaining 21 patients (63.6%) who received antibiotics, in the absence of any compelling cause the antibiotic therapy was inappropriate: in 14 patients (42.4%) the average duration of antibiotic administration after surgery was 3.9 days; in seven patients (21.2%) the antibiotic treatment was started ≥ 1 day before surgery; in five patients (15.2%) the antibiotics used was piperacillin which was not recommended in the guidelines; in three patients (9.1%) a combination of two antibiotics was used .

The present study has demonstrated that, although the adherence to separate aspects of prophylaxis was favourable, adherence to all aspects of the guidelines for surgical prophylaxis was not attained. It is noteworthy that the criteria for assessment of adherence were strict, and that the guidelines recommended a prudent use of antibiotics. Timentin® was identified as the antibiotic, which was used inappropriately for prophylaxis for all the three groups. The most probable reason appears to be the ease of administration (single antibiotic), broad spectrum of activity and its recommended use in perforated appendices.

In contrast to the present study, most studies in other countries have assessed the quality of prophylaxis according to an international or a national standard. Only a few have studied adherence to local guidelines.[84-86] One report from a tertiary teaching hospital in Brazil[84] showed that in only 3% of the antibiotic prophylaxis were given according to hospital guidelines, in terms of antibiotic choice, duration, dose and timing. In the present study, concordance with local guidelines on duration, dose and timing for prophylaxis was higher than 90%. In the study by Finkelstein et al.[86] performed in Israel, adherence to duration and timing was less than in the present study. In the study by Vaisbrud et al.[85] also performed in Israel, the adherence was almost similar to this study, especially for timing of the first dose.

A questionnaire for perioperative antibiotic prophylaxis in selected Spanish hospitals showed that, of all the 84% surgical procedures where PAP was used, 77% of these procedures where according to locally developed guidelines. It once again showed that compliance was higher with locally developed guidelines, a situation found in 77% of the selected Spanish hospitals.[87]

In past decades, many papers have described optimal prophylaxis, and guidelines for surgical prophylaxis have been developed. Despite the availability of these guidelines, recent studies assessing the current practice of prophylaxis throughout the world have shown that over-consumption of antimicrobial drugs and inappropriate timing remains a problem in surgical prophylaxis.[29, 41, 43, 44, 46, 88-90] In a recent multicentre study of surgical antimicrobial prophylaxis in the Netherlands by van Kasteren et al.[91], it was found that the most important barriers to local guideline adherence were lack of awareness due to ineffective distribution of the most recent version of the guidelines, lack of agreement by the surgeons with the local guidelines, and environmental factors, such as organizational constraints in the surgical suite and in the ward

4.4 Ward antibiotics

Prescribing of ward antibiotics was a clinical decision taken by the surgeon based on the morphology of the appendix. According to the in-hospital guidelines all patients with inflamed appendix even with a non-perforated appendix were to be given two doses of Timentin® post-surgically. In the case of peritoneal soiling detected post-surgically, Timentin® was to be prescribed four times daily for up to five days. There were 221/250 (88.4%), 25/28 (89.3%) and 110/130 (84.6%) patients given ward treatment with antibiotics in Group - I, II and III (Table 3.13). Where no ward antibiotic treatment was given this was considered appropriate. Nine different antibiotic regimes were prescribed post-surgically for treatment in Group - I, most (210/221 patients) were prescribed Timentin® for ward treatment, which was the recommended in the guidelines for treatment. In group - II, Timentin® was prescribed for 24/25 patients given ward treatment. 102/110 patients were prescribed Timentin® in group - III (Table 3.14).

