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Prophylactic Antibiotic Administration for Prevention of Surgical Site Infection in Urological Laparoscopic Surgeries

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ABSTRACT

Background: The purpose of this study is to investigate the occurrence of surgical site infection (SSI) in our cases after laparoscopic surgery with prophylactic antibiotics administration (PAA) of 1-2 days or 3 days duration. Methods: Two hundred and nine patients were enrolled in this study. SSIs were categorized as urinary tract and/or wound infection. Laboratory data relating to infection such as serum white blood cell (WBC) and C-reactive protein (CRP) were investigated after surgeries and compared to the data before surgeries. Data were collected and analyzed retrospectively. Results: There were 4 SSI patients in total. SSI was 4/125 (3.2 %) cases of PAA of 1-2 days (shorter) duration patients and there was 0/84 (0 %) of PAA of 3 days (longer) duration. Longer group showed the tendency of lower SSI ratio even though the difference did not reach statistically significant (p=0.0978) because of small number of SSI cases and ratios. Change of serum WBC at 4th day from pre-surgery was significantly suppressed in longer group than shorter group. Conclusions: Our data showed 3-days of PAA might be better to be selected according to the cases especially such as, for instance, immune-compromised hosts. Future prospective study with more number of patients may be necessary for further evaluation.

INTRODUCTION

Laparoscopic surgery has become standard in the urological field for kidney, prostate, and bladder surgery. Laparoscopic surgery is in general minimally invasive for patients and may offer a shorter duration of hospitalization and less need for pain relief. In addition, it should provide a lower rate of surgical site infection (SSI) occurrence. This could be partly because of the smaller wound and lower blood loss from laparoscopic surgery.

In this situation, prophylactic antibiotic administration (PAA) is generally used for prophylaxis for infections complication (21) but there is a tendency to give patients a longer duration of PAA than guidelines recommendation (18). Guidelines suggest that prophylactic

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administration for this purpose can be stopped within 48-72 hours after surgery. First or 2nd generation cephalosporines or penicillins with beta-lactamase inhibitors are one of the recommendations and are widely used (12). Some reports have found a 1-2 % SSI occurrence in urological laparoscopic surgery with PAA (21, 22), and an outcome may be similar to open surgery.

In our country, surgical training system has been changed (that is, training as a general resident for 2 years after graduation from medical school) and the medical environment has changed due to increases in medical lawsuits. This may have inclined physicians to use longer duration PPA, especially in the physicians who do not know or understand the guidelines.

This study investigated retrospectively the relationship between the duration of PAA and the occurrence of SSI in urological laparoscopic surgeries using clinical markers related to infections especially comparing the within 2 days of PAA with 3 days of PAA.

METHODS

Patients and SSI

Urological laparoscopic surgeries were performed and data were gathered from the Department of Urology, Kobe University Hospital. The patients who were given 1-3 days of PAA in the study period (from January 2008 to December 2010) were selected. Sugeries included laparoscopic nephrectomy and nephroureterectomy, retroperitoneoscopic nephrectomy and nephroureterectomy, laparoscopic adrenalectomy, laparoscopic partial nephrectomy and retroperitoneoscopic partial nephrectomy, laparoscopic or retroperitoneoscopic pyeloplasty, and laparoscopic prostatectomy. Details are shown in Table I.

Table I. Patients' backgrounds

	Longer duration group*	Shorter duration group*	p-value
N	84	125	
Age (median)	25-87(64)	18-83(65)	0.1382
Diseases			
Renal tumor	37	44	0.1988
Adrenal tumor	18	19	0.2507
Prostate cancer	17	42	**0.0329****
Urotherial cancer	9	16	0.6469
Retroperitoneal tumor	1	2	0.8051
Uretero-pelvis junction obstruction	1	2	0.8051
Others	1	0	0.2214

*Longer duration group: the patients group with 1-2 days -antibiotic administration
*Shorter duration group : the patients group with 3 days -antibiotic administration
**Bold: Statistically significant

Surgical procedure were performed via 3 ports in adrenalectomy, 3-4 ports in nephrectomy, nephroureterectomy or pyeloplasty, and 5 ports in laparoscopic prostatectomy. As preventative measure for infectious complication, no preoperative shaving was undertaken, sterilization by iodine based disinfectant were performed preoperatively, and we

covered the surgical wound by wound-membrane dressing. Surgical staplers were removed as a rule at a week after surgery.

SSI after laparoscopic surgeries was defined according to Centers for Disease Control (CDC) guidelines (6, 20) as infection occurring within 30 days after the operation. In addition, the laboratory data relating to infections (serum white blood cells (WBC) and C-reactive protein (CRP)) were examined. In detail, data the next day after surgery (day 1), day 4, and day 7 were taken and compared with the day before surgery. We used as a rule 4 kinds of antibiotics for preventing SSI: cephazolin (CEZ), sulbactam/ampicillin (SBT/ABPC), cefotiam (CTM), or tazobactam/piperacillin (TAZ/PIPC). The details are shown in Table II. We correlated sex, age and the kind of prophylactic antibiotics used with SSI and the laboratory data relating to infection mentioned above in our analyses.

