Modified Antibiotic Regimen for Pediatric Complicated Appendicitis to Reduce Infectious Morbidity in Taiwan

We compared our previous hospital-based antibiotic protocol and an optimum modified one by reviewing hospital records of children younger than 18 years with complicated appendicitis between 2010-2016. The modified protocol showed no infectious morbidity, which is significantly different from that of our previous protocol (mortality rate, 21.4%). An optimum hospital-based antibiotic protocol for complicated appendicitis can reduce the infectious morbidity rate without increasing hospital cost.

Keywords: *Abscess, Cost, Emergency, Management*.

The infection rate of appendicitis may increase to up to 23% when perforation occurs [1]. A 3-antibiotic regimen (cefmetazole, gentamycin, and metronidazole) was in use in our hospital to decrease postoperative infection. However, wound infection and intra-abdominal abscess were noted in some cases of complicated appendicitis (perforated or gangrenous appendicitis). We found that 29% of our patients had a positive *Pseudomonas sp.* culture of the appendix that was not covered by the above three antibiotics. We switched our antibiotic regimen to piperacillin and tazobactam and metronidazole, based on bacterial cultures sensitivity tests of all complicated appendicitis cases in our hospital. This new regimen, followed by oral ciprofloxacin, has been in use in our department since April, 2013. Standardized guidelines for patient care can help reduce infectious morbidity [2]. We assumed that this protocol would decrease the infectious complication rate. However, its net cost is higher than that of the old protocol. Thus, we aimed to investigate the differences in hospitalization duration and cost between the previous and new antibiotic protocols.

This study was approved by the Research ethics review committee of our hospital. Charts of all patients (aged younger than 18 years (n=87) who presented to our department from January, 2010 to August, 2016 with complicated appendicitis were reviewed retrospectively. Laparoscopic appendectomy was performed with a 7-mm Jackson-Pratt drainage tube in all patients. A 3-antibiotic regimen, followed by an oral antibiotic, was employed before April, 2013, thereafter, pipiracillion- tazobactam and metronidazole, and subsequent oral ciprofloxacin were used. Patients were divided into two groups according to their antibiotic regimen *viz*. Group 1 patients received three antibiotics (cefmetazole 25 mg/kg 6-hourly, gentamycin 2.5 mg/kg 12-hourly, and metronidazole 10 mg/kg 8-hourly). Group 2 patients received piperacillin-tazobactam 112.5 mg/kg and metronidazole 10 mg/kg 8-hourly, followed by oral ciprofloxacin. Antibiotics were administered intravenously until patients were afebrile for >24 hours and their appetite had recovered. All patients were followed up in our outpatient department until full recovery.

Hospital costs in this study are estimates based on the current pricing in our institution. The expense excluded the cost of emergency room (ER) services and imaging studies performed in the ER, and was calculated in United States dollars. Unpaired 2-tailed Student t-test and chi-square test were used to compare data between both groups. P <0.05 was considered significant. All analyses were performed using SPSS version 20.0. (IBM Corp., Armonk, NY).

The patient demographics and clinical outcomes are presented in ***Table* I**. The durations of intravenous and oral antibiotics in group 2 were 3.95 and 5.8 days, respectively. Nine patients in group 1 developed postoperative complications, including 7 wound infections and 2 intra-abdominal abscesses (P<0.0001 when compared to group 2). Three of these patients visited the ER because of a wound infection or postoperative fever. The two patients with intra-abdominal abscess were re-admitted. Therefore, the total admission duration ranged from 4-16 (mean, 8.89) days. The total cost increased significantly to $3613.34 (mean, $1824.00; P=0.03) in patients with infectious

Table I Characteristics of Children With Complicated Appendicitis

Characteristics	*Group 1 (n=42)*	*Group 2 (n=45)*
Age, y	11 (4.13)	11 (3.87)
Weight, kg	42.49 (18.72)	42.78 (16.64)
Males	57%	64%
CRP, mg/dL	13.81 (11.26)	12.78 (10.14)
Admission, d	7 (1.93)	6.84 (1.25)
Total cost USD*	1507.5 (498.7)	1579.09 (457.3)
Infection[#]	9 (21.4)	0

CRP: *C-reactive protein*; **Cost per patient; all P>0.05 except* [#]*P<0.0001.*

complications compared to patients who recovered uneventfully.

The study limitations were the retrospective, single-centre design and small sample population. Piperacillin-tazobactam has been recently demonstrated to be as efficacious as traditional 3-antibiotic therapy [4,5].

The daily costs of receiving intravenous antibiotics in our hospital in group 1 and 2 were $18.27 and $88.73, respectively, for a child weighing 40 kg. However, we found no difference in cost with the optimum regimen, which is mainly related to the significant decrease in infectious morbidity. Group 2 patients did not require further antibiotic treatment and hospitalization. Generally, the cost of managing infectious complications was significantly higher in our study than in previous studies [6]. Therefore, we have improved the quality of our medical care by the decreasing infection rate without increasing cost.

It is important to use an effective empirical antibiotic to control severe infection, but at the same time, we should prevent antibiotic resistance. Therefore, our principle is to monitor the duration of antibiotic use, which can reduce the possibility of resistance [7]. Therefore, piperacillin-tazobactan was not used for >7 days in our patients.

We suggest that bacterial culture and sensitivity tests should be performed for every case of complicated appendicitis, and antibiotic protocol guided by these reports. Reducing postoperative infectious morbidity in complicated appendicitis using an optimum hospital-based antibiotic protocol can reduce hospital stay without increasing expenses.

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