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Optimizing the timing of antimicrobial prophylaxis in surgery: an intervention study

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The timing of surgical antimicrobial prophylaxis was determined before and after an intervention programme of education of surgeons, anaesthetists and nurses on the subject of antimicrobial drug prophylaxis, and the subsequent implementation of new protocols of single dose prophylaxis administered within one hour before incision. This prospective study was performed in three surgical departments of a university hospital. For comparison, the timing of prophylaxis was also determined in an operating department of a community hospital. The timing improved considerably in the departments of the university hospital where the intervention was carried out: administration of the first dose within one hour before incision increased from 39% to 69% in department A and from 64% to 80% in department B. Before the intervention, seven out of 16 prophylactic doses were given after inflation of the tourniquet. After the intervention all doses of prophylactic antibiotics were administered before inflation of the tourniquet. Initially, the intervals of multidose prophylaxis varied widely. In the second review, single-dose prophylaxis increased from 21% to 78% in department A and from 31% to 85% in department B. We conclude that the intervention succeeded in improving the quality of surgical prophylaxis.

Introduction

Timing of intravenous antimicrobial prophylaxis in surgery is considered to be optimal about 30 min before incision, i.e. at induction of anaesthesia (Abramowicz, 1989), and for commonly administered antimicrobials, adequate concentrations are then present in the tissues at incision and for 2 h thereafter (DiPiro *et al.*, 1984). The rationale is to be found in the experimental work of Burke (1961) and the clinical trials of Stone *et al.*, (1976). Protection against infection is maximal when the antibiotic is present in the tissues before microbial inoculation of the wound occurs. In distal limb orthopaedic

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surgery, the antibiotic should be injected before the application of the tourniquet to reach protective concentrations in the limb (Katz & Siffert, 1982). Administration more than 1 h preoperatively has resulted in a higher rate of infective complications in gynaecological surgery (Galandiuk *et al.*, 1989). Recently, significantly fewer wound infections were noted in those patients where the drug was given preoperatively instead of up to 2 h after incision (Classen *et al.*, 1992). One or more additional postoperative doses is unlikely to offer benefit (Dellinger *et al.*, 1994). We assessed the effect of implementing accepted guidelines for specific surgical procedures (Abramowicz, 1989) on the quality of timing of surgical antimicrobial prophylaxis.

Materials and methods

Setting and patient population

This prospective study was conducted in three separate operating departments: surgery (A), orthopaedic surgery (B) and otorhinolaryngology (C), of the 948-bed University Hospital, Nijmegen. The operating departments were staffed by a rotating pool of 40 anaesthetists. The timing of antimicrobial prophylaxis was registered as part of a general quality-of-use review of the use of antimicrobials in these departments. During one month in 1990, and again in 1992, all consecutive operations were reviewed by an infectious diseases physician and a pharmacist in training. In a 326-bed community hospital, an infection control nurse (MN) collected data on the administration of antimicrobial prophylaxis in 500 consecutive operations by three anaesthetists using an identical method.

Method of the review

Recorded times of injection of the antibiotic by the anaesthetist, of induction of anaesthesia, incision and end of the operation were copied from the anaesthesia record after the return of the patient from the operating room. The partially-computerised anaesthesia record allowed time-recording with an error of no more than 5 min. In the university hospital, for multidose prophylactic regimens lasting 24 h or more, the times of second and third injections of antibiotics were copied from the patient medication sheet in the ward.

Intervention

After the first review, a report on each department was sent to their chiefs of staff. The report was accompanied by recommendations for an alternative antibiotic policy. The principal goal was to introduce a universal surgical prophylaxis standard of a single-dose cephalosporin for all but dirty procedures (DiPiro *et al.*, 1984), with a second injection during the procedure for interventions lasting more than three hours. Cefazolin was to be given at incision (with metronidazole where an anaerobic spectrum was needed). The reports were discussed by the surgical staff, and the recommendations were formulated into new protocols for prophylaxis. After approval by the Antibiotic Committee, a presentation of the report and the protocol was made in the departments. In most departments, the first dose of surgical antimicrobial prophylaxis was given by the anaesthetist in the operating room. An inquiry (questionnaire by mail) in the department of anaesthesia showed deficient communication between anaesthetists and

surgeons on the subject of administration and timing of prophylaxis and the wish of the anaesthetists to standardise prophylaxis. The results of the inquiry were presented at the time of introduction of the protocols. The whole intervention took approximately 14 months. The implementation of the protocols was assisted by junior pharmacists who organized briefings for nurses in the operating departments and in the wards. The standardized prophylaxis guidelines were displayed in the wards and the operating rooms. Operating room drug stocks were reorganized.