Therefore the appropriateness level in terms of antibiotic choice for ward treatment was high in the range of 91 - 92.7% (Table 3.15) with no significant difference between the groups ($p > 0.05$). This was slightly higher than the 85% level of appropriateness of ward antibiotic choice for the five month follow-up period (till April 2002) reported by Mallik.[1] The use of unnecessary ward antibiotics doses administered shows a downward trend from 29.9% to 16.4% (Table 3.17) with significant difference between Groups - I and III ($p<0.05$). This may be explained by an increase use of Timentin® in Group – III as Timentin® prophylaxis may have given increased confidence to surgeons regarding lack of subsequent infections (Table 3.9). The level for the appropriateness for the time of administration of ward antibiotics has been continually high ranging from 84.6% to 92.7% (Table 3.18) with no significant difference ($p>0.05$) within the groups. These relate to information taken from patient charts rather than observation.

The implication of over- and underutilization of surgical antimicrobial prophylaxis should be considered. The costs for overutilization of surgical prophylaxis include unnecessary drug utilization and its attendant preventable adverse events and the potential for increased resistance of organisms that are exposed to environmental pressure with antimicrobials. Underutilization of surgical prophylaxis ultimately may increase the rate of surgical site infections and subsequent associated costs such as increased hospital lengths of stay, pharmacy costs for antibiotics, diagnostics laboratory tests, and increased wound care needs.[51]

4.5 Total appropriateness

The total appropriateness of the prescribing was a combination of the following factors: (i) the surgeons prescribed an appropriate theatre antibiotic regime (ii) an appropriate post operative ward antibiotic regime (iii) an appropriate combined theatre and ward antibiotic dosage. No prophylaxis was considered inappropriate, where as no treatment was considered appropriate. In Group-I there were 115/250 (54.7%) patients who achieved total appropriateness followed by 13/28 (54.2%) patients in Group-II and 34/130 (31.5%) patients in Group - III (Table 3.22). There was a significant difference between Groups-I and III. The total appropriateness showed a declining trend over the three year survey period.

4.6 Interventions

Interventional strategies that have been shown to improve antibiotic prescribing patterns include antibiotic monitoring systems, hospital formularies and clinical guidelines to limit the availability of antibiotics to prescribers. Changing prescribers' attitude through participation in continuing medical education has been found to reduce the misuse and overuse of antibiotics.[92]

Interventions fall into two categories, educational or persuasive, and restrictive or coercive. Educational interventions for example, pharmacy bulletins and newsletters, lectures, conferences, and handbooks are preferred, but it is perceived that, alone, they are of limited value in terms of facilitating judicious antibiotic usage. Moreover, without constant reinforcement to maintain their impact will be only temporary.[93] Educational interventions are more likely to result in improving prescribing when they are carried out by senior opinion leaders, involving

participants in interactive learning sessions, when prescribers are given feed back about their own practices, and when there are repeated contacts with them.[92] Restrictive interventions especially to control antibiotic usage have been shown to be more effective than educational strategies and their impact is more enduring. Bamberger and Dahl compared the impact of voluntary restriction of selected antibiotics with that of a strict control policy. When restriction was voluntary, only 24.2% of the usage of these drugs was in compliance with local guidelines, compared with 85.4% when restriction was enforced. Nonetheless, restrictive interventions are only effective if they are enforced, and enforcement may lead to adversarial relations between prescriber and healthcare workers (usually pharmacists).[94]

On the other hand multifaceted interventions have been shown to be more likely to improve performance than single interventions with ongoing follow-up.[95, 96] A defining characteristic of the follow-up programme is that it informs the physician of the implications of his/her antibiotic use rather than prescribing or controlling physician prescribing behaviour. Interventions that control prescribing behaviour are likely to raise physician objections on the grounds of restricting therapeutic freedom; this feature of the follow-up programme may well explain the acceptance of the programme by physicians and increased profitability associated with prophylactic antibiotic use. The impact of the follow-up programme is not restricted to the consumption and costs of prophylactic antibiotics. A more appropriate use of antibiotics is also likely to have a beneficial effect on hospital ecology and clinical outcomes.[97] A study by Awad at el. found that multifaceted interventions involving audit and feedback combined with either academic detailing or seminars appeared more effective than audit and feedback alone in changing prescribing practices of antibiotics.[92]

A randomised controlled trial of academic detailing by Avorn and Soumerai[98], indicated that face-to-face education of the practising physician was an effective means of reducing less than optimal prescribing decisions and the differences in prescribing remained highly significant, with no sign of diminution in effect nine months after the start of the office-based intervention.

