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Application of guidelines on preoperative antibiotic prophylaxis in León, Nicaragua

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ABSTRACT

Background: To determine adherence to the guideline for preoperative antibiotic use in Nicaragua.
Methods: An observational study in the University Hospital of León, Nicaragua. All surgical patients in the departments of general surgery, orthopaedics, gynaecology and obstetrics, and paediatrics during a four-week period were included. Patients with infections prior to surgery were excluded. Main outcome measures were the proportion of patients that received appropriate preoperative antibiotics based on wound classification, suspected pathogens, administered antibiotics (type and dose), therapy duration and timing according to the local protocol.
Results: In the study, 297 patients received a total of 395 antibiotics with 2595 doses for a total of 1087 days. Only 68% of patients received antibiotic prophylaxis for indications mentioned in the protocol. Antibiotics were given without indication or as treatment in 23%. In 9% of the cases no preoperative antibiotic therapy was given (no indication for 6%, but indicated for 3%). Of the 201 patients with an indication for prophylaxis, 25% received more antibiotic therapies than indicated. Antibiotic choice was discordant with the protocol in 69%, dose in 20%, and both the moment of administration and duration in 78%. Overall adherence was achieved in 7% of patients. Complete protocol violations were observed in 12%. The 243 patients in the prophylaxis group received 1707 doses, 83% of which were administered unnecessarily.
Conclusion: Protocol violations are frequent in preoperative antibiotic prophylaxis in Nicaragua leading to considerable overprescription. Educational strategies to reinforce protocolised antibiotic use are essential for reducing costs and antibiotic resistance rates.

KEYWORDS

Adherence, antibiotic prophylaxis, protocol, surgical site infection

INTRODUCTION

When appropriate antibiotic prophylaxis is used, the incidence of surgical site infections is between 2 and 5% and the associated mortality is 0.6%.[1,2] Inadequate prophylaxis leads to an increased incidence of surgical site infections of up to 15%.[3-5] Studies have shown inappropriate antibiotic prophylaxis, hyperglycaemia, preoperative condition (ASA score), wound classification and the duration of the operation to be independent risk factors for such infections.[3,6] The aetiology of surgical site infections is dependent on the location of the surgery, the bacterial load in the tissue or blood perioperatively and the integrity of host defenses.[2,4,6] Adequate prevention of such infections is important because they are associated with increased mortality and hospital costs of up to tenfold.[2,4,6-8] Inappropriate use of antibiotics (including overprescription and the unnecessary use of broad-spectrum antibiotics) can also lead to increased bacterial resistance.[9,10] A sound and restrictive policy minimises antibiotic resistance, prevents surgical site infections and is cost-effective.[11-13]

Protocols for antibiotic prophylaxis have been designed worldwide to optimise local administration of antibiotics. Monitoring and intervention can be effective in increasing the adherence to a protocol as has been shown in studies in which the appropriateness of antibiotic prophylaxis was increased from around 50 to 95 to 100% by the stricter implementation of an existing protocol.[14,15]

As baseline data are lacking in Nicaragua, we set out to evaluate the adherence to guidelines for preoperative antibiotic use in León, Nicaragua.

METHODS

Preoperative antibiotic guidelines

In Nicaragua, the Ministry of Health published two documents on preoperative antibiotic treatment in the mid-1990s. In 1997, a nationwide project was initiated to promote rational use of medications on the basis of these documents.[16] In 2000, the University of León and the Ministry of Health collaborated on this topic and published a final protocol for the preoperative use of antibiotics.[17] To detect deviations from the protocols in Western countries, the widely accepted Dutch protocol formulated by the SWAB (Dutch Working Party on Antibiotic Policy) was used as a reference.[18] Even though there are some minor differences between Dutch hospitals, the SWAB guidelines are used in this study as the official Dutch national protocol for comparison purposes. The Nicaraguan and Dutch protocols were compared on a number of points: wound classification, most likely pathogens, suggested antibiotics (primary and secondary), and ideal moment of administration.