Outcome measures

The review was repeated in identical form two years later. The effect of the intervention was measured in operating departments A and B, where the timing was found to be unsatisfactory. The number of nosocomial infections (defined as active infections not present or incubating at the time of admission) per 100 bed-days treated with antibiotics is given as an indicator of the effect of prophylaxis.

In most cases, chi-square tests were applied to establish systematic differences. Fisher's exact test was used to compare the timing in relation to tourniquet application, and variance ratio F-tests for comparing variations in dosage intervals.

Results

Timing of the first dose in the university hospital

In the first review, the timing of 276 intravenous prophylactic prescriptions was studied in operating departments A, B and C of the university hospital. Thirty nine (14%) prescriptions were excluded from the analysis, because the timing of the first antibiotic dose was not noted or the anaesthesia record was missing. Prophylactic injections were divided into three groups: injections given more than 1 h before incision, within 1 h before incision, and after incision. There was a significant difference in the frequency distribution of the injections between the departments A, B and C ($P < 0.001$). The frequency distribution of the injections in the departments A and B is shown in Figure 1. The number of injections given within 1 h before incision and those given after incision differed widely between the three departments. In department A, 32 (39%) of the total number of injections were given within 1 h before incision, in department B this amounted to 32 (64%) and in department C to 65 (78%). Almost all surgical prophylaxis was administered by the anaesthetist in the operating room. Only the prophylactic antimicrobials against endocarditis were administered by the nurses in the wards at 8 h (i.e. often more than 1 h before incision). Therefore, the number of injections given more than 1 h before incision was low for all departments: three (3%) in department A, two (4%) in department B and one (1%) in department C. In department A we looked at the differences between scheduled ($n = 63$) and emergency ($n = 41$) procedures. The timing data were not statistically different between both types of procedures ($P = 0.94$).

In the second review, 161 prophylactic injections were studied in departments A and B. The timing of prophylaxis in departments A and B after intervention is also shown in Figure 1. In department A, the frequency distribution of injections was significantly different from those in the first review ($P < 0.001$). In department B, no significant changes were seen ($P = 0.15$). After the intervention, almost 70% (A) and 80% (B)

were given within 1 h before incision and no injection was given more than 1 h preoperatively.

Timing of the first dose in the community hospital

In the community hospital, intravenous prophylaxis was given in 128 out of 500 operations (26%). In 12 (9%), the time recordings of induction and/or intravenous administration were missing. The timing of prophylaxis was studied for 116 procedures. Anaesthetists administered the prophylactic drugs in the operating room. However, the first scheduled patient of the day was given the prophylactic drug by the ward nurse. Although 81 (70%) injections were given before the incision, 30 (26%) injections were given for more than 1 h preoperatively. Overall, there was suboptimal timing in 56% of the procedures.

Tourniquet use

In the first review, 16 procedures in the university hospital were performed under tourniquet control (Figure 2). In seven procedures, prophylaxis was given after inflation of the tourniquet. In the second review, all of eight prophylactic doses were administered within 30 min before inflation of the tourniquet ($P = 0.054$).

