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Research article

Risk of surgical site infection and efficacy of antibiotic prophylaxis: a cohort study of appendectomy patients in Thailand

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Abstract

Background: No data currently exist about use of antibiotics to prevent surgical site infections (SSI) among patients undergoing appendectomy in Thailand. We therefore examined risk factors, use, and efficacy of prophylactic antibiotics for surgical site infection SSI among patients with uncomplicated open appendectomy.

Methods: From July 1, 2003 to June 30, 2004 we conducted a prospective cohort study in eight hospitals in Thailand. We used the National Nosocomial Infection Surveillance (NNIS) system criteria to identify SSI associated with appendectomy. We used logistic regression analysis to obtain relative risk estimates for predictors of SSI.

Results: Among 2139 appendectomy patients, we identified 26 SSIs, yielding a SSI rate of 1.2 infections/100 operations. Ninety-two percent of all patients (95% CI, 91.0–93.3) received antibiotic prophylaxis. Metronidazole and gentamicin were the two most common antibiotic agents, with a combined single dose administered in 39% of cases. In 54% of cases, antibiotic prophylaxis was administered for one day. We found that a prolonged duration of operation was significantly associated with an increased SSI risk. Antibiotic prophylaxis was significantly associated with a decreased risk of SSI regardless of whether the antibiotic was administered preoperatively or intraoperatively. Compared with no antibiotic prophylaxis, SSI relative risks for combined single-dose of metronidazole and gentamicin, one-day prophylaxis, and multiple-day antibiotic prophylaxis were 0.28 (0.09–0.90), 0.30 (0.11–0.88) and 0.32 (0.10–0.98), respectively.

Conclusion: Single-dose combination of metronidazole and gentamicin seems sufficient to reduce SSIs in uncomplicated appendicitis patients despite whether the antibiotic was administered preoperatively or intraoperatively.

Background

Data regarding risk factors and use of antibiotics in surgical patients are essential for preventing and treating surgical site infections (SSI). Appendectomy is one of the most common surgical procedures [1] with SSI complicating 1–5% of appendectomy cases [2-4]. One established risk factor for SSI in appendectomy is the duration of operation [1].

While antibiotic prophylaxis is common in surgical procedures [5], inappropriate use of antibiotics occurs in 25–50% of general elective surgeries [6-10]. The efficacy of antibiotic prophylaxis in patients undergoing appendectomy has been examined in several randomized and observational studies [4,11-19] showing that appropriate use of antibiotics reduces the risk of SSI following appendectomy by 40–60%.

In Thailand, some hospitals had their own internal antibiotic prophylaxis guidelines. However, standardized national guidelines for antibiotic prophylaxis among appendectomy patients have not yet been established. Simple appendicitis is treated according to surgeons' discretion, which results in use of many different agents.

No study has been conducted of the efficacy of antibiotic prophylaxis on risk of SSI in patients undergoing appendectomy in Thailand. We aimed to examine risk factors for SSI, the use of antibiotic prophylaxis, and the efficacy of antibiotic prophylaxis in reducing SSI among appendectomy patients in Thailand.

Methods

This prospective multicenter cohort study was conducted from 1 July 2003 to 30 June 2004 in eight Thai hospitals (four tertiary care teaching hospitals and four geographically dispersed general hospitals). The participating hospitals were Chiangkham Hospital, Saraburi Hospital, Bhumibol Adulyadej Hospital, Vachira Phuket Hospital, Naradhiwas Rajanagarindra Hospital, Rayong Hospital, Chumphon Khet Udomsakdi Hospital, and Udonthani Hospital. The project was approved by the Ethical Review Committee for Research in Human Subjects, the Thai Ministry of Public Health, and the Ethical Committee and/or the directors of the participating hospitals. After attending a one-day training session on data collection and diagnostic criteria, infection control nurses in each hospital prospectively collected and recorded data.

