

Efficacy of Short-Term versus Long-Term Post-Operative Antimicrobial Prophylaxis for Preventing Surgical Site Infection after Clean Neurosurgical Operations

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Objective: Surgical site infection (SSI) is a problem constantly uppermost in the minds of all surgeons, although the actual rate of occurrence is only 1–5% in general surgery. In neurosurgical fields, there have been a few papers published about efficacy of post-operative antimicrobial prophylaxis (PAMP) to prevent SSI, compared to well known effectiveness of pre-operative antibiotics. Thus, infection rates of short-term PAMP groups and those of long-term PAMP groups were investigated to evaluate the effectiveness of PAMP and the efficacy of short-term PAMP compared to long-term PAMP for prevention of SSI.

Methods: Between April 2010 and April 2012, we retrospectively analyzed the data of 35 patients in the aneurysmal neck clipping groups (short-term PAMP group: PAMP for 3 days and fewer, long-term PAMP group: PAMP for 10 days and more) and 79 patients in the microdissectomy groups (short-term PAMP group: 3 days and fewer, long-term PAMP group: PAMP for 6 days and more).

Results: In aneurysmal neck clipping groups, SSI occurred 23.1% of short-term PAMP group and 9.1% of long-term PAMP group ($p=0.3370$). And in microdissectomy groups, SSI occurred 6.7% of short-term PAMP group and 4.1% of long-term PAMP group ($p=0.9840$).

Conclusion: There is no significant difference between the short-term PAMP group and the long-term PAMP group in terms of SSI, regardless of operation type. We therefore suggest that short-term PAMP usage could be an appropriate therapy for preventing SSI in clean neurosurgical operations.

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KEY WORDS: Antibiotic prophylaxis · Surgical wound infection · Neurosurgical procedure.

Introduction

Surgical site infection (SSI) is a problem constantly uppermost in the minds of all surgeons, although the actual rate of occurrence is only 1–5% in general surgery.^{7,9)} SSI leads to increases in the cost of care as well as, prolonged hospital stays. Furthermore, in the field of neurosurgery, SSI may result in increased morbidity and mortality, or may induce critical neurologic deficits that have a direct impact on quality of life.

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It is well known that pre-operative antimicrobial prophylaxis (AMP) can reduce SSI acquired at the time of surgery and has been routinely employed in many surgical fields.^{1,2,3,15)} However, in neurosurgical field post-operative antimicrobial prophylaxis (PAMP) has been employed practically to cover the SSI not only acquired at the time of surgery but also after the surgery. In other surgical fields short-term PAMP (PAMP for less than one day) was recommended instead of long-term PAMP (PAMP for more than one week), because long-term PAMP may induce numerous side effects such as hypersensitivity reaction or increasing prevalence of antibiotic-resistant bacteria.¹¹⁾ Few papers have been published about the efficacy of short-term PAMP to prevent SSI in neurosurgical field. Despite general recommendation of short-term PAMP, prolonged antibiotic use is still common-

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ly reported in clinical settings in our neurosurgical community. To evaluate the effectiveness of PAMP and the efficacy of short-term PAMP compared to long-term PAMP for prevention of SSI, we performed a retrospective study analyzing the rates of occurrence of SSI with short-term PAMP compared to those of long-term PAMP after clean, elective neurosurgical operations.

Materials and Methods

Patients

Between April 2010 and April 2012, operations were performed under general anesthesia in a total of 639 patients at our institute. Out of these patients, excluding patients who underwent emergency surgery, we selected 134 patients of elective aneurysmal neck clipping in brain surgery and microdiscectomy in spine surgery upon whom the uniform standard surgical protocol was performed. Of these group, only patients who were treated with prophylactic antibiotics and showed no pre-operative infection signs of infection were eligible for the study. Patients were excluded if they 1) were prescribed post-operative antibiotics for a duration inappropriate to our criteria; 2) were received previous antibiotic injections for any reason prior to the operation except AMP; 3) had, pre-operatively, other confirmed infections (e.g., urinary tract infection or upper respiratory infection); 4) expired within 30 days after the operation (Figure 1). After application of all exclusion criteria, there were 35 patients in the aneurysmal neck clipping group (Group A) and 79

patients in the microdiscectomy group (Group B). Each group was further subdivided into two subgroups (A1, A2, B1 and B2) according to the duration of PAMP. There were the short-term groups (group A1: PAMP for 3 days and fewer and group B1: PAMP for 3 days and fewer) and the long-term groups (group A2: PAMP for 10 days and more and group B2: PAMP for 7 days and more). We retrospectively analyzed the data from those 114 patients to investigate the incidence of SSI and to evaluate the efficacy of reducing post-operative prophylactic antibiotics. Surgical wound follow-up continued until 30 days after operation.