Table II. Prophylactic antibiotics and duration of administration

	Longer duration group**	Shorter duration group**	Total	p-value
SBT/ABPC*	45	71	116	0.682
CEZ*	18	18	36	0.1993
CTM*	12	23	35	0.4165
TAZ/PIPC*	4	4	8	0.5754
others	5	9	14	0.715
Duration of Antibiotic administration				
1 days	0	6	6	
2 days	0	119	119	
3 days	84	0	84	

*SBT/ABPC: sulbactam/ampicillin; CEZ: cefazolin; CTM: cefotiam; TAZ/PIPC: tazobactam/piperacillin
**Longer duration group: the patients group with 1-2 days -antibiotic administration
**Shorter duration group : the patients group with 3 days -antibiotic administration

Statistical analyses

Statistical analyses were performed by student-t tests using JSTAT (Java Virtual Machine Statistics Monitoring Tool) with $p < 0.05$ considered to indicate statistical significance.

RESULTS

Patient characteristics

Of the 209 patients we examined in this study, 81 patients were diagnosed with renal tumor, 59 with prostate cancer, 37 with adrenal tumor, and 25 with urothelial cancer. The details are shown in Table I. There were some clean-contaminated cases in both shorter and longer duration of PAA groups but the distribution was not significantly different ($p > 0.05$) (data not shown).

Prophylactic antibiotic administration (PAA)

SBT/ABPC was most often used as prophylactic antibiotics for the prevention of SSIs after surgery. The details of the antibiotics used are shown in Table II.

SSI occurrence and PAA

Patients took from 1 to 3 days of antibiotics; the median was 2 days. Therefore, we divided the patients into 2 groups: 1) longer duration antibiotics (3 days) and 2) shorter duration antibiotics (1-2 days) and compared SSI occurrence between these 2 groups. The patients' backgrounds and prophylactic antibiotics according to this category were shown in Table I and II. We had 4 SSI occurrences in all 209 laparoscopic surgeries; 1) 0/84 cases (0 %) in longer PAA group and 4/125 cases (3.2 %) in shorter PAA group, and this difference was not statistically significant partly because of small number of SSI cases and ratios (p=0.0978). In 4 cases of SSI of shorter PAA group, SBT/ABPC was used in 3 cases (Table III). Details of SSI cases were shown in Table IV. They were recovered by the switch to 3rd or 4th generation of cephalosprines or to carbapenems and/or ureteral stenting.

Table III. Prophylactic antibiotics in SSI cases

	Longer duration group**	Shorter duration group**	Total
SSI*	0	4	4
CEZ*	0	1	1
CTM*	0	0	0
SBT/ABPC*	0	3	3
others	0	0	0

*SSI: surgical site infection; CEZ: cefazolin; CTM: cefotiam; SBT/ABPC: sulbactam/ampicillin
**Longer duration group: the patients group with 1-2 days -antibiotic administration
**Shorter duration group : the patients group with 3 days -antibiotic administration

Table IV. SSI cases

	Infection (occurrence date) (operation)	PAA*
case 1	infection in bladder-urethral anastomostic part (unknown) (radical prostatectomy)	CEZ (shorter PAA**)
case 2	wound infection (5POD***) (nephroureterectomy)	SBT/ABPC (shorter PAA)
case 3	wound infection (3POD) (partial nephrectomy)	SBT/ABPC (shorter PAA)
case 4	pyelonephritis (5POD) (nephroureterectomy)	SBT/ABPC (shorter PAA)

PAA*: prophylactic antibiotic administration
shorter PAA**: shorter duration of prophylactic antibiotic administration
POD***: post-operation day

Laboratory data change

In addition, we analyzed the laboratory data regarding infections such as serum white blood cell (WBC) and C-reactive protein (CRP) at day 1, 4, and 7 after surgery and compared with the data before surgery. The change of serum WBC at day 4 from the date of pre-surgery was suppressed significantly in longer PAA group (p=0.0006) and on the contrary that of CRP at day 1 was suppressed in shorter group from unknown reasons (p=0.0144) (Table V).

Table V. Comparison data of serum WBC and CRP before and after surgery

	before-surgery	1st day*		4th day*		7th day*	
WBC(/mm^3)			p-value**		p-value		p-value
longer group***	5752±1558	8826±2507		6366±1793		6421±2027	
shorter group***	5902±1597	9502±2419	0.0541	7365±2178	**0.0006**	6807±1634	0.2209
CRP(ug/ml)							
longer group	0.1989±0.2521	4.709±3.045		5.208±4.149		2.084±2.676	
shorter group	0.2546±0.7464	3.636±3.069	**0.0144**	6.117±4.410	0.1521	2.645±2.554	0.2049

*1st day: 1st day after surgery
p-value: Statistics is from the comparison between longer group and shorter group with serum WBC and CRP change from pre-surgery data.
***Longer duration group: the patients group with 3 days -antibiotic administration
***Shorter duration group : the patients group with 1-2 days -antibiotic administration
Bold: Statistically significant

