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Original article

Prescribing regimens of prophylactic antibiotic used in different surgeries

Palikhe N[1], Pokharel A[2]
[1]Lecturer, Dept of Pharmacology, KMC, [2]Lecturer, Dept. of Pharmacology, KUMS

Abstract

Aim and Objective: The main objective was to study the different types of regimen of prophylactic antibiotic in different surgeries in hospitals of western region, particularly, Pokhara valley and the hospitals were Western Regional Hospital (WRH) and Manipal Teaching Hospital (MTH).

Methodology: A descriptive, quantitative, retrospective study were used to evaluate the patients' undergone surgery in the year 2059 BS (15th April 2002 – 14th April 2003). The total of 950 patients, 450 from WRH and 500 from MTH were taken from the medical record for the study. Data about different types of prophylactic antibiotic regimen was collected.

Conclusion: The most common surgery in MTH is dilatation and curettage (D and C) and in WRH is caesarean section (CS). In both hospitals Ampicillin+Cloxacillin was the most commonly used regimen, 12.4% in WRH and 34% in MTH. In WRH ciprofloxacin and cefotaxime was also used by 12.4%. Ciprofloxacin and gentamicin (12%) combination was the third commonly used regimen in WRH where as ciprofloxacin (28.4%), Ampi+Cloxa and gentamicin (22.4%) in MTH.

Key words: Antibiotic prophylaxis, Surgery

The reduction of postoperative wound infection during the past 25 years has been attributed to improvements in aseptic and surgical techniques and to the use of antibiotics as prophylactic agents[1]. First generation cephalosporins are considered the most adequate drugs for the majority of the procedures[2-4]. In spite of extensive knowledge about the effectiveness of antibiotic prophylaxis; administrative regimens are often inappropriate in practice[5-8].

Administration of prophylaxis should be done within three hours after the start of the operation otherwise it significantly reduces its effectiveness but for maximum effect, it should be given just before or just after the start of the operation[9]. Prophylaxis should be started preoperatively in most circumstances, ideally with in 30 minutes of the induction of anesthesia. However, there may be situation where overriding factors alter the normal timing of administration. For example, during a cesarean section prophylaxis should be delayed until cord is clamped in order to prevent the drug reaching the neonate. The case of only those people who doesn't have a surgical history in past 1 month and who have no infection prior to surgery is taken. All these criterias' developed in reference to international guidelines for considering antibiotic as a prophylactic use to conduct the study.

In Nepal, there is no proper guideline for antibiotic prophylaxis in surgery. The practice is generally based on the influence of senior doctors, with the reference of books, and journals. The practice of use of prophylactic antibiotic in different surgeries is now becoming mandatory because of increased chance of hospital-acquired infection and also for prevention of postoperative infectious morbidity. But the regimen for prophylactic antibiotic is different in hospitals. Higher generation of cephalosporins and combination of two antibiotics are found to be prescribed in hospitals in surgeries. The inappropriate use of antimicrobial agents has resulted not only in unnecessary expense or overuses of antimicrobial agents but also in the development of drug-resistant bacteria. Ideally, an appropriate spectrum of prophylactic antimicrobial agents for surgery should be saturated in the body fluids and at the surgical site during the operation but they should be terminated as soon as possible to avoid the occurrence of resistant organisms. So, this study aims to determine the practice of prophylactic antibiotic in different surgeries in one region of Nepal.

Correspondence
Ms Nami Palikhe
Dept. of Pharmacology
Kathmandu Medical College, P.O. Box: 21266
Email:p_namu@hotmail.com

Nowadays there is a social movement toward quality in all-human activities, including medical activity. It is important that health professionals participate in studies and implementation of quality programs, including assessments of personal practice patterns. Certainly, the use of antibiotic as a prophylactic deserves to be periodically evaluated. In this procedure, the observation of the guideline would result in cost reduction, and moreover, lower adverse reaction risks, infection morbidity reduction, length of stay reduction, and microbial resistance reduction would be expected.