Infection definition

We determined SSI using the diagnostic criteria of SSI defined by the United States Centers for Disease Control and Prevention (US CDC), which include localized signs including operation site pain, tenderness, swelling, redness, and wound discharge and categorized into deep, superficial and organ SSI (e.g., meningitis, peridural abscess in brain surgery or discitis, peridural abscess in spine surgery).^{13,15)}

Aseptic techniques, pre-procedural preparation

All operative procedures were performed in one operation room according to our aseptic operative protocols. Hand and forearm antiseptic scrubbing of surgeon was performed for more than 3-minutes before aseptic surgical attire was done. The incision area was initially scrubbed with 7% betadine soap and then widely and meticulously prepared and painted with a solution of 80% alcohol and 10% beta-

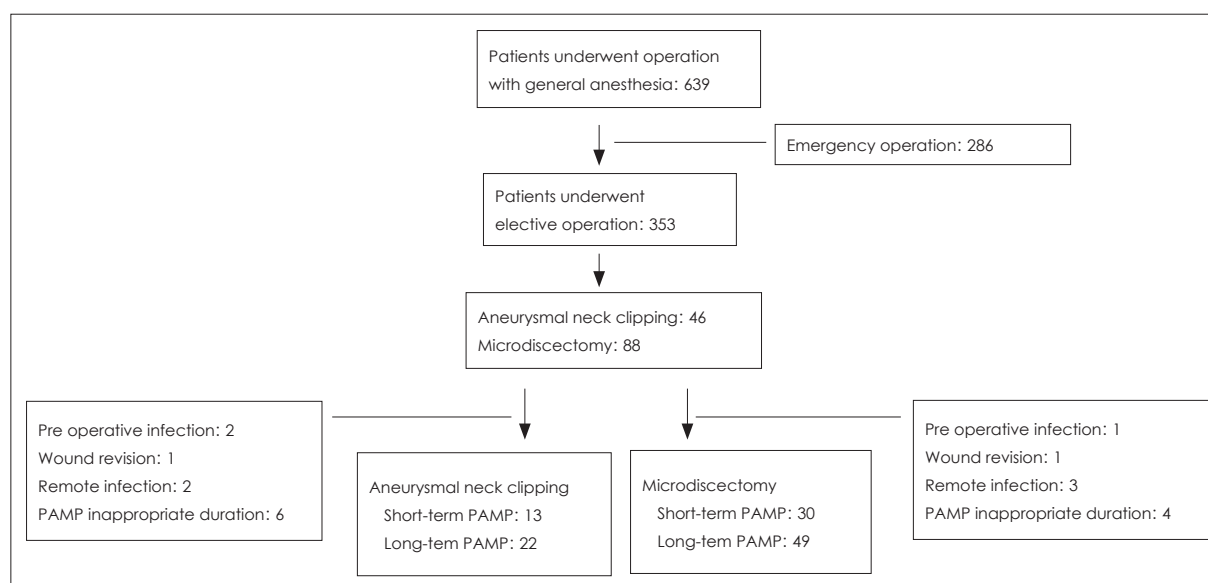


FIGURE 1. Patient population profile. PAMP inappropriate duration: patient who prescribed post-operative antibiotics from 4 days to 9 days after surgery in aneurysmal neck clipping group and patient who prescribed post operative antibiotics from 4 days to 6 days after surgery in microdiscectomy group. PAMP: post operative antimicrobial prophylaxis.

dine. In cases of brain surgery, hair-shaving was performed immediately before the surgery by doctors directly in the operating room. A single dose of pre-operative prophylactic antibiotic (the same antibiotic that was prescribed after the operation) was injected into all patients within 1–2 hours prior to the surgery, and an additional dose was injected every 4 hours if the operation required a prolonged procedure.^{6,15)}

