J Infect Chemother (2007) 13:172–176
DOI 10.1007/s10156-007-0514-y

ORIGINAL ARTICLE

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Success of countermeasures against respiratory infection after digestive surgery by strict blood and fluid resuscitation

Received: January 4, 2007 / Accepted: February 19, 2007

Abstract This prospective controlled study included 5859 cases of digestive surgery from September 1987 to August 2002. The study was divided into six 2.5-year periods, A–F. During and after period B, cefazolin was used for surgery of the esophagus, stomach, and gall bladder, and cefotiam for colon resection, hepatectomy, and pancreatectomy. During period A, total parenteral nutrition (TPN) was administered for 6 (±4.6) days before surgery, on average. During and after period B, TPN was confined to patients who were incapable of oral intake. During thoracic esophageal cancer surgery, frozen plasma was administered at 10 ml/h, colloid osmotic pressure was maintained, and water was prevented from accumulating in the third space. Mechanical respiratory support was not needed during or after period B. The incidence rate of respiratory infection decreased to 1.7% during period A, and to 0.7%–1.1% during and after period B. During and after period B, in particular, early respiratory infection cases after surgery decreased significantly to 0.1%–0.3%. In period A, among the respiratory infectious bacteria isolated, MRSA was the most frequent, followed by *Pseudomonas aeruginosa*. After period B, *P. aeruginosa* was the most frequent bacterium isolated. Over all periods, there was no significant difference in resistant ratios in *P. aeruginosa*. Because of consistent infusion management during the perioperative period, artificial breathing became unnecessary and, as a result, the prevalence of early respiratory infection decreased significantly.

Key words Respiratory tract infection · Ventilator-associated pneumonia · MRSA · Digestive tract surgery · SSI · Postoperative infection

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Introduction

Many measures for protection against surgical site infections after digestive surgery have been discussed.[1,2] However, although cases of respiratory infection after surgery are not frequent, these cases are very severe and refractory, which makes prognosis after surgery very difficult. Methicillin-resistant *Staphylococcus aureus* (MRSA) and multiple-drug-resistant *Pseudomonas aeruginosa* (MDRP) are often isolated from the patient's airways.[3] Furthermore, any respiratory tract infection becomes a source of hospital infection. Accordingly, such cases are very important, and could result in the success or failure of the prevention of hospital infection.

Most respiratory infection cases are so-called ventilator-associated pneumonia (VAP). Although a cross-infection measure for patients managed by artificial breathing is discussed in the Infectious Disease Society of America (IDSA) guidelines and the American Thoracic Society (ATS) guidelines, and there are VAP guidelines from various standpoints from the Centers for Disease Control and Prevention (CDC) and the Healthcare Infection Control Practices Advisory Committee (HICPAC), there are few reports of measures that have been successful in significantly decreasing VAP. We implemented various measures against the occurrence of MRSA in the 1980s, and were able to keep the isolation rate of MRSA at less than 1% of all infections after all digestive surgery.[4] Among these measures, the implementation of measures against respiratory infection after surgery was the most difficult. Here, we report that respiratory infection after digestive surgery has decreased significantly as a result of the measures implemented against infection over a period of 15 years.

Methods

This study included 5895 surgical patients who underwent digestive tract surgery from September 1987 to August 2002. The details of the patients and the procedures used are given in Table 1. Respiratory infection after surgery was defined as cases that presented an infiltrating shadow on a chest X-ray film and general infectious signs, including fever, increased white blood cell count, and elevated levels of C-reactive protein (CRP), according to the National Nosocomial Infections Surveillance (NNIS) System criteria.[5] The analytical data acquired from respiratory isolates from sputum and other respiratory materials that could be fully evaluated were combined, and the drug susceptibilities of MRSA and *Pseudomonas aeruginosa* (*P. aeruginosa*) in particular were compared according to the Clinical and Laboratory Standards Institute (CLSI) criteria.

The study was divided into six 2.5-year periods, A–F, and a comparative investigation was conducted. The selection of drugs and the methods of administration of prophylactic antibiotics (which has been reported elsewhere[4]) are described below.