Operating room (OR) logbooks were reviewed daily to identify uncomplicated open appendectomies meeting the inclusion criteria. We excluded appendectomies incidental to other operative procedures and the patients who were on antibiotic therapy. Patients' names, hospital numbers, and wards were identified via OR records. Medical records, operative notes, anesthetic records, diagnostic imaging reports, microbiological and biochemical data, and data on the operative procedure (duration and type of operation) were reviewed by study nurses and attending physicians. The American Society of Anesthesiologists (ASA) score of patient physical status was abstracted from anesthetic records. Data on the use of antibiotic prophylaxis included timing of first antibiotic prophylaxis dose, antibiotic agent, and duration of antibiotic therapy. These were obtained from patients' medical and anesthetic records. Following review, pertinent data were recorded on preprinted data collection forms.

Outpatient records of discharged patients and medical records of readmitted patients were also reviewed for evidence of infections developing after hospital discharge. Completed data collection forms were edited and analyzed at the study data processing center.

Definitions

We used criteria of the US Centers for Disease Control and Prevention (CDC) NNIS System to diagnose SSI. Infections were classified as superficial incisional, deep incisional, or organ/space SSI [20]. The ASA score was used to characterize the patients' physical status as 1 (healthy), 2 (mild systemic disease), 3 (severe systemic disease), 4 (severe life-threatening systemic disease), or 5 (moribund) [21]. Patients' final diagnoses and operations were coded according to the International Classification of Diseases 10th Revision (ICD-10) and the International Classification of Diseases 9th Revision, Clinical Modification (ICD-9 CM), respectively. The appendectomy procedures were also classified according to the NNIS [22].

We defined uncomplicated appendicitis as acutely inflamed appendicitis without perforation (clean-contaminated wound). Patients with gangrenous appendicitis, peritonitis, or abscess formation were not included.

Statistical analysis

The rate of SSI was computed by dividing the number of infections by the number of operations performed and multiplying by one hundred.

Contingency tables were constructed to analyze the relations between SSI and the other study variables: use and duration of antibiotic prophylaxis, sex, age, length of preoperative stay, type of operation, ASA score, and duration of operation. We conducted logistic regression analysis to estimate the relative risk (RR) of SSI for the main study variables.

All analyses were performed using STATA statistical software, version 7 (Stata Corp, College Station, TX).

Results

Patient and operation characteristics

During the study period, 2139 patients, 53.1% of them women, underwent open appendectomy. The median age was 26 years (interquartile range 16 to 39). Twenty-one percent of patients were hospitalized preoperatively with a median length of preoperative stay of 1 day (interquartile range 1 to 1). For postoperative or total hospital stay, median length was 3 days (interquartile range 2 to 4). Among 2139 operations, 72.4% were classified as emergency. The median operation duration was 58 minutes (interquartile range 42 to 83).

SSI rates

Twenty-six SSIs were identified in 2139 operations, yielding an overall SSI rate of 1.2 infections/100 operations. Superficial and deep incisional SSIs occurred most frequently (46.2% each). Of the 26 SSIs, 15 (57.7%) were detected after hospital discharge, and a half, within seven days after surgery. The median onset of SSI was 8 days (interquartile range 5–11).

Risk factors

The following variables were associated with the risk of SSI in the crude analyses: duration of antibiotic prophylaxis, age, elevated ASA score, prolonged preoperative hospital stay, duration of operation, emergency surgery, and sex. However, after adjustment, only prolonged duration of operation remained significantly associated with an increased risk of SSI (RR = 3.29; 95% CI 1.44–7.52) (Table 1).

The use of antibiotic prophylaxis

Prophylactic antibiotics were administered in the course of 1972/2139 (92.2%) operations. In 89.8% of these cases, antibiotics were given preoperatively, but they were given within one hour before the incision in only 38.9% of cases. The most common prophylactic antibiotics were metronidazole and gentamicin (64.2%). The combination of a single dose of metronidazole and gentamicin was used in 38.8% of cases. Antibiotic prophylaxis was administered for one day in 54.2% of cases. The median duration of antibiotic prophylaxis was 1 day (interquartile range 1 to 2). Antibiotic prophylaxis was extended for over one day in 38.0% of patients (Table 2).