Restrictions are sometimes enforced without creating an awareness of the problem being addressed and this may lead to unexpected consequences. For example, restriction of one antibiotic may decrease its use, the use of other antibiotic

in the same therapeutic class may increase.[99] Shenfield et al.[100] reported an unintended increase in the use of potent codeine phosphate for mild pain when the right to prescribe detropropoxyphene was restricted in one hospital. Reilly et al.[101] reported an increased use of gentamicin after cephalosporins were restricted. Recco et al.[102] showed a dramatic reduction in the use of restricted antibiotics. A corresponding rise in some unrestricted antibiotic was noted. When cefotetan was withdrawn from the theatre in July 2004 following the change in guidelines, it was expected that the prescribing for prophylaxis should have shifted from cefotetan to combination of cephazolin and metronidazole. But instead usage shifted more towards Timentin. One possible reason can be lack of awareness for the changed guidelines, as intervention carried in hospital did not have the desired impact. In a review by Cabana et al.[103] 46 surveys measured the lack of awareness as barrier to adherence to guidelines. The percentage of respondents identifying lack of awareness as a barrier was as high as 84% and as low as 1% and with a median of 54.5%. In 36% of the 46 surveys, at least 10% of the respondents were not aware of the guidelines.

The intervention carried out at PMH in May 2004, where the hospital did not make change to the prescribing guidelines until the stock of cefotetan was near exhausted and second intervention in July 2004, which was not a complete multifaceted intervention to prescribing doctors lacked the same impact as that performed by Mallik[1] in December 2001. A multifaceted intervention with academic detailing and regular follow-up carried out by Mallik[1] appears to more effective than those carried in May 2004 and July 2004 at PMH. Ideally pharmacists should be involved in pursuing the objective through continually monitoring of prescribing, providing information to new doctors and nurses and assisting in the process of drug review this include improved communication with all newly arrived surgical and other related staff, and providing them with information about antibiotic polices.[104]

4.7 Limitation and Areas of future research

The randomised controlled trial is considered the gold standard for providing a high level of scientific validity. The methodology used for a randomised controlled trial is not directly applicable to drug use studies involving intervention since the intervention cannot usually be contained or blinded to one group of prescribers. A retrospective study uses existing data that have been recorded for reasons other than research. The weakness in this design is that, it relies on accuracy of written record or recall of individuals and the results can be hypothesis generating.

As the study did not collect data on patterns of antimicrobial resistance, rates of adverse drug events, morbidity and mortality rates, the question of the cost effectiveness or cost benefit of the follow-up programme in stimulating a more appropriate use of prophylactic antibiotics is an important avenue for further research.

5 Conclusion

In conclusion, inappropriate antibiotic use for prophylaxis in appendectomy procedures was found to be common. The two interventions (in May 2004 and July 2004) carried in the hospital did not have desired impact on prescribing for prophylaxis. This would indicate that issuing of changed guidelines and withdrawal of the drug being replaced did not positively influence appropriate prescribing. Timentin® has been identified as being used inappropriately for prophylaxis. To facilitate compliance with the protocol, more efficient control measures should be developed and implemented, and prospective and continuous monitoring of antibiotic use is required. Attempts to highlight discrepancies through regular audits in conjunction with an educational program can lead to appropriate action to improve the standards of practice in antibiotic prescribing for prophylaxis.

For further improvement, anaesthesia protocols could be configured to add drug administration including prophylaxis for routine surgical procedures according to the guidelines. Compared to standard operating procedures, the suggested antibiotics could be represented in the protocol in a defined colour, playing the role of an optical reminder in the anaesthesia record in the hope of leading to a more appropriate use of antibiotics in surgical procedures. Apart from the widespread proactive methods outlined above, respective health authorities should implement tougher measures to halt inappropriate prescribing patterns associated with injudicious use of antibiotics.