In period A, the third-generation cephems (a subgroup of β-lactam antibiotics, including cephalosporins and cephamycins) and aminoglycoside drugs were administered, and the duration of medication was 11.4 (±3.7) days, on average. During and after period B, cefazolin was selected for use with surgery of the upper digestive organs, including esophageal resection and gastrectomy, as well as the gall bladder, and cefotiam was selected for colon resection, hepatectomy, and pancreatectomy. During period B, the duration of administration of prophylactic antibiotics was shorter, 5.1 (±1.4) days, and was gradually shortened still further. During period F, the duration of administration of prophylactic antibiotics was only 1.3 (±0.3) days.

In period A, total parenteral nutrition (TPN) was administered before gastrectomy and esophageal resection, as follows. For cases of esophageal cancer and gastric cancer, TPN using a commercial formulation was administered at 40.0 Kcal/day as 91.6 ml/day for 6 (±4.6) days, on average.

During and after period B, TPN administration before surgery for esophageal and stomach cancer patients was confined to those patients who were unable to receive oral nutrition. TPN was administered for 8 (±2.2) days, on average. The infusion volume was reduced to 72.4 (±4.9) ml/h, targeted to a urine specific gravity of 0.012–0.020. During thoracic esophageal resection, 10 ml/h fresh frozen plasma (FFP) was administered in order to maintain colloid osmotic pressure and prevent pulmonary edema.[4] During and after period D, instead of FFP, methyl predonine was administered at 12.5 mg/kg in order to prevent water from accumulating in the third space.[6]

In period A, prophylactic mechanical respiratory support after the operation was provided for patients with thoracic esophageal resection, but during and after period B, the infusion therapy described above was conducted, and mechanical respiratory support after surgery became unnecessary.

During and after period B, the volume of infusion was strictly controlled in nutrition management after thoracic esophageal resection.

Regarding the arrangement of patients' rooms in the surgical ward, in period A, patients with infection after surgery and patients in the terminal stage of a malignant tumor were accommodated in a recovery room of the surgical ward, but from periods B to D, the recovery room was used only for patients after surgery under general anesthesia and those needing breathing management (excluding patients needing short-term breathing management after prolonged general anesthesia). Patients with any infection and patients in the terminal stage of a malignant tumor were excluded from this type of recovery room.[4] However, in period E, our hospital had no choice but to accommodate patients with respiratory infections in the surgical ward in order to enhance the emergency medical services of the hospital. Although it was regrettable, in period F the hospital selected patients to occupy the recovery room. However, because the surgical indications for thoracic esophageal cancer were changed in 2003, cases of thoracic esophageal cancer are not included in this study. Given this background, the incidence time and rate of respiratory infection after surgery, the complications after surgery, the respiratory bacteria isolated and the drug resistance to them, and the death rate were all considered.

Statistical analyses were done using Student's *t*-test, the χ^2 test, and Fisher's exact test. Differences were considered to be statistically significant at $P < 0.05$.

Results

There were no significant differences in disease between cases with each disease (Table 1). There was no significant difference in the incidence of postoperative infection over all periods (Table 2). During period A, all cases who underwent esophagectomy, gastrectomy with thoracotomy, or hepatectomy were treated under mechanical respiratory support. During and after period B, all the patients in this study were treated under spontaneous respiration with nasal oxygen therapy. Mechanical respiratory support was not needed during or after period B.

There were two types of postoperative respiratory tract infection. Early respiratory tract infection occurred after respiratory distress following surgery, and the early respiratory infection after surgery (referred to as early respiratory infection) occurred, on average, 2.3 (±1.8) days after surgery (Table 3). Respiratory infection complicated by multiple organ failure (MOF) caused by serious intraabdominal infection due to suture insufficiency of the digestive tract (referred to as late respiratory infection) occurred, on average, 23.1 (±11.9) days after surgery. In period A, the incidence of respiratory infection after surgery was 1.7% (14/833), and of these cases, the rate of early respiratory infection was 1.3% (11/833), and the rate of late respiratory infection was 0.4% (3/833). During and after period B, but excluding period D, respiratory infection after surgery decreased significantly to 0.7%–1.1%. During and after period B, early respiratory infection decreased significantly to 0.1%–0.2% compared with period A. There was no significant difference in the incidence of late respiratory infection between period A and periods B to E.