Antibiotics

Before April 2011, empirically the patients who underwent brain surgery were treated with a prophylactic 3rd generation cephalosporin, twice a day (2,000 mg every 12 hr) for 10 days or more (13 days, on average) and those who underwent spine and/or peripheral surgery were treated with a 1st generation cephalosporin, three times a day (1,000 mg every 8 hr) for about 7 days after operation as per routine.^{15,16,21)} However after May 2011, when the Health Insurance Review and Assessment service, a national institute of public health in our country, recommended short-term use of post-operative antibiotics to prevent overuse, we discussed with department of infectious diseases in our institute about reducing usage of PAMP and decided to implement PAMP for maximum 3 days after surgery. Thus, we prescribed 2nd generation antibiotics, twice a day (1,000 mg every 12 hr) to almost all patients for 3 days and fewer for prophylaxis after clean, elective surgery. In cases of post-operative SSI, antibiotics were changed following determination of susceptibility and used for more than 3 days until the infection was completely controlled.

Statistical analysis

Categorical variables were compared using Fisher's exact test or the chi-square test, and continuous variables were compared using the Student's *t*-test. A *p* value of less than 0.05 was considered having significance. Statistical analysis was performed with STATA/SE 11.0 (StataCorp LP, College Station, TX).

Results

Incidence of SSI

Group A: Aneurysmal neck clipping group

Baseline characteristics, such as sex, age, underlying disease (diabetes mellitus, hypertension, and obesity), and smoking history were similar in the two subgroups. In addition, there was no significant difference between the two subgroups with regard to the mean duration of the operation

(Table 1). SSI occurred in three of 13 patients (23.1%) in group A1 and two of 22 patients (9.1%) in group A2 (Table 3). However, there was no statistically significant difference in the rate of SSI between the two subgroups (*p*=0.3370).

Group B: Microdiscectomy group

As with group A, there were no statistically significant dif-

TABLE 1. Demographic data of aneurysmal neck clipping group

	Group A1 (n=13)	Group A2 (n=22)	<i>p</i> -value
Sex			0.2925
Men	6	6	
Women	7	16	
Age	49.17 ± 11.04	54.67 ± 9.90	0.1507
Hypertension			0.7260
Present	5	7	
Absent	8	15	
Diabetes mellitus			0.5193
Present	0	2	
Absent	13	20	
Smoking history			0.4630
Yes	3	9	
No	10	13	
BMI	22.65 ± 3.10	23.11 ± 2.27	0.6126
Operation time	418.46 ± 107.28	363.41 ± 102.16	0.1399

Continuous variables are expressed as mean ± standard deviation, A1: aneurysmal neck clipping with short-term PAMP group, A2: aneurysmal neck clipping with long-term PAMP group. BMI: body mass index, PAMP: post-operative antimicrobial prophylaxis

TABLE 2. Demographic data of microdiscectomy group

	Group B1 (n=30)	Group B2 (n=49)	<i>p</i> -value
Sex			0.1739
Men	19	22	
Women	11	27	
Age	51.17 ± 15.77	50.67 ± 13.77	0.8842
Hypertension			0.2416
Present	7	19	
Absent	23	30	
Diabetes mellitus			0.9077
Present	5	10	
Absent	25	39	
Smoking history			0.5558
Yes	8	9	
No	22	40	
BMI	24.32 ± 3.18	24.40 ± 3.95	0.9284
Operation time	148.67 ± 89.80	141.22 ± 87.81	0.7180

Continuous variables are expressed as mean ± standard deviation, B1: microdiscectomy with short-term PAMP group, B2: microdiscectomy with long-term PAMP group. BMI: body mass index, PAMP: post-operative antimicrobial prophylaxis

ferences in baseline characteristics in the two subgroups (Table 2). SSI occurred in 6.7% in group B1 and 4.1% in group B2 (Table 3). No statistically significant differences were found between two subgroups in SSI ($p=0.9840$) (Table 3).

Surgical site infected patients

There were five surgical site-infected patients in group A (Table 4) and four patients in group B (Table 5). The mean ages was 55.1 years and male to female ratios of surgical site-infected patients was 1:3, respectively. Two of the surgical site-infected patients had underlying diabetes mellitus, and 4 of the 9 patients had a smoking history. 89% of infected patients (8 of 9) were obese or overweight (BMI: body mass index for Asian population, underweight <18.5, normal: 18.5–22.9, overweight: ≥ 23 , obese class I: 25.0–29.9, obese class II: ≥ 30). The average operation time of infected pa-

tients in group A was 429 minutes, which was longer than the average operation time of the entire group A (383.86 minutes, on average) (Figure 2). The average operation time of infected patients of group B (190 minutes) was longer than the entire group B's mean operation time (144.05 minutes) (Figure 3).