The doses of antibiotic prophylaxis administrated in this study were metronidazole 500 mg, gentamicin 80 mg, penicillin 2 million units, amoxicillin 500 mg, amoxicillin/clavulanate 1.2 g, ampicillin 1 g, cloxacillin 1 g, cefazolin 1 g, cephalexin 1 g, cefotaxime 1 g, ceftriaxone 2 g, ceftazidime 1 g, cefdinir 100 mg, cefoxitin 1 g, ofloxacin 200 mg, norfloxacin 400 mg, cotrimoxazole 480 mg, chloramphenical 1 g, fosfomycin 1 g, clindamycin 600 mg, and amikacin 500 mg.

Table 1: The association between selected risk factors and surgical site infections

Risk factors	N	Infection	Rate*	Relative risk			
				Crude	95% CI	Adjusted**	95% CI
Duration of antibiotic prophylaxis							
None	167	5	3.0	1.00	Reference	1.00	Reference
1 day	1159	12	1.0	0.34	0.12–0.97	0.30	0.10–0.89
>1 day	813	9	1.1	0.36	0.12–1.09	0.29	0.09–0.92
Duration of operation							
≤ 1.0 hour	1738	16	0.9	1.00	Reference	1.00	Reference
>1.0 hour	401	10	2.5	2.75	1.24–6.11	3.29	1.44–7.52
Age							
1–20 years	808	6	0.7	1.00	Reference	1.00	Reference
21–40 years	853	14	1.6	2.23	0.85–5.83	2.15	0.82–5.68
41–60 years	382	5	1.3	1.77	0.54–5.85	1.91	0.57–6.48
>60 years	96	1	1.0	1.41	0.17–11.81	2.11	0.22–20.76
Type of operation							
Elective	591	9	1.5	1.00	Reference	1.00	Reference
Emergency	1548	17	1.1	0.72	0.32–1.62	0.78	0.33–1.83
Total	**2139**	**26**	**1.2**	**-**	**-**	**-**	**-**

* Rate = # infections/100 operations

**Adjusted for sex, age, length of preoperative stay, type of operation, ASA score, and duration of operation

Table 2: Characteristics of antibiotic prophylaxis administration

Characteristics	Number	%	Infection	Rate*
Antibiotic prophylaxis (N = 2139)				
No	167	7.8	5	3.0
Yes	1972	92.2	21	1.1
Time of first antibiotic dose administration (N = 1972)				
>1 hour preoperatively	1004	50.9	8	0.8
≤ 1 hour preoperatively	767	38.9	9	1.2
Intraoperatively	47	2.4	0	0.0
Postoperatively	154	7.8	4	2.6
Antibiotic agent (N = 1972)				
Combination Metronidazole and Gentamicin	1266	64.2	13	1.0
Single dose combination	766	38.8	8	1.0
Combination within 1 day	130	6.6	1	0.8
Combination > 1 day	370	18.8	4	1.1
Others**	706	35.8	8	1.1
Single dose	108	5.5	2	1.9
Multiple dose or combination within 1 day	155	7.9	1	0.6
Combination > 1 day	443	22.4	5	1.1
Duration of antibiotic prophylaxis*** (N = 2139)				
None	167	7.8	5	3.0
1 day	1159	54.2	12	1.0
>1 day	813	38.0	9	1.1

* Rate = infections/100 operations

** Others: Penicillin, amoxicillin, amoxicillin/clavulanate, ampicillin, cloxacillin, cefazolin, cephalexin, cefotaxime, ceftriaxone, ceftazidime, cefdinir, cefoxitin, ofloxacin, norfloxacin, cotrimoxazole, chloramphenical, fosfomycin, clindamycin, and amikacin.