Table 1. Operative sites and diseases found in the patients studied

Organ	Disease	Period					
		A	B	C	D	E	F
Esophagus	Tumor	21	19	18	15	16	17
	Others	1	1	1	4	0	0
Stomach	Tumor	194	186	181	159	178	184
	Others	33	39	18	31	21	24
Liver	Tumor	7	11	15	18	15	14
	Others	4	0	0	0	0	0
Gallbladder	Stone	137	199	203	201	277	321
	Tumor	7	9	7	7	8	8
Pancreas	Tumor	12	12	16	17	14	13
	Others	0	0	0	3	0	0
Colon	Tumor	135	185	216	228	211	234
	Perforation	17	18	15	16	10	14
	Others	2	3	3	2	5	8
Appendix		153	217	129	125	182	259
Other		110	95	83	92	106	165
Subtotal		833	899	905	918	1043	1261
Total							5859

Table 2. Incidence of postoperative infections

Infectious sites (incidence)	Period					
	A(833) 12.9%(108)	B(899) 11.1%(100)	C(905) 10.9%(99)	D(918) 12.0%(110)	E(1043) 13.7%(143)	F(1261) 10.9%(136)
SSI	8.9%(74)	8.6%(77)	8.2%(74)	9.6%(88)	11.1%(116)	9.8%(123)
Sup. SSI	6.4%(52)	6.5%(59)	5.7%(52)	6.9%(63)	7.0%(73)	6.7%(84)
Deep SSI	2.6%(22) (4[a])	2.0%(18) (3[a])	2.4%(22) (3[a])	2.3%(25) (4[a])	3.2%(33) (6[a])	2.6%(33) (5[a])
Resp.	1.7%(14) (4[a])	0.7%(7) (3[a])	0.8%(7) (2[a])	1.0%(9) (4[a])	1.1%(11) (5[a])	0.7%(9) (4[a])
Cath.	2.0%(17)	1.7%(15)	2.1%(19)	2.3%(21)	1.8%(19)	0.6%(7)
UTI	1.2%(10)	0.9%(8)	1.2%(11)	1.4%(13)	1.1%(11)	0.6%(7)
EC	1.2%(10) (1[a])	0	0	0	0.2%(2)	0
MRSA inf.	4.1%(34) (4[a])	0.2%(2) (2[a])	0.2%(2) (2[a])	0.4%(4) (3[a])	2.7%(28) (6[a])	1.4%(18) (5[a])
Fatal rate	0.6%(5)	0.3%(3)	0.3%(3)	0.4%(4)	0.6%(6)	0.3%(4)

SSI, surgical site infection; Sup., superficial; Resp., respiratory tract infection; Cath., catheter-related infection; UTI, urinary tract infection; EC, enterocolitis; inf., infections

[a], fatal cases

Table 3. Incidence of postoperative respiratory tract infection (September 1987 to August 2002)

Cases with surgery	Period						
	A 833	B 899	C 905	D 918	E 1043	F 1261	Statistics
Early RI	1.3%(11)	0.1%(1)	0.1%(1)	0.2%(2)	0.2%(2)	0.2%(2)	A:B–F $P < 0.05$
Late RI	0.4%(3)	0.6%(5)	0.7%(6)	0.8%(7)	0.9%(9)	0.6%(7)	NS
Case with res. dis.	0	0.7%(1)	0	0	0	0	
Total incidence	1.7%(14)	0.7%(7)	0.8%(7)	1.0%(9)	1.1%(11)	0.7%(9)	A:B,C,E,F $P < 0.05$

RI, respiratory tract insfection. dis., respiratory disease

In period A, MRSA and *P. aeruginosa* were commonly isolated from patients who developed postoperative respiratory infection (Table 4). During and after period B, the incidence of MRSA decreased slightly compared with that in period A, but was not significantly different. During and after period B, *P. aeruginosa* was the commonest cause of postoperative respiratory infection. Throughout all periods, 6.3% (1/16) of isolated MRSA had a strain resistant to arbekacin, but no strain resistant to vancomycin or teicoplanin. Among 32 strains of isolated *P. aeruginosa* in period A, 36.4% (4/22) of strains isolated soon after surgery had resistance to imipenem. Among 37 strains of *P. aeruginosa* isolated from late respiratory infections, 37.8% (14/37) showed resistant properties, but there was no significant difference between strains isolated early and late after surgery.