Design, setting and study population

We conducted an observational study during a four-week period in 2005 in the University Hospital of León, Nicaragua. All consecutive persons of any age undergoing surgery in the departments of general surgery, orthopaedics, gynaecology and obstetrics, and paediatrics were eligible for inclusion into the study. We excluded patients with current infections or contaminated wounds prior to surgery by review of the patient records. When an infection became apparent during the operation, the initial prophylaxis was switched to treatment. Therefore, only the initial dose given prior to surgery was evaluated.

Measurements

During the study period, all patient records from the participating departments were checked on a daily basis for new surgical procedures as well as to follow up the patients already included in the study. For our research purposes, a case record form was developed which included information on patient characteristics, surgical procedures and antibiotic treatments for each subject. Wound classification was obtained from the antibiotic ordering form which was sent to the hospital pharmacy for each patient prior to surgery. When the wound classification was not reported, the wound was classified from the operation report according to the Nicaraguan protocol standards for that type of surgical procedure.[16]

Follow-up data were updated daily with regard to additionally administered doses, changes in type of antibiotic medication and administration intervals as well as for signs of postoperative wound infections. If more than one antibiotic was prescribed, they were evaluated separately. Subsequently, a final assessment of all antibiotics per patient was made. Antibiotic therapy given to patients at discharge was not included. All antibiotics administered within 1.5 hours before surgery were recorded as being concordant with the Nicaraguan protocol.[16] When the patient record indicated 'antibiotics given in the operating theatre', such antibiotics were regarded as being given at the start of anaesthesia. The authors did not attend the surgical procedures themselves, thus not influencing the timing and administration of antibiotics by their presence. All other moments of administration in relation to the surgery were treated as protocol violations. All antibiotics prescribed were compared with the Nicaraguan protocol.

RESULTS

A comparison of the Nicaraguan and Dutch protocols (*table 1*) shows only minor differences between them. The moment of administration is stricter in Nicaragua but the criteria for a second dose during surgery are the same. Moreover, the Nicaraguan protocol does not differentiate between contaminated and dirty wounds. The Nicaraguan and Dutch protocols use the same definition for surgical site infections.

Of the 297 patients, the majority of procedures were carried out in women (80%) and the mean age was 29 years (standard deviation 18 years). Most patients were from the obstetric wards (45%), followed by general surgery (21%), gynaecology (15%), paediatrics (10%) and orthopaedic wards (8%). Comorbidity was present in 12% of these patients, and 2% had a known allergy to antibiotics. Of all surgical wounds, 77% were clean-contaminated, 14% were clean and 9% were contaminated-dirty. The mean duration of the surgical procedure was 56 minutes (standard deviation 39 minutes). Only 1.4% of patients had an infection postoperatively.

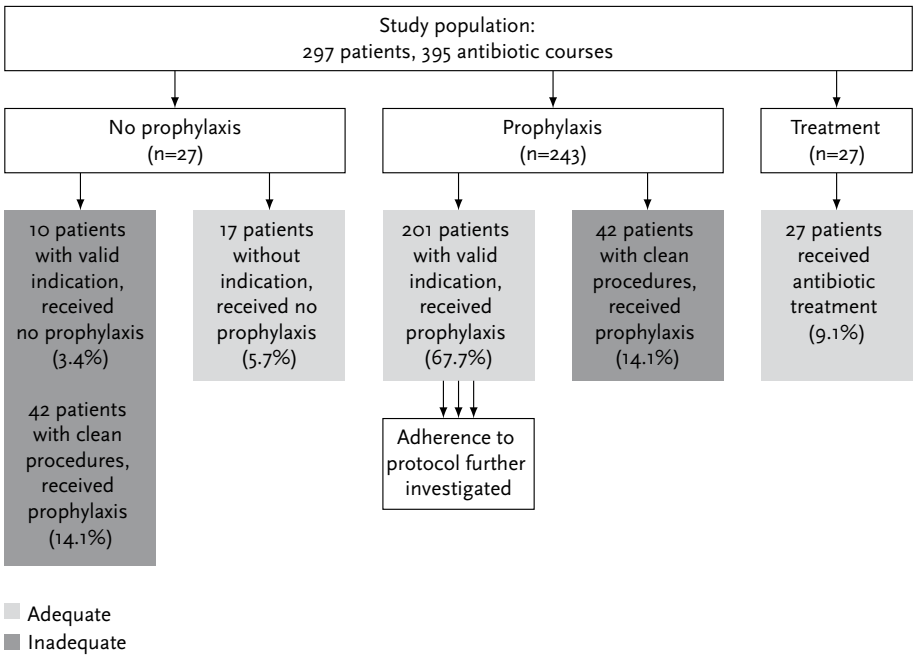
In all, 395 antibiotic therapies were prescribed for these 297 patients (*figure 1*). The majority, 201 patients (68%), received antibiotics for an appropriate prophylaxis indication. However, 69 cases (23%) received antibiotics either without indication since the procedure could be considered a clean one (42 patients, 14.1%) or as antibiotic treatment (27 patients, 9.1%) for a contaminated wound. Contaminated wounds are susceptible to infections due to the presence of bacteria in the wound and therefore require more intensive treatment than prophylaxis alone.