Materials and methods

The prescribing pattern of antibiotic prophylaxis for different regimen was investigated in different surgeries of major hospitals in Pokhara valley. A descriptive, quantitative, retrospective study were used to evaluate the patients' undergone surgery in the year 2059 BS (15^{th} April 2002 – 14^{th} April 2003). Medical records of in- patients of age fall between 18 - 65 years having no surgical history in past 1 month, absence of infection prior to surgery and patient undergoing gastrointestinal surgery, gynecological and obstetrics surgery, ENT surgery, biliary tract surgery, urological surgery etc where antibiotic prophylaxis is recommended by the literatures were reviewed retrospectively. Hospital numbers of all the patients' who had undergone surgery in the 2059 BS were noted from the record book of medical record section. Out of all the surgery cases in one year of both hospitals, 500 from MTH and 450 from WRH were collected by the systematic random sampling method. Data about patient, surgery and antibiotic prophylaxis were collected.

Results

1. Common Surgery in two hospital

Table 1: Common Surgeries in WRH and MTH

S. No.	Type of Surgery	WRH, n (%)	MTH, n (%)
		Total	Total
1.	CS	140 (31.1)	69 (13.8)
2.	Cholecystectomy	110 (24.4)	36 (7.2)
3.	Hysterectomy	68 (15.1)	105 (21.0)
4.	D and C	40 (8.9)	108 (21.6)
5.	Herniorraphy	32 (7.1)	37 (7.4)
6.	Prostectomy	20 (4.4)	16 (3.2)
7.	Others	40 (8.9)	129 (25.8)
Total		450 (100)	500 (100)

2. Cholecystectomy

The most commonly used antibiotic regimen was Ampi/Genta (38.2%) in WRH and Ampi+Cloxa with Genta (36.1%) in MTH. Penicillin group of antibiotics together with gentamicin was the preferred regimen in WRH. Quinolone group of antibiotic i.e. ciprofloxacin was also used in WRH together with gentamicin. In MTH, penicillin group of antibiotics (for example, Ampi+Cloxa) and cephalosporins (i.e. Cefuroxime, second generation cephalosporins) and ciprofloxacin were mainly used as prophylaxis for cholecystectomy.

Table 2: Regimen of Antibiotic used for Prophylaxis in Cholecystectomy

S. NO.	WRH (N=110)*		MTH (N=36)**	
	Antibiotic/s	n (%)	Antibiotic/s	n (%)
1.	Ampi / Genta	42 (38.2)	Ampi + Cloxa / Genta	13 (36.1)
2.	Ampi + Cloxa	32 (29.1)	Ampi + Cloxa	10 (27.8)
3.	Ampi + Sulbactum	16 (14.5)	Cefuroxime	8 (22.2)
4.	Ampi + Cloxa / Genta	14 (12.7)	Cipro	5 (13.9)
5.	Cipro / Genta	6 (5.5)		

*Out of 110, in 66 cases Metro was used along with respective regimen.

** Out of 36, in 20 cases Metro was used along with respective regimen.

Ampi- Ampicillin, Genta- Gentamicin, Cloxa- Cloxacillin, Cipro- Ciprofloxacin.

3. Dilatation and Curettage (D and C)

The most commonly used antibiotic for prophylaxis in dilation and curettage (D and C) was ciprofloxacin by 50% and 56.5% in WRH and MTH respectively.

In WRH amoxicillin (20%) and in MTH Ampi+Cloxa (28.7%) was the second mostly used antibiotic for prophylaxis.

Table 3: Regimen of Antibiotic used for Prophylaxis in D and C

S. NO.	WRH (N=40)*		MTH (N=108)**	
	Antibiotic/s	**n (%)**	**Antibiotic/s**	**n (%)**
1.	Cipro	20 (50)	Cipro	61 (56.5)
2.	Amoxy	8 (20)	Ampi + Cloxa	31 (28.7)
3.	Ampi + Cloxa	4 (10)	Ampi	10 (9.25)
4.	Cefotaxime	4 (10)	Cefotaxime	3 (2.8)
5.	Cipro / Amikacin	2 (5)	Ampi + Cloxa / Genta	3 (2.8)
6.	Ampi	2 (5)		

