

Antibiotic use in patients with abdominal injuries: guideline by the Korean Society of Acute Care Surgery

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Purpose: A task force appointed by the Korean Society of Acute Care Surgery reviewed previously published guidelines on antibiotic use in patients with abdominal injuries and adapted guidelines for Korea.