Table 1. *Protocol comparison*

	Léon, Nicaragua	**Utrecht, the Netherlands**
Time of administration	90-15 minutes before incision	120-30 minutes before incision
Additional dose*	Every 3-4 hours with: operation length >3 x $t^{1}/_{2(antibiotic)}$, blood loss >2 litres, extracorporal circulation	
Wound classification	Clean (surgery without trauma or infection, with asepsis, without opening airways, intestinal tract or urogenital system and without implantation of prostheses): no prophylaxis indicated	Clean (elective surgery, closed without drains, no infection found, good asepsis, without opening airways, intestinal tract or urogenital system): no prophylaxis indicated
	Clean-contaminated: controlled opening of the airways, intestinal tract, biliary tract or urogenital system. Penetrating abdominal trauma without signs of visceral damage or infection during surgery, cardiothoracic surgery, large vessel surgery	Clean-contaminated: controlled opening of the airways, intestinal tract, biliary tract or urogenital system Contaminated: open traumatic wounds, leakage from intestinal tract, open urogenital or biliary tract with infected urine or bile, infection without pus
	Contaminated-dirty: therapy required, all surgery that is not clean or clean-contaminated	Dirty-infected: traumatic wounds with necrosis, corpus alienum or (faecal) infection, perforated viscera, acute bacterial infection with pus
Surgical site infection	Manifest after a surgical procedure (within 48 hours) and have a direct relation to this procedure	

*The rules for administering an additional dose are the same in both countries.

Figure 1. *Patient flow chart*



No antibiotics were received by 27 patients since they were not indicated in a clean procedure (17 patients, 5.7%) or prophylaxis was indicated but not prescribed (10 patients, 3.4%). All 96 patients who did not receive prophylactic antibiotic treatment were not followed up further.

In total, 201 patients with an indication for prophylaxis received 282 antibiotic therapies. In 51 patients (25.4%) an additional antibiotic therapy was prescribed, contrary to the protocol. Of these 282 prescriptions, antibiotic choice was discordant with the hospital protocol in 68.8%, dose in 19.9%, moment of administration in 77.7% and duration in 78.4%. Overall, 690 violations of any aspect were recorded in the 282 antibiotic therapies. Overall adherence to the protocol was achieved with only 21 (7.4%) antibiotic therapies, 38 (13.5%) were in accordance with the protocol on all but one item, 41 (14.5%) on two items and 149 (52.8%) were only correctly prescribed for one item

(mostly a correct dose). In 33 cases (11.7%) the antibiotics were not in accordance with any of the items mentioned in the protocol. There were no statistically significant differences in protocol adherence between the different surgical wards.