* Out of 40, in 32 cases Metro was used along with respective regimen.
**Out of 108, in 36 cases Metro was used along with respective regimen.
Amoxy –Amoxycillin Ampi-Ampicillin, Genta- Gentamicin, Cloxa---Cloxacillin, Cipro—Ciprofloxacin

4. Caesarean Section (CS)

In WRH Cipro with Cefotaxime (31.4%) was mostly used regimen, whereas as in MTH, it was Ampi+Cloxa with Genta (43.5%). Cefotaxim with Genta (25.7%) and Ampi+Cloxa (31.9%) were the second mostly used regimen in WRH and MTH respectively.

The prophylactic antibiotic regimens in both hospitals include penicillin and cephalosporin and quinolone groups.

Table 4: Regimen of Antibiotic used for Prophylaxis in CS

S. NO.	WRH (N=140)*		MTH (N=69)**	
	Antibiotic/s	n (%)	Antibiotic/s	n (%)
1.	Cipro / Cefotaxim	44 (31.4)	Ampi + Cloxa / Genta	30 (43.5)
2.	Cefotaxime / Genta	36 (25.7)	Ampi + Cloxa	22 (31.9)
3.	Cefotaxime	24 (17.5)	Ampi / Genta	10 (14.5)
4.	Cipro / Genta	22 (15.7)	Ceftazidime	5 (7.2)
5.	Ampi + Cloxa	14 (10)	Cefotaxime / Genta	2 (2.9)

*Out of 140, in 86 cases Metro was used along with respective regimen.
**Out of 69, in 58 cases Metro was used along with respective regimen.
Ampi- Ampicillin, Genta- Gentamicin, Cloxa- Cloxacillin, Cipro- Ciprofloxacin.

5. Hysterectomy

In WRH Cipro with Cefuroxime (17.6%), Cipro with Cefotaxime (17.6%) Cefotaxime (17.6%) alone were used mostly whereas in MTH, Cipro (60%) was mostly used for the prophylaxis. Ampi+Cloxa with Genta was second mostly used antibiotic for prophylaxis.

Table 5: Regimen of Antibiotic used for Prophylaxis in Hysterectomy

S. NO.	WRH (N=68)*		MTH (N=105)**	
	Antibiotic/s	n (%)	Antibiotic/s	n (%)
1.	Cipro / Cefuroxime	12 (17.6)	Cipro	63 (60)
2.	Cipro / Cefotaxime	12 (17.6)	Ampi + Cloxa / Genta	24 (22.9)
3.	Cefotaxime	12 (17.6)	Ampi + Cloxa	8 (7.6)
4.	Cipro / Genta	10 (14.7)	Amikacin / Genta	7 (6.7)
5.	Cipro	8 (11.8)	Cefotaxime	3 (2.8)
6.	Ampi + Cloxa	6 (8.9)		
7.	Cefotaxim / Genta	4 (5.9)		
8.	Cipro / Amikacin	4 (5.9)		

* In all cases, 68 cases in WRH Metro was used along with respective regimen.
**Out of 105, in 99 cases Metro was used along with respective regimen.
Ampi- Ampicillin, Genta- Gentamicin, Cloxa- Cloxacillin, Cipro- Ciprofloxacin.

6. Herniorrhaphy

The commonly used regimen in WRH was Ampi + Cloxa with Genta (56.3%) whereas in MTH it was only Ampi + Cloxa (70.3%). Cipro with Genta (25%) in WRH and Ampi+ Cloxa with Genta (21.6%) in MTH were the second mostly used regimen.