Table 4. Changes in bacterium isolated from respiratory tract

Strain	Phase					
	A 31	B 11	C 16	D 11	E 15	F 14
MRSA	45.2%(14)	9.1%(1)	12.5%(2)	18.2%(2)	20.5%(3)	14.3%(2)
P. aeruginosa	25.8%(8)	45.5%(5)	37.5%(6)	72.7%(8)	46.7%(7)	42.9%(6)
Klebsiella spp.	6.5%(2)	18.2%(2)	12.5%(2)	9.1%(1)	0	7.1%(1)
Enterococcus spp.	6.5%(2)	9.1%(1)	6.3%(1)	0	13.3%(2)	14.3(2)
Acinetobacter spp.	3.2%(1)	0	6.3%(1)	0	6.7%(1)	7.1%(1)
Citrobacter spp.	3.2%(1)	0	0	0	6.7%(1)	7.1(1)
Other bacterium	3.2%(1)	9.1%(1)	12.5%(2)	0	6.7%(1)	0
Candida spp.	6.4%(2)	9.1%(1)	12.5%(2)	0	0	0

P. aeruginosa, Pseudomonas aeruginosa

Discussion

Much of the postoperative infection after digestive tract surgery is surgical site infection.[1,2] There are only a small number of cases of respiratory tract infection after digestive tract surgery, but they are serious and have resistant bacteria,[3] Furthermore, because they would become a reservoir of hospital infection, their prevention is very important. However, there have been extremely few reports of measures that have resulted in a significant decrease in respiratory tract infections after surgery.

We experienced a rapid increase in MRSA in the late 1980s, and we changed the prophylactic antibiotics for surgery after implementing many measures in an attempt to decrease MRSA infections. Furthermore, we reduced the incidence of postoperative MRSA infections significantly by recognizing the importance of implementing measures against respiratory infection.[4] Our use of perioperative antibiotic therapy has been introduced into many medical institutes in Japan.[7] After that, we were successful at keeping the respiratory infection rate below 1.1% in all patients who underwent digestive surgery over a period of 15 years. The most frequent cause of respiratory infection after digestive surgery is VAP. Of the available measures for the prevention of VAP, only management in single rooms and the implementation of measures against cross-infection have been widely used, but VAP cannot be reduced significantly and continuously with these measures.

Given this fact, we developed a management procedure which would be effective in preventing respiratory infection after digestive surgery, so that respiratory failure after surgery could be prevented and mechanical respiratory support would become unnecessary.[4] Because respiratory failure tends to occur after thoracic esophageal cancer surgery and stomach cancer surgery involving thoracotomy, we attempted a consistent management procedure throughout the periods before, during, and after surgery to prevent respiratory failure as a measure against infection. We paid particular attention to the management of intravenous infusion during the perioperative period.

We assumed that if an intravenous high-calorie infusion is given to a patient suffering from inadequate nutrition and who had a low level of plasma albumin before surgery, the volume of water in the third space would increase and could cause respiratory failure after surgery. Therefore, we prevented water from accumulating in the third space by reducing the total dose of intravenous nutrition for 3 days immediately before surgery in cases that required TPN. During and after surgery, we attempted to maintain the colloid osmotic pressure using FFP made from the patient's own blood, which had been removed before surgery.

A further problem in preventing respiratory infection is that many cases are caused by drug-resistant bacteria. What is most important in implementing this measure is the selection of the appropriate prophylactic antibiotics.