The 201 patients who were given prophylaxis received 211 (of 282) antibiotic therapies perioperatively, 71 courses (25%) were given additionally at a later time. Of all 211 initial therapies 78% of the antibiotics were administered outside the correct dosing interval; 63% were administered after the operation, with a mean delay of 6.9 hours. Fifteen percent of the antibiotics were administered ≥90 minutes before entering the operating theatre, on average 8.8 hours before surgery. Only 22% were administered in the correct dosing interval. Eleven percent of antibiotics were administered between 90 minutes before entry and entering the operating theatre. Another 11% were administered in the operating theatre. For these, it was not possible to establish a more precise moment of administration and it was assumed that they were given prior to incision.

Protocols for prophylaxis propose the preferential use of certain antibiotics over others. An overview of the types of antibiotics used in patients in whom prophylaxis was given for a valid indication is shown in *table 2*. Ampicillin (58.3%) and cefazolin (13.0%) were most often prescribed. Cefazolin and cefoxitin are the antibiotics that are most often administered correctly according to the protocol (*table 3*). Ampicillin and ceftriaxone are not mentioned in the protocol, but they are often prescribed for prophylactic purposes.

The 243 patients in the prophylaxis group (*figure 1*) received a total of 322 antibiotic therapies or 1707 doses for a total of 721 days in the four-week study period. According to the protocol, 1409 of these 1707 doses (83%) were administered unnecessarily for 411 days, as regulations indicated that fewer doses would have been sufficient. There were no patient characteristics, wards or types of antibiotic which could significantly predict overprescription.

Table 2. *Administration of antibiotics of the study population (n=201)*‡

Antibiotic received	% of total	No. of doses	No. of days
Ampicillin	58.3%	793	272
Cefazolin*	13.0%	177	93
Gentamicin*	9.8%	133	90
Penicillin	5.7%	77	25
Cefoxitin*	4.7%	64	33
Ciprofloxacin	2.3%	31	24
Ceftriaxone	1.3%	17	12
Metronidazole*	1.2%	16	8
Amoxicillin*	0.6%	8	6
Others**	3.2%	44	26
Total	*100%*	*1360*	*589*

‡**Initial, first-choice therapies only;** ***antibiotics mentioned in the prophylactic protocol;** ****dicloxacillin, amikacin, cephalexin, clindamycin, nitrofurantoin, cefadroxil.**

Table 3. *Local prophylaxis guideline**

Type of surgery (clean-contaminated)	Recommended antibiotics
Head and neck surgery	1. Cefazolin 2. Clindamycin + gentamicin
Stomach/duodenal/biliary surgery	1. Cefazolin 2. Clindamycin + gentamicin
Colorectal surgery, appendectomy (nonperforated)	1. Cefoxitin 2. Clindamycin + gentamicin
Penetrating abdominal trauma	1. Cefoxitin ± gentamicin 2. Clindamycin + gentamicin
Vaginal surgery, caesarean section, abdominal hysterectomies	1. Cefazolin 2. Clindamycin ± metronidazole
Cardiovascular surgery	1. Cefazolin 2. Vancomycin

***In the local guidelines, for each type of surgery, two choices of antibiotic prophylaxis are given.**

DISCUSSION

When the Dutch and Nicaraguan protocols are compared, there are few differences in the timing of antibiotic prophylaxis and wound classification.[16-18] Furthermore, the expected pathogens for each type of surgery and the primary antibiotics recommended are generally the same (results not shown). However, about half of the antibiotics used (*table 2*) are not mentioned as a suitable prophylactic drug either in the Nicaraguan or Dutch protocols. Of these drugs, ampicillin is used in León by the gynaecologists as standard prophylaxis for caesarean sections. This use is not supported by the local infectious diseases specialist and there are no bacterial resistance or sensitivity data that warrant its use. Therefore, these cases were considered protocol violations. Many of the studied patients underwent a caesarean section and the use of ampicillin thus influences the results significantly.