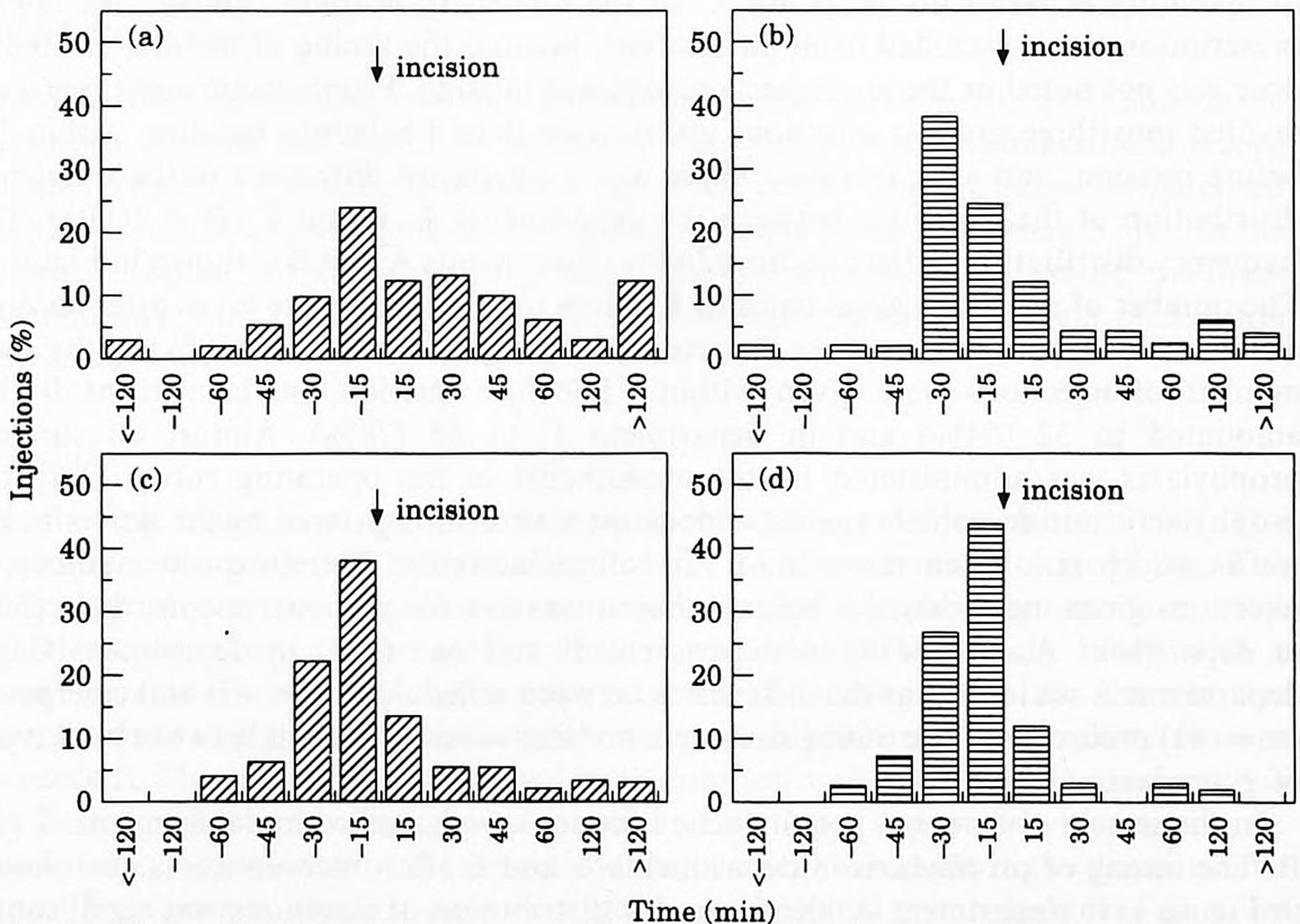


Figure 1. Timing of antimicrobial prophylactic injections in surgical departments before (a), (b) and after (c), (d) intervention. (a) Department A, $n = 104$; (b) department B, $n = 50$; (c) department A, $n = 120$; (d) department B, $n = 41$. Time = 0 is the time of incision.