*** Median = 1 day (interquartile range 1–2 days)

Efficacy of antibiotic prophylaxis

Antibiotic prophylaxis was associated with decreased risk of SSI, while timing of administration – preoperatively vs. intraoperatively – had no effect on risk. Compared with no antibiotic prophylaxis, receiving one-day, or multiple-day antibiotic prophylaxis was each associated with about one third of the SSI risk, adjusted RR were 0.30 (0.11–0.88) and 0.32 (0.10–0.98), respectively (Table 3). This reduced risk was also found when receiving only a single dose of metronidazole in combination with gentamycin (adjusted RR = 0.28 (0.09–0.90)), Data on duration, administration time, and antibiotic agent associated with SSI, adjusted for age, sex, ASA score, and duration of operation, are shown in Table 3.

Discussion

This prospective cohort study conducted in eight Thai hospitals showed that a prolonged duration of operation was a significant risk factor for SSI among patients undergoing appendectomy. Conversely, antibiotic prophylaxis was inversely related to the risk of SSI in such uncomplicated appendicitis patients. Single-day antibiotic prophylaxis was found to be as effective as multiple-day antibiotic prophylaxis in reducing SSIs and administering prophylaxis before the incision or intraoperatively did not affect the risk. A combined single dose of metronidazole and gentamicin seemed sufficient to reduce risk of SSI in uncomplicated appendicitis patients.

Study strengths and weaknesses

The strengths of this study are its large sample size and prospective cohort design with complete early follow-up. Furthermore, we were able to include all patients admitted with uncomplicated appendicitis, who underwent open surgery in all of the eight hospitals.

Among the study limitations was the failure to account for differences in surgical technique, preoperative and post-operative practices. However, appendectomies are performed quite uniformly in Thailand and we consider large variation in these practices unlikely. Owing to high cost of post-discharge surveillance, we were unable to follow all patients for 30 days after surgery. Curtailed follow-up may cause underestimation of the SSI rate. Still, the SSI rate in our study (1.2%) was similar to that observed in the NNIS system report (1.3%) [2]. Some SSIs were potentially misclassified when the exact layer of tissue or organ/space involved in the infection was unclear. To limit such misclassification, an expert was consulted in these cases. In addition, the surgeon and at least one person from the infection control team had to agree to the diagnosis and classification of SSI in all cases.

Risk factors

A prolonged duration of operation has been reported as a risk factor for SSI in other studies [1,23,24]. Earlier investigations have also reported increasing age [25], and emer-

Table 3: Association between surgical site infections and duration, timing, and antibiotic prophylaxis agent, adjusted for age, sex, ASA score, and duration of operation

Predictor variable	N	Infection	Rate*	Relative risk			
				Crude	95% CI	Adjusted**	95% CI
Duration of antibiotic prophylaxis							
None	167	5	3.0	1.00	Reference	1.00	Reference
1 day	1159	12	1.0	0.34	0.12–0.97	0.30	0.10–0.88
>1 day	813	9	1.1	0.36	0.12–1.09	0.32	0.10–0.98
Time of first antibiotic dose administration							
None	167	5	3.0	1.00	Reference	1.00	Reference
>1 hour preoperatively	1004	8	0.8	0.26	0.08–0.81	0.22	0.07–0.70
≤ 1 hour preoperatively or interoperation	814	9	1.1	0.36	0.12–1.09	0.33	0.11–1.02
Postoperatively	154	4	2.6	0.86	0.23–3.28	0.78	0.20–3.00
Antibiotic agent							
None	167	5	3.0	1.00	Reference	1.00	Reference
Single dose combination metronidazole and gentamicin	766	8	1.0	0.34	0.11–1.06	0.28	0.09–0.90
Combination metronidazole and gentamicin within 1 day	130	1	0.8	0.25	0.03–2.18	0.22	0.03–1.98
Combination metronidazole and gentamicin > 1 day	370	4	1.1	0.35	0.09–1.34	0.29	0.08–1.12
Others***	706	8	1.1	0.37	0.12–1.15	0.37	0.12–1.15