First of all, we considered that it is important not to select a broad-spectrum drug, which has the risk of inducing a microbial substitution phenomenon in the airway. Although there has been no report of microbial substitution in the airway induced by an antibacterial drug, Takahata et al.[8] examined the multiplication of MRSA within the intestine of an MRSA-carrying rat, and showed that MRSA does not grow in response to the administration of cefazolin or cefotiam, and we have previously reported that the growth of MRSA was reduced by the administration of cefazolin or cefotiam.

The arrangement of patients in the ward during the perioperative period is very important from the viewpoint of the prevention of infection caused by drug-resistant bacteria.

Irrespective of the existence or nonexistence of respiratory infection, during respiratory management we have basically kept patients in single rooms, or used shared rooms only for patients with similar conditions. Conventionally, in cases where bacteria that could be significant sources of hospital infection were isolated and signs of infection were observed, patients with respiratory infection have been managed in single rooms, or several patients with similar conditions have been in shared rooms. However, even if the signs of infection are not observed, patients exhaling bacteria which could be significant sources of hospital infection, including MRSA or MDRP, should be treated in the same way.

After cultivating the bacteria in a patient's respiratory secretions, any patient shown to be exhaling epidemiologically significant bacteria, including MDRP, is generally placed in a single room. However, it takes several days to obtain the results of a bacterial culture, and this measure against cross-infection, because it originates from the patient, is not implemented until the result is obtained. According to a recent report, hospital-acquired pneumonia cannot be prevented even if patients infected with respiratory MRSA are managed individually in a single room or collectively in a shared room.[9] In other words, even if the patients with a respiratory infection are separated from other patients, there is no reduction in the cases of respiratory cross-infection. We consider that patients receiving artificial breathing management by endotracheal intubation or by tracheotomy have a perpetual risk of respiratory infection and of becoming a source of cross-infection, and therefore they should be separated from other patients before the epidemiologically significant bacteria are isolated from the airway.

During and after period B, by designating the recovery room of the surgical ward as an uncontaminated area, and restricting the movements of patients with respiratory infections to that area, we were able to manage them in the intensive care unit (ICU) and in a unit for their exclusive use in the surgical ward.[4] However, in period E, because an emergency service was established and the recovery room of the surgical ward was used for the management of emergency inpatients, MRSA infection also spread among digestive surgery patients. After that, the use of the recovery room was strictly limited, and as a result the incidence of MRSA infection again decreased.

As described above, the incidence of pneumonia is high during respiratory management of patients, so they should be managed in a separate room whenever possible. On the other hand, it is extremely important to know the drug susceptibility of bacteria isolated from a respiratory infection in order to choose the appropriate treatment for a respiratory infection after surgery. In this study, among the bacteria isolated from respiratory infections after surgery, MRSA and *P. aeruginosa* were the commonest worldwide, as reported by many researchers.[10,11,12] In particular, most *P. aeruginosa* isolated long after the initial infection was imipenem-resistant. In practice, because it takes several days before the result of a drug-susceptibility test is obtained, when a respiratory infection has to be treated, an empirical therapy is adopted. In the case of a respiratory infection complicated by MOF, in particular, it is desirable to take into consideration the possibility of the presence of multidrug-resistant bacteria when selecting drugs.

With the methods described above, early respiratory infection can be prevented. However, the choice and implementation of measures against a late respiratory infection remain extremely difficult. As many studies have reported, in the case of patients who have developed MOF, a decrease in respiratory infection cannot be expected, because it is difficult to completely cure the primary infectious disease. Our fatal cases in period F had anastomotic leakage and postoperative abdominal abscess. They had been in a condition of multiple organ failure for a month, and we could not remove the source of infection.

This study was not a randomized control study. However, respiratory infection has a very strong tendency to cross-infection, and it is impossible to prevent cross-infection completely in a ward or in an ICU. Accordingly, when assessing measures as good or bad, it is inappropriate to distinguish between patients in the same ward during the same period. If there is no significant change in the contents of subject cases, surgical procedures, or surgeons, a historical study over a long period is considered to be an excellent way to approach the possible eradication of the affects of cross-infection.

This study has shown that changes in fluid resuscitation in the perioperative phase are effective against respiratory tract infection. However, the prevention of respiratory infection complicated by MOF is very difficult.

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