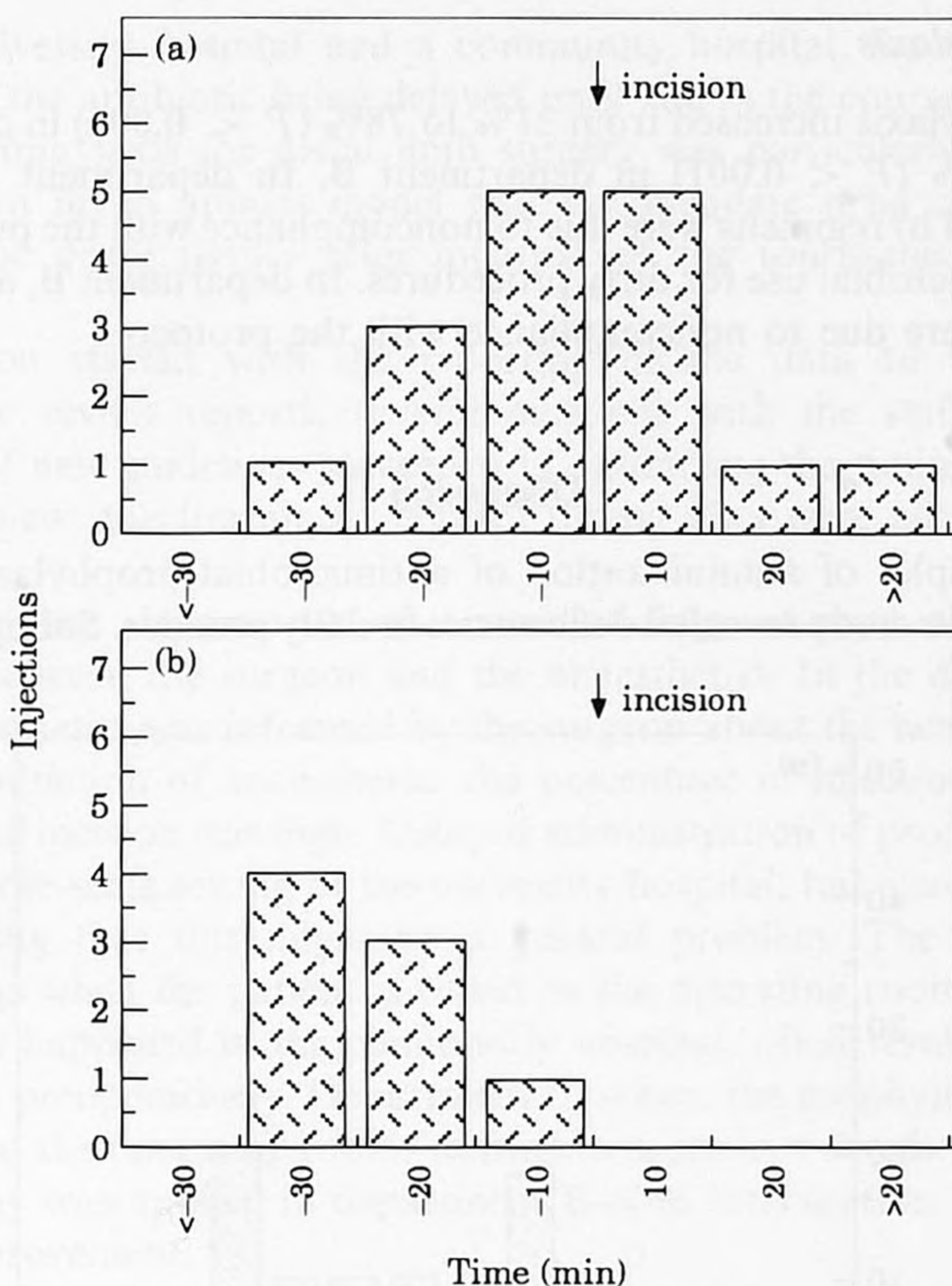


Figure 2. Timing of antimicrobial prophylaxis in distal limb surgery, (a) before intervention ($n = 16$) and (b) after intervention ($n = 8$). Time = 0 is the inflation of the tourniquet.