* Rate = infections/100 operations

** Adjusted for age, sex, ASA score, and duration of operation

*** Others: Penicillin, amoxicillin, amoxicillin/clavulanate, ampicillin, cloxacillin, cefazolin, cephalexin, cefotaxime, ceftriaxone, ceftazidime, cefdinir, cefoxitin, ofloxacin, norfloxacin, cotrimoxazole, chloramphenical, fosfomycin, clindamycin, and amikacin.

gency surgery [26] as risk factors of SSI. Our study did not show substantial association between these factors and the risk of SSI. Under-accounting for other predictors of SSI not included in our analysis might explain our failure to observe an association between age or emergency surgery and SSI.

The use of antibiotic prophylaxis

Twenty-one different antibiotic agents were administered to appendectomy patients in our study, highlighting the lack of consensus among Thai surgeons in prescribing practices. Metronidazole plus gentamicin were most commonly used agents, and our study confirmed their effectiveness in reducing SSIs reported by others [18,19]. The prophylaxis was effective despite the fact that timing of prophylaxis followed international guidelines in only 39% of the cases [27,28]. This finding corroborates the notion that the timing of the administration – pre-, intra- or post-operation – may not be crucial for preventing SSIs [1]. At the same time, higher SSI rate was reported among patients who received antibiotic prophylaxis after surgical incision [29], probably because the antibiotic serum concentration at the surgical closure is strongly associated with SSI [30].

The American Society of Health System Pharmacists (ASHP) [27] recommends prophylaxis with cephalosporins for uncomplicated appendicitis [27,28], with metronidazole and gentamicin only considered an alternative in cases of penicillin allergy. However, the combination of metronidazole plus gentamicin may have an economic advantage. A Thai study indicated that the estimated cost for these combined agents was 210 baht per 24 hours, compared with 1160 baht for cefoxitin [31]. Adverse effects were not documented for our patients.

Extended duration of antibiotic prophylaxis was less frequent in our study than in a Malaysian study [32], but our finding is consistent with other studies conducted in France [8] and Spain [9].

The improper use of antibiotic agents and inappropriately prolonged duration of antibiotic prophylaxis are likely to cause antimicrobial resistance [33-38]. Surgeons and surgical departments need to update their practices of antibiotic prophylaxis to comply with standard guidelines [27,28] and updated evidencebase [1].

Efficacy of antibiotic prophylaxis

Antibiotic prophylaxis is associated with a decreased risk of postoperative SSIs. This finding is in agreement with other studies [4,14-19]. In addition, our data indicate that in uncomplicated appendicitis cases, one-day antibiotic prophylaxis is just as effective in reducing SSIs as multiple-day antibiotic prophylaxis. Thus, our study does not offer justification for routine administration of oral antibiotics upon hospital discharge as in a previous study [39]. Furthermore, our findings correspond to findings in other reports [27,40], a single-dose antibiotic [40], such a combined a single dose of metronidazole and gentamicin, was efficient to reduce SSIs in uncomplicated appendicitis [27].

Conclusion

A prolonged duration of operation was associated with increased risk of SSI among appendectomy patients, while antibiotic prophylaxis was associated with decreased risk. A combined a single dose of metronidazole and gentamicin administered preoperatively or intraoperatively appears sufficient to reduce SSIs in patients with uncomplicated appendicitis. We recommend that preoperative antibiotic prophylaxis be administered to all patients undergoing appendectomy.

Abbreviations

SSI Surgical site infection

NNIS National Nosocomial Infection Surveillance

ASA American Society of Anesthesiologists

RR Relative risk

CI Confidence intervals

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

HTS, NK and MN conceptualized the study. NK and the Surgical Site Infection Study Group assisted with the data collection. NK was responsible for data management and data analysis. HTS, NK, MN and HCS were responsible for interpretation of data. HTS, MN, HCS, SJ and VC provided advice and review. NK, HTS, MN, HCS, SJ and VC collaboratively wrote the manuscript. All authors read and approved the final manuscript.

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