Discussion

Many reports discuss the prevention of SSI, and these reports reveal the importance of such factors as pre-operative AMP, length of hospital stay, hair removal, skin preparation techniques, operating time, surgeon's skills, antisepsis and sterile post-operative wound care techniques in reducing SSI.^{10,15,19,20,22} Among these factors, surgical antimicrobial prophylaxis, in particular, has been shown to reduce the incidence of post-operative neurosurgical wound infections in numerous randomized clinical trials.^{1,2,4,19} Korinek et al,¹² for example, reported that AMP in neurosurgical operations to be effective in preventing

TABLE 3. Distribution patterns of surgical site infected patients

	Group A1 (n=13)	Group A2 (n=22)	p-value
Infection			
Present	3	2	
Absent	10	20	
Rate	23.1%	9.1%	0.3370
	Group B1 (n=30)	Group B2 (n=49)	p-value
Infection			
Present	2	2	
Absent	28	47	
Rate	6.7%	4.1%	0.9840

A1: aneurysmal neck clipping with short-term PAMP group, A2: aneurysmal neck clipping with long-term PAMP group, B1: microdisectomy with short-term PAMP group, B2: microdisectomy with long-term PAMP group, PAMP: post-operative antimicrobial prophylaxis

TABLE 4. Characteristics of SSI patient in aneurysmal neck clipping group

Case	Group	Sex	Age	Infection type	Operation time	DM	Smoking	BMI
1	A1	M	43	D	10 hr	N	N	29.41
2	A1	F	52	S	8 hr 25 min	N	Y	20.60
3	A1	F	25	S	5 hr	N	N	26.58
4	A2	F	67	D	7 hr 20 min	Y	Y	23.18
5	A2	F	61	S	5 hr	N	Y	28.11

A1: aneurysmal neck clipping with short-term PAMP group, A2: aneurysmal neck clipping with long-term PAMP group, M: male, F: female, DM: diabetes mellitus, BMI: body mass index, D: deep infection, S: superficial infection, Y: yes, N: no, PAMP: post-operative antimicrobial prophylaxis, SSI: surgical site infection

TABLE 5. Characteristics of SSI patient in microdisectomy group

Case	Group	Sex	Age	Infection type	Operation time	DM	Smoking	BMI
6	B1	M	62	S	5 hr 10 min	N	N	26.06
7	B1	F	58	D	3 hr 25 min	N	N	26.24
8	B2	F	61	D	2 hr 15 min	Y	Y	25.15
9	B2	F	67	S	1 hr 50 min	N	Y	35.03

B1: microdisectomy with short-term PAMP group, B2: microdisectomy with long-term PAMP group, M: male, F: female, DM: diabetes mellitus, BMI: body mass index, D: deep infection, S: superficial infection, Y: yes, N: no, PAMP: post-operative antimicrobial prophylaxis, SSI: surgical site infection

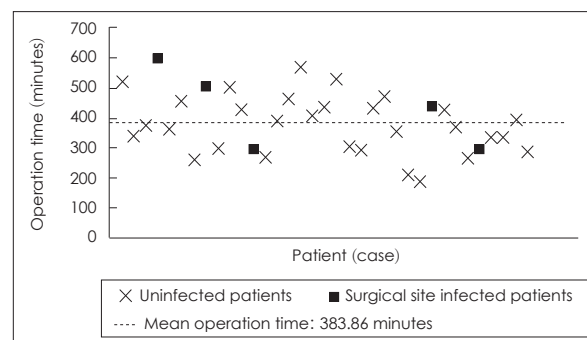


FIGURE 2. Operation time of group A.

surgical site infections even in patients at low risk of infection. AMP decreased infection rates from 9.7% to 5.8% in all patients ($p < 0.0001$) and from 10.0% to 4.6% in low risk patients ($p < 0.0001$). Most SSI is acquired at the time of surgery and main role of pre-operative antibiotics is to reduce the bacterial infection before and during surgery. However, some of SSI such as meningitis is not acquired at the time of surgery. Thus, the rationale of using PAMP is to reduce SSI which is not acquired at the time of surgery compared to pre-operative antibiotics which cover only SSI acquired at the time of surgery. Nevertheless, the use of prophylactic antibiotics in neurosurgical field has long been controversial.^{4,5,8,11,14,17} And, to our knowledge, there have been no recent studies performed in neurosurgical field to evaluate the efficacy of PAMP.