Continuous surveillance of antibiotic use and resistance levels is warranted to maintain efficacy and safety of antibiotic treatment. Therefore it's a shared responsibility of the hospital including clinical pharmacists to maintain continuos compliance with the local guidelines.

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Appendix

Presentation

A Retrospective Study to Assess Antibiotic Prescribing for Pediatric Appendectomy Procedures

MA Abid[1], VB Sunderland[1], MJ Roberts[2], and L Stafford[1]

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[2] Department of Pharmacy, Princess Margaret Hospital for Children, WA;

This study was presented at the following conference:
Australasian Pharmaceutical Science Association, Melbourne, Australia, 4-7th Dec 2005.

Objective: To retrospectively evaluate antibiotic use in paediatric appendectomy procedures following a prescribing intervention in December 2001.

Methodology: The analysis was conducted in patients <18 years old undergoing non-perforated appendectomy procedures at Princess Margaret Hospital for Children, WA. Data collection and analysis were divided into three parts. Part I involved patients from May 2002 to April 2004 (period following the post-intervention follow up conducted from December 2001-April 2002 by Mallik et al.[1]). In May 2004, Western Australian Therapeutic Advisory Group (WATAG) advisory note recommended a change from the use of Cefotetan for surgical prophylaxis to Cephazolin plus metronidazole. Part II of the study involved patients between May 2004 (when the WATAG note was released) and June 2004 (when the hospital enforced the change); while part III involved patients from July 2004 to April 2005. Demographic, clinical and antibiotic prescribing data were collected.

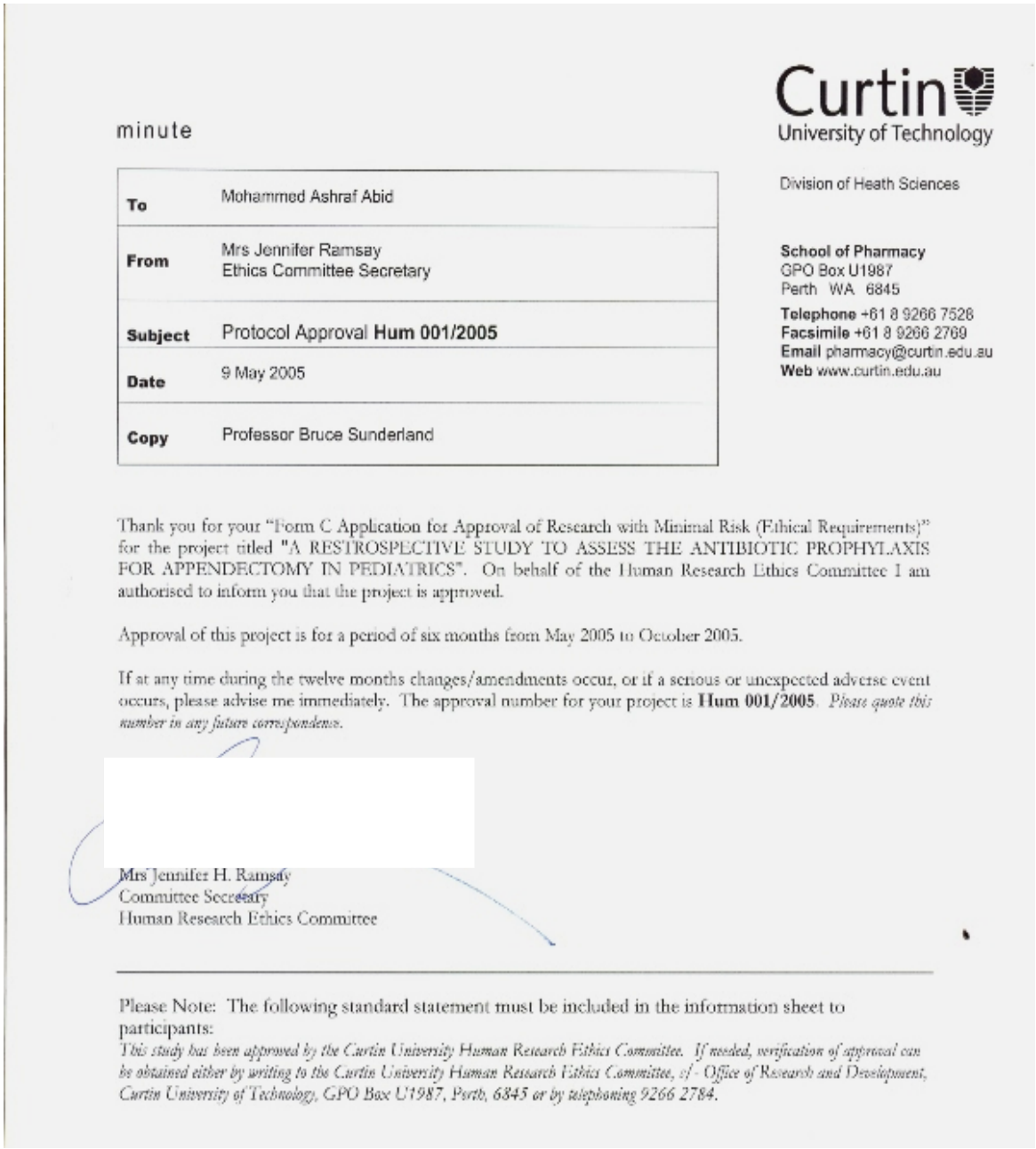
Results: 408 patient records were evaluated across the three parts of the study. An appropriate prophylactic drug regimen was prescribed in 68.5%, 66.7% and 39.8% of patients in parts I, II and III respectively, with a significant difference in appropriate drug choice between parts I and III ($p < 0.05$). There was no significant difference