The study data indicate that protocol violations are frequent in preoperative antibiotic prophylaxis in Nicaragua, which leads to considerable overprescription of antibiotics. It has been established in numerous studies that the use of preoperative prophylaxis reduces

the rate of surgical site infections and it is now accepted as standard care (and recommended by the Centre for Disease Control).[3-5] It was shown that for 68% of patients the appropriate choice to administer antibiotics is made. In addition in 5% of the cases the appropriate decision of not administering prophylaxis was made. However, when the indication was appropriate, antibiotic choice, duration, dose and timing were discordant with hospital guidelines in many patients. Van Kasteren *et al.* conducted a similar study in 13 Dutch hospitals and found antibiotic choice to be discordant with hospital guidelines in 8%, duration in 18%, dose in 11% and timing in 50%.[19] Considering these much lower discordance rates with the protocol, we may conclude that there is still room for improvement in adherence to the protocol in Nicaragua. A more recent study showed that the implementation of the SWAB guidelines improved long-term adherence.[13] This resulted in a decrease in inappropriate antimicrobial use and lowered costs without impairing patient outcome.

Of particular concern is the timing of the prophylaxis in Nicaragua. The majority of antibiotics are administered outside the correct preoperative dosing window. Most antibiotics were administered too early or too late leading to ineffective antibiotic blood levels at the time of surgery. A limitation of this study is the inability to comment on the 9% of antibiotics administered in the operating theatre, because it is unclear if the antibiotic was given before or after the incision. In future studies one could consider a method to record the timing more precisely. In some cases antibiotics were given for periods longer than 24 hours. Studies have shown, however, that effective prophylaxis can be established with short courses of less than 24 hours and that longer administration not only has no benefit but may be detrimental due to an increased incidence of resistance.[2,20] Moreover, during a caesarean section, guidelines advise antibiotic prophylaxis just after cutting the umbilical cord, but in this study, only 14 caesarean sections (11%) were performed correctly as advised. In 21 patients (16%), prophylaxis was given before the caesarean section and in 94 patients (73%) prophylaxis was given on the ward, 0.5 to 24 hours after the caesarean section.

Currently prophylactic antibiotics take up a large part, up to 30% or more, of the prescribed antibiotics in hospitals.[14] Adherence to local guidelines could keep costs to a minimum. Literature suggests various cost-effective strategies to improve protocol adherence. Prado *et al.* show that when the pharmacy is given a central role in the administration of prophylaxis, the appropriateness of the indication increased from 56 to 100%, while the costs decreased by 40%.[15] Moreover, Zwar et al. found that giving feedback on prescription behaviour increased the appropriateness of the prescriptions.[21] Welschen *et al.* conclude that by organising a group education and consensus meeting and monitoring prescriber behaviour, prescription errors decreased by 12% compared with controls.[22] Alerany *et al.* showed that integrating all the above strategies resulted in an increase in the adherence from 51 to 95% in operations requiring prophylaxis.[14] They used an antibiotic prophylaxis chart in the operating theatres, pharmacy-controlled administration and education and prescriber feedback. It can be noted that the main causes of misuse in the article by Alerany *et al.* were timing and choice, which were also problematic in this study.

In León, antibiotics must be ordered from the pharmacy prior to the operation. A specific form must be completed for all procedures, including clean ones. It is the only form on which the wound classification has to be indicated and if not filled in completely, the information might be lost. This form was completed for only 25% of the study subjects. It is important for future prescriptions to stress the value of filling in this form. An effort to consistently classify the wounds might result in a better awareness and understanding of the protocol and, subsequently, the adherence to it.

General population statistics show that an allergy to antibiotics occurs in roughly 5 to 10% of the population.[23] Thus a 2.4% allergy rate in our study population could be an underestimation.
The incidence of surgical site infections or postoperative infections ranges from 2.5 to 10% depending on the type of surgery.[8,24] It was not part of the objective to study the effectiveness of the protocol in terms of prevention of surgical site infections.

CONCLUSION

Adherence to the preoperative antibiotic therapy protocol is far from optimal and in concordance with the Nicaraguan guidelines leading to more than half of the antibiotic doses administered unnecessarily according to the protocol rules. This is a huge toll on the budget of the hospital and obviously also plays a major role in the formation of antibiotic resistance. Successful prescription of antibiotic prophylaxis is dependent on the national policy on the control of antimicrobials, quality of the local protocols, their implementation, hospital staff education, monitoring, and feedback interventions to increase the adherence.

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