According to our results, in the aneurysmal neck clipping groups the infection rate of the short-term PAMP group (23%) was higher than that of the long-term PAMP group (9%). Similarly, in the microdissectomy groups, the infection rate of the short-term group (7%) was higher than that of the long-term group (4%). Overall, the reason why our study shows higher infection rate than the average of 1–5% in general surgery is that even if the standard of infection has been adhered to diagnostic criteria of US CDC, the analysis criteria included the suspected infection as well as the definite proven infection.^{7,9,18} However, there was no statistically significant difference between the two groups in SSI development ($p = 0.3370$; $p = 0.9840$). And, there was an obvious difference in infection rate between short-term PAMP and long-term PAMP groups of aneurysmal neck clipping patients. Maybe the reason is that precise comparison is not able to be acquired due to the small sample size. Therefore, further studies with bigger sample size will be needed.

The results of the analysis presented here suggest that short term PAMP could be appropriate for patients who undergo aseptic operation with clean elective neurosurgical procedures such as aneurysmal neck clipping or microdissectomy. However, these results cannot be considered representative of all neurosurgical operations. And it is difficult to extrapolate from this study whether short-term PAMP for SSI is appropriate in all neurosurgical fields. The results of our study show only that short-term PAMP could be appropriate compared to long-term PAMP in clean elective neurosurgical operations.

The characteristics of wound-infected patients may be important to consider for determining how long PAMP should be prescribed (Table 4, 5). Long-operation time is a well-known risk factor for SSI.²² It cannot be overlooked that, in the present study, a larger portion of surgical site

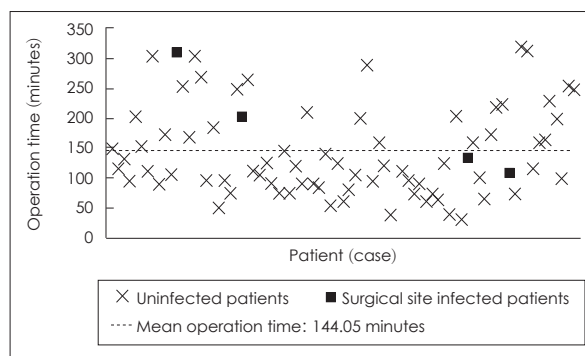


FIGURE 3. Operation time of group B.

infected patients (5 of 9) had a long operation compared to the average of uninfected patients although there was no statistical significance. In cases of surgical site-infected patients in the aneurysmal neck clipping group, 3 of 5 patients had a long time operation (60%). Similarly, about half of the wound-infected patients in group B had a longer operation time than average. Other risk factors for SSI include obesity, smoking history, and underlying diseases such as diabetes mellitus.^{13,15} The sample size of the wound-infected patients in both groups was not large enough to achieve the estimated power in statistical evidence in this study. However, wound-infected patients in the current study have at least two risk factors on average. For example, patient No. 1 was obese and underwent a long operation, while patient No. 4 was a heavy smoker who had diabetes mellitus as an underlying disease. He also underwent an operation with a longer duration than the mean operation time (Table 4). Similarly, among the patients of group B, patient No. 6 was obese and underwent a long operation (Table 5). Although we were unable to provide statistical evidence of this hypothesis, our results suggest that, even in clean neurosurgical procedures, patients who undergo unexpectedly long operations and have at least one risk factor such as old age, obesity, diabetes mellitus, or smoking history might be considered for treatment with long-term antimicrobial prophylaxis (Figure 2).

Conclusion

There were no significant differences between the short-term PAMP groups and the long-term PAMP groups in the incidence of SSI. We therefore suggest that short-term PAMP usage is an appropriate regimen for preventing SSI in clean, elective neurosurgery. However, further study is needed to address this issue in high-risk patients who undergo long operation and/or have underlying risk factors.

■ The authors have no financial conflicts of interest.

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