DISCUSSION

Laparoscopic surgeries have become widespread in the urological field. They involve less stress to patients (16) and should offer a lower rate of SSI occurrence and post-surgical complications than open surgery. They are considered beneficial to patients so that it has been accepted and spread in a way (3,5,13) including oncological safety (2,17). Howard et al. compared SSI occurrence between open surgery and laparoscopic surgery and concluded that laparoscopic surgery for colorectal resection showed lower SSI than open surgery, and that longer surgical time was one of the risks for SSI (7). Our case showed the surgical time did not affect SSI occurrence (data not shown). On the contrary, Montgomery et al. stated that wound infections may occur less frequently with hand-assisted laparoscopic surgery (HALS) than with open surgery but more often than with standard laparoscopic surgery (14). Nakamura et al. suggested that it was advisable to select the laparoscopic surgical approach and to undertake high-pressure washing of the wound just before closure of the abdomen wound in order to prevent wound infection after surgery for colorectal cancer (15).

Regarding the duration of prophylactic antibiotic administration (PAA), Takeyama et al. stated that in their clean or clean-contaminated urological laparoscopic surgery series the comparison of 1-day PAA with 3-day PAA had no apparently significant difference as to SSI occurrence (21). Moreover, as to the kind of PAA, even though the recommendation in the

guideline exits, there were no prospective investigations of comparison or 2-arms study to our knowledge (12). George et al. stated that in their transperitoneal urological laparosopic surgery series there were 2.5 % cases of SSI and body mass index and operative time were significant predictive factor for SSI occurrence (4). However, our data showed the trend that longer PAA had lower SSI than shorter PAA even though the difference did not reach statistical significance. We need to pay attention to the caution of statistical analyses; this is because the SSI case number and ratio is generally so small that it could not be easy to have statistical significance from the characteristics and limit of statistics. In this situation, there is still a lack of evidence showing how much and how long PAA should be performed (12), even though guidelines were established in 2007 in our country. There are few studies comparing shorter or less amounts of PAA with longer or greater amounts of PAA in laparoscopic urologic surgeries as mentioned above (12). The recommendations may be based on single studies of PAA in laparoscopic urologic surgery or comparison studies between laparoscopic and open urologic surgery (9). Therefore, the results in the current study may provide some evidence of utility of longer duration of PAA even though it differs from the conclusions of several studies. Our next study will utilize for instance the comparison of one day with 2-day duration of PAA with the single kind of prophylactic antibiotics.

The selection of antibiotics should be based on the surgical pollution category. For instance, a different kind of antibiotics should be used in laparoscopic nephrectomy and nephroureterectomy because the latter could be clean-contaminated surgery (11). Importantly, the targeted bacteria may be mainly gram-positive bacteria in the former (clean) but mainly both gram-positive and negative in the latter. Our cases included clean-contaminated cases and there was no significant difference between longer and shorter PAA groups as to surgical pollution category (data not shown).

The guidelines and our study include the antibiotics with beta-lactamase inhibitors (12) and this might be based on the increase and spread of extended spectrum beta-lactamase (ESBL) producing bacteria. However, especially in clean surgery such as laparoscopic nephrectomy or adrenalectomy, the target bacteria to be inhibited are largely gram-positive bacteria as mentioned above. ESBL-producing bacteria are considered in most cases to be gram-negative bacteria such as *Escherichia coli* or *Klebsiella* (1). Clean-contaminated surgery cases which open urinary tract and especially the cases with urinary tract infections might need antibiotics with beta-lactamase inhibitor while other cases may use 1^{st} or 2^{nd} generation cephalosporins (12).

On the other hand, Kusachi et al. concluded that shorter duration of PAA (18.2 ± 2.7 hours) showed significantly higher ratio of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated SSI occurrence after digestive surgery than longer duration groups (96.1 ± 11.2 hours or 66.9 ± 11.1 hours) (10). In different viewpoints, Steiner et al. stated that prophylaxis by 1 g ceftriaxone offer pharmacoeconomic advantage in transperitoneal open nephrectomy (19). Our cases included 2 wound infection cases and they were caused by MRSA and the kind of PAA was SBT/ABPC and the duration of PAA was 2 days in both cases, suggesting MRSA isolation might be assumed especially in wound infection.

Our data on surgical time showed no definite influence on SSI occurrence. This conclusion varies from other studies (8), suggesting urological laparoscopic surgeries may give low stress under safe surgery regardless of surgical time.

CONCLUSION

The current study suggested that 3 days duration of PAA for urological laparoscopic surgery tended to suppress SSI occurrence (0 %) and serum WBC elevation at day 4 after surgery compared to 1-2 days of PAA (4/125: 3.2 %), suggesting that 3-days of PAA might be better to be selected according to the cases especially for instance such as immune-compromised hosts. Future prospective study with more number of patients may be necessary for further evaluation.

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