Table 6: Regimen of Antibiotic used for Prophylaxis in Herniorrhaphy

S. NO.	WRH (N=32)*		MTH (N=37)**	
	Antibiotic/s	**n (%)**	**Antibiotic/s**	**n (%)**
1.	Ampi + Cloxa /Genta	18 (56.3)	Ampi + Cloxa	26 (70.3)
2.	Cipro/Genta	8 (25)	Ampi + Cloxa / Genta	8 (21.6)
3.	Cipro	6 (18.7)	Ampi	3 (8.1)

*Out of 32, in 20 cases Metro was used along with respective regimen.
** Out of 37, in 10 cases Metro was used along with respective regimen.
Ampi- Ampicillin, Genta- Gentamicin, Cloxa- Cloxacillin, Cipro- Ciprofloxacin

7. Prostectomy

In WRH combination of four antibiotics were mostly used, that was, Ampi+Cloxa with Genta and Cefotaxim in 50% of cases. Whereas in MTH combination of Ampi+Cloxa with Genta (62.5%) were mostly used. In WRH Ampi with Genta (20%) and in MTH Cipro with Genta (18.8%) were the second mostly used regimens.

Table 7: Regimen of Antibiotic used for Prophylaxis in Prostectomy

S. NO.	WRH (N=20)*		MTH (N=16)**	
	Antibiotic/s	n (%)	Antibiotic/s	n (%)
1.	Ampi+Cloxa/Genta/Cefotaxime	10 (50)	Ampi + Cloxa / Genta	10 (62.5)
2.	Ampi / Genta	4 (20)	Cipro / Genta	3 (18.8)
3.	Cipro / Genta	4 (20)	Ampi + Cloxa	2 (12.5)
4.	Ampi+Cloxa/Genta/Amikacin	2 (10)	Amikacin	1 (6.2)

*Out of 20, in 4 cases Metro was used along with respective regimen.
**Out of 16, in 5 cases Metro was used along with respective regimen.
Ampi -Ampicillin, Genta- Gentamicin, Cloxa---Cloxacillin, Cipro—Ciprofloxacin

8. Other surgeries

The surgeries other than mentioned earlier were included in the category of "Others". In WRH mostly used regimen was cipro along with cefotaxime and genta (35%), followed by cipro alone (25%) and Ampi+Sulbactum.(20%). For MTH others were Circumscision, Hymenectomy, Fistulectomy, Oesophagoscopy, Urethrolithotomy, Laminectomy, Laparotomy, Omentoplasty.

Among others there were also Tympanoplasty (N=24) and Haemorrhoidectomy (N=32), but these surgeries were not found in WRH. Because of this reason, these surgeries were kept in category of others, and the individual analyses of the regimen used were identified for MTH.

Table 8.1: Regimen of Antibiotic used for Prophylaxis in others[#] in WRH

S. NO.	WRH (N=40)*	
	Antibiotic/s	n (%)
1.	Cipro/ Cefotaxime/ Genta	14 (35)
2.	Cipro	10 (25)
3.	Ampi + Sulbactum / Genta	8 (20)
4.	Cipro / Genta	4 (10)
5.	Ampi / Genta	4 (10)

*Out of 40, in 18 cases Metro was used along with respective regimen.
Others in WRH are urethrotomy, cystolithotomy, fistulectomy, laparotomy.
Ampi-Ampicillin, Genta- Gentamicin, Cloxa---Cloxacillin, Cipro—Ciprofloxacin

Table 8.2: Regimen of Antibiotic Prophylaxis in Haemorrhoidectomy in MTH

S. NO.	MTH (N=32)*	
	Antibiotic/s	**n (%)**
1.	Ampi + Cloxa / Genta	15 (46.9)
2.	Ampi+Cloxa	11 (34.3)
3.	Ampi	3 (9.4)
4.	Cipro	2 (6.3)
5.	Amoxy	1 (3.1)

* *Out of 32, in 24 cases Metro was used along with respective regimen.

Table 8.3: Regimen of Antibiotic used for Prophylaxis in Tympanoplasty in MTH

S. NO.	MTH (N=24)*	
	Antibiotic/s	n (%)
1.	Ampi+Cloxa	16 (66.7)
2.	Cipro	6 (25)
3.	Amoxy	2 (8.3)

*No metro was used along with regimens.

Table 8.4: Regimen of Antibiotic used for Prophylaxis in others except Haemorrhoidectomy and Tympanoplasty in MTH

S. NO.	MTH (N=73)*	
	Antibiotic/s	n (%)
1.	Ampi + Cloxa	42 (57.6)
2.	Ampi + Cloxa / Genta	11 (15.1)
3.	Amikacin / Genta	6 (8.2)
4.	Cipro	5 (6.8)
5.	Ampi / Genta	5 (6.8)
6.	Ceftriaxone	4 (5.5)

*Out of 73, in 18 cases Metro was used along with respective regimen.