between the parts with respect to appropriate prophylactic drug dose ($p>0.05$). Appropriateness rates for antibiotic choices for ward treatment were high at 91.0%, 92.0% and 92.7%, with no significant differences. There was a significant difference between the three parts regarding the number of doses for ward treatment, with inappropriateness rates of 29.9%, 40% and 16.4% ($p<0.05$). The overall appropriateness rates (drug choice plus dose in theatre and ward) across the study were 54.7%, 54.2% and 31.5%, with a significant difference ($p <0.05$) between parts I, and III.

Conclusion: Issues have been identified with the inappropriate prescribing of Ticarcillin with Clavulanic acid for prophylaxis, with potential implication for increased bacterial resistance. Further prescribing interventions may be required to improve compliance with hospital guidelines.

1. Mallik A, Sunderland VB, Roberts MJ, Turner S, Lilley BJ. Impact of an Educational Program on Antibiotic use in Paediatric Appendectomy Procedures. Journal of Pharmacy Practice and Research 2005;35(1):21-4.

Curtin University of Technology Human Research Ethics Committee Approval Letter



minute

Curtin
University of Technology

To	Mohammed Ashraf Abid
From	Mrs Jennifer Ramsay Ethics Committee Secretary
Subject	Protocol Approval **Hum 001/2005**
Date	9 May 2005
Copy	Professor Bruce Sunderland

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Thank you for your "Form C Application for Approval of Research with Minimal Risk (Ethical Requirements)" for the project titled "A RESTROSPECTIVE STUDY TO ASSESS THE ANTIBIOTIC PROPHYLAXIS FOR APPENDECTOMY IN PEDIATRICS". On behalf of the Human Research Ethics Committee I am authorised to inform you that the project is approved.

Approval of this project is for a period of six months from May 2005 to October 2005.

If at any time during the twelve months changes/amendments occur, or if a serious or unexpected adverse event occurs, please advise me immediately. The approval number for your project is **Hum 001/2005**. *Please quote this number in any future correspondence.*

Mrs Jennifer H. Ramsay
Committee Secretary
Human Research Ethics Committee

Please Note: The following standard statement must be included in the information sheet to participants:
This study has been approved by the Curtin University Human Research Ethics Committee. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University of Technology, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784.