Dosage interval

At the first review in the university hospital, we studied 100 antimicrobial drug regimens that were started in the operating room as prophylaxis or therapy and were continued postoperatively. The intervals between the first and subsequent doses were measured. In the wards, intravenous antibiotics were administered by nurses in fixed schedules of 6- or 8-hourly administrations. In department A, patients returning from the recovery room were shifted into the fixed schedules without taking into account the doses given in the operating room. In department B, nurses calculated the correct interval by checking the time of the first dose on the anaesthesia record. There were 40 8-hourly regimens in department A and 29 in department B. The distribution of the intervals for A and B is shown in Figure 3. The average interval between first and second dose was 7 h 40 min (range 0 h 30 min–13 h 30 min) for A and 7 h 30 min (range 1 h 10 min–11 h) for B. A significantly higher standard deviation was found for department A compared with B ($P = 0.01$). The average interval between the second and third dose in ward A was 7 h 45 min (range 4–11 h). The standard deviation was significantly smaller compared with that of the first interval in A ($P < 0.001$).

We did not study dosage intervals in the second review as, after the introduction of single-dose prophylaxis, only a small number of postoperative doses were recorded.

Single-dose prophylaxis

Single-dose prophylaxis increased from 21% to 78% ($P < 0.001$) in department A and from 31% to 85% ($P < 0.001$) in department B. In department A, two thirds of multiple dosing (24 h) regimens were due to noncompliance with the protocol. One third consisted of antimicrobial use for dirty procedures. In department B, all multiple dosing (24 h) regimens were due to noncompliance with the protocol.

Discussion

Though the principles of administration of antimicrobial prophylaxis in surgery are well-established, our study revealed deficiencies in daily practice. Suboptimal timing was