9. Commonly used regimen

In both hospitals Ampi+Cloxa was the most commonly used regimen, 12.4% in WRH and 34% in MTH. In WRH Cipro/Cefotaxim was also used by 12.4%. Cipro/Genta (12%) combination was the third commonly used regimen in WRH where as Cipro (28.4%) and Ampi+Cloxa/Genta (22.4%) in MTH. The variation in the use of antibiotic regimen was found in WRH compared to MTH. Most of the guidelines preferred first generation of cephalosporin (cefazolin) for the antibiotic prophylactic but in our study penicillin was found to be mainly used in both hospital.

Table 9: Commonly used regimen in two hospitals

S. No.	Regimen WRH	n (%)	Regimen MTH	n (%)
1.	Ampi+Cloxa	56 (12.4)	Ampi+Cloxa	170 (34.0)
2.	Cipro/Cefotaxime	56 (12.4)	Cipro	142 (28.4)
3.	Cipro/Genta	54 (12.0)	Ampi+Cloxa/Genta	112 (22.4)
4.	Ampi+Genta	50 (11.1)		
5.	Cipro	44 (9.8)		

Ampi- Ampicillin, Genta- Gentamicin, Cloxa- Cloxacillin, Cipro- Ciprofloxacin

Discussion

Different guidelines on antibiotic prophylaxis in surgery recommend the prophylaxis for biliary surgery including elective or emergency cholecystectomy[10,11]. American Society of Health System Pharmacists (ASHP)[10] recommends a single dose of cefazolin 1g (as the sodium) administered intravenously at induction of anaesthesia for open procedures in the biliary tract. Western Australian Drugs and Therapeutics Committee recommends a single agent cefotetan 2g IV at the time of induction or metronidazole 500mg IV infusion ending at the time of induction plus at the time of induction cephalothin 2g IV or cefazolin 1g IV or gentamicin 2mg/Kg IV[12]. According to American Family Physician's[11] recommendations for antibiotic prophylaxis for procedures of the biliary tract d

epends on the presence of specific risk factors. In general, prophylaxis for elective cholecystectomy (either open or laparoscopic) may be regarded as optional. Risk factors associated with an increased incidence of bacteria in bile and thus of increased risk for postoperative infection include age over 60 years, disease of the common duct, diagnoses of cholecystitis, presence of jaundice and previous history of biliary tract surgery[13]. In most cases of symptomatic cholelithiasis meeting high-risk criteria, cefazolin is an acceptable agent. Agents with theoretically superior antimicrobial activity have not been shown to produce a lower postoperative

infection rate. But in our study, only 22.2% of cases in MTH utilize the cephalosporins as a prophylactic agent, i.e. cefuroxime. Studies have shown that there was no significant difference in effectiveness of first generation cephalosporins as compared with second and third generations as an antibiotic prophylaxis in reducing the postoperative complications in surgery.

Bacteria isolated from bile during surgery are those most likely to be associated with wound infection. *E.coli, Klebsiella,* and E*nterococcus* are the most likely pathogens in case of indications leading to cholecystectomy. Other gram-negative bacilli, *Streptococci,* and *Staphylococci* are occasionally isolated. Anaerobic bacteria are uncommon, but *Clostridium* is the most common when isolated. A quinolone, such as, ciprofloxacin may also be effective for coverage of gram-negative organisms, although data for context of prophylaxis are not available.

The prophylactic regimen of penicillin and cephalosporins in the hospitals were justified[14]. But the practice of quinolone i.e. Ciprofloxacin was controversial. Ciprofloxacin is excreted in breast milk[15,16]. A pharmacokinetic study in rabbits found milk: plasma ratio of 3.6 for this drug[17]. One brief report did not find a detectable level of ciprofloxacin in the serum of an infant whose mother was taking this drug[16]. One study of 10 women who received 750mg every 12hrly, milk levels of ciprofloxacin ranged from 3.79 mg/L at 2 hr post-dose to 0.2 mg/L at 24 hr[18]. There is one case report of pesudomembranous colitis in infant of a mother who self-medicated with ciprofloxacin for 6 days[19]. Though the American Academy of Pediatrics consider the drug as compatible with breastfeeding because the amount of the drug absorbed by the infants is small, but little is known about the safety of long term use[20]. In one study, there was no statistically significant difference in growth and development between the control group and neonate who received ciprofloxacin[21]. But still ciprofloxacin is regarded as a controversial drug in infant, because of the risk of the joint deformities. In summary, due to the paucity of information, the use of fluoroquinolone antibiotics in breastfeeding mothers requires a risk-vs-benefit assessment.

Ampicillin alone was the mostly recommended prophylactic antibiotic by study[14] . It was also the most commonly used antibiotic for prophylaxis for CS by physician in one study in Thailand and they gave the reasons as ampicillin was perceived to cover organisms in the genitourinary tract and is simple, cheap, readily available, and with very few side effects[22].

The risk of postoperative febrile morbidity is reduced to a comparable extent by broad-spectrum penicillins, such as ampicillin, and cephalosporins[23] . A review of the Cochrane Library by Hopkins L and Smaill F[14] concluded that both ampicillin and first-generation cephalosporins have similar efficacy in reducing postoperative endometritis. There is no evidence that a more broad-spectrum agent produces greater efficacy in the reduction of infectious morbidity following cesarean section. The results indicate that multiple dose regimens do not offer any added benefit when compared with single dose regimens[24-25]. Furthermore, single dose regimens are likely to be less expensive. The advantages of a single dose regimen are obvious and might ensure universal utilization of prophylactic antibiotics for cesarean section, especially in under-resourced countries.

There is an evidence that a less expensive, narrow-spectrum cephalosporins is as effective as more expensive, broader spectrum cephamycins and cephalosporins as prophylaxis for patients[25]. Among cephalosporins, single IV dose of cefazolin and that of cefonicid, both provides a similar degree of prophylaxis against infection[26].

Multiple dose regimens and combinations of antibiotic were given in both hospitals. Even third generation cephalosporins like cefotaxime and ceftazidime were also given in the hospitals. Trials comparing different regimens show no clear advantage to a combination of antibiotics over single agents. Likewise, the use of three to five doses, rather than a single dose of antibiotics for prophylaxis of infection with cesarean section does not appear to confer any additional benefit[27-28].

Despite the theoretical need to cover gram negative and anaerobic organisms, studies have not demonstrated a superior result with broad-spectrum antibiotics compared with cefazolin. Therefore cefazolin was the recommended agent for CS.

The ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery[10] recommended a regimen for women undergoing vaginal hysterectomy, abdominal hysterectomy or radial hysterectomy was a single IV dose of cefazolin 1g or cefotetan 1g at the induction of anesthesia. An alternate was cefoxitin 1g IV at the induction of anaesthesia.

The Western Australian Drugs and Therapeutics Committee's preferred option for a vaginal hysterectomy and abdominal hysterectomy was a single agent of cefotetan 2g IV at the time of induction or cephalothin 2g plus metronidazole 500mg IV ending the infusion at the time of induction[12]. So, finally first generation cephalosporins were the choice of an agent for hysterectomy.

In general, prophylaxis is considered optional. For hernia repairs entailing the insertion of mesh, prophylaxis is considered desirable since morbidity

of infected mesh in the groin is substantial. However, no prospective trials demonstrate the effectiveness or necessity of this practice. If prophylaxis is desired or indicated for these procedures, cefazolin is the recommended agent[10].

The Western Australian Drugs and Therapeutics Committee had recommended the use of gentamicin 2mg/Kg IV at the time of induction for the patient's undergoing prostectomy[11].

The results obtained from the study revealed that there was a practice variation in the use of an antibiotic prophylaxis in both hospitals. The hospitals infrequently met the international published guidelines for antibiotic prophylaxis and compliance varied by type of procedure and also within the procedure.

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