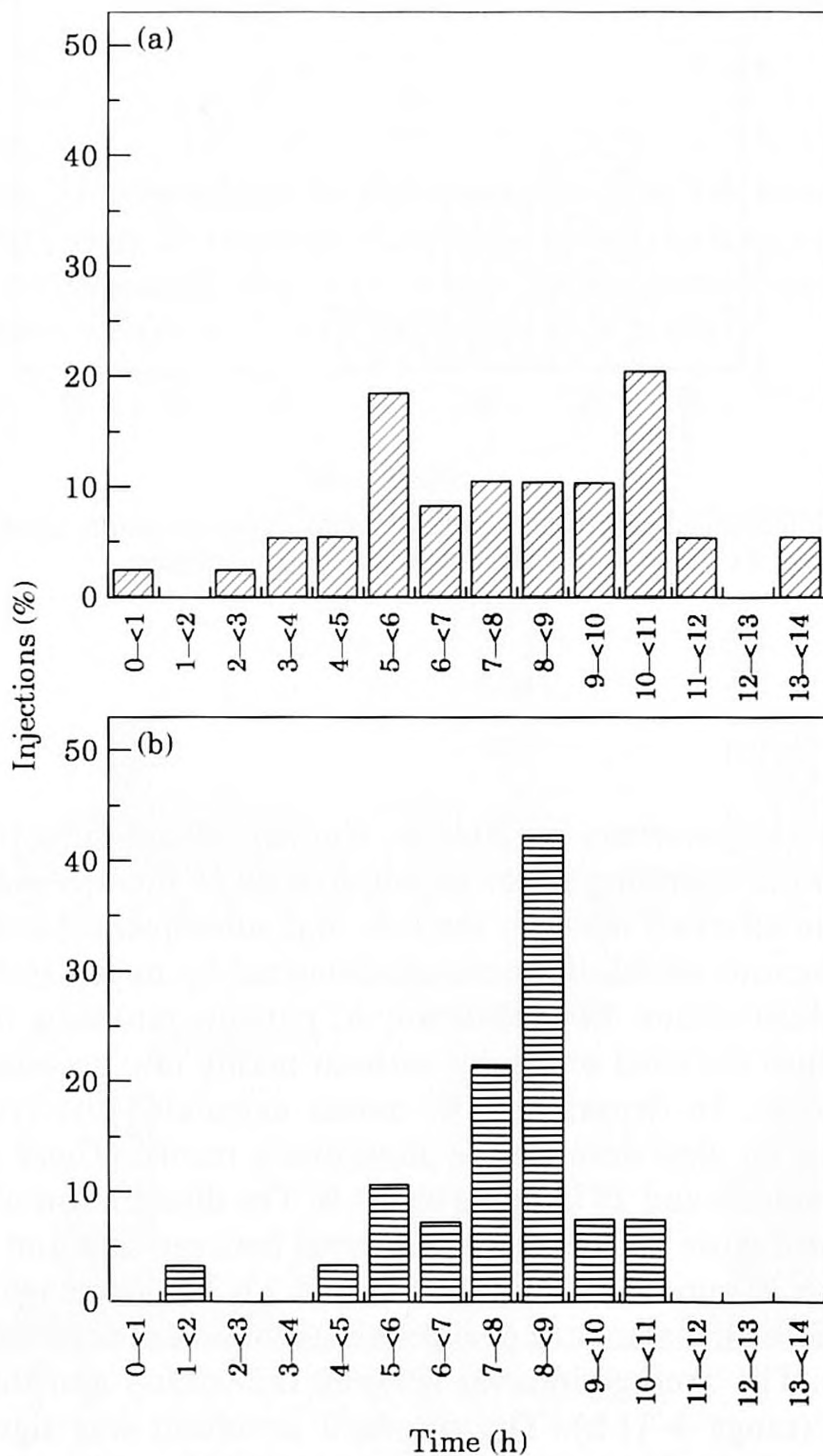


Figure 3. Interval between first antimicrobial drug dose in the operating room and second postoperative dose for $n = 40$ 8-hourly regimens in department A (a) and $n = 29$ 8-hourly regimens in department B (b) (before intervention).

recorded in a university hospital and a community hospital, for many patients the administration of the antibiotic being delayed until late in the course of the procedure. The timing of prophylaxis for distal limb surgery was particularly disturbing, since it has been shown in an animal model that no adequate drug concentrations can be attained in the distal tissues after inflation of the tourniquet (Katz & Siffert, 1982).

Our intervention started with the reporting of the data to the surgeons and anaesthetists. The review reports, several meetings with the staff and finally, the implementation of new guidelines succeeded in optimizing the timing of the first dose. In the second review, the tourniquet control timing data were all within the correct range.

The inquiry in the department of anaesthesiology showed the importance of communication between the surgeon and the anaesthetist. In the departments A and B where the anaesthetist was informed by the surgeon about the need for prophylactic drugs after the induction of anaesthesia, the percentage of injections of prophylactic drugs after surgical incision was high. Delayed administration of prophylaxis was found not only in the large-scale setting of the university hospital, but also in the community hospital, suggesting that this might be a general problem. The administration of prophylactic drugs when the patient is called to the operating room after being given premedication, as happened in the community hospital, often resulted in doses given for more than 1 h preoperatively. Department C, where the prophylactic drug was sent with the patient to the operating room, seemed to score best for the timing of the first dose. This strategy was applied in department B after intervention, but did not result in significant improvement.

Our data in department A showed widely varying intervals between the first and second prophylactic dose and therefore resulted in inappropriate pharmacokinetics and probably inadequate prophylaxis. Patients returning at irregular times from the operating room to the wards were administered the second dose following the fixed medication times—for example 6 h–14 h–22 h—in 8-hourly regimens. Once the patient remained in the ward, the regular time schedule of the nursing staff provided good quality of prescribing, as was described by others (Denton, Morgan & White, 1991).

In 1990, many surgeons involved in this study adhered to 24 h prophylaxis regimens, because they felt it to be unsafe to switch to a single-dose regimen. The inconsistency of the 24 h prophylaxis practices revealed by the review helped us to convince the staff to implement protocols of single-dose regimens. In the second review, all surgeons used single-dose prophylaxis, although some of them continued to use 24 h prophylaxis in selected cases.

Optimizing of the timing of administration results in a reduction in wound infection rates as shown by Classen *et al.* (1992). In our study, not only the timing, but also the choice of drug and duration of prophylaxis changed after the intervention, following the guidelines for optimal prophylaxis (Abramowicz, 1989). Although we did not prospectively study the incidence of postoperative wound infections during the study periods, there are some indicators that the new policy improved the quality of prophylaxis. The number of nosocomial infections treated with antibiotics/100 bed-days was 1.38 in the first study period and 0.90 in the second. The average length of stay, as an indicator of postoperative infectious complications, has continued to decrease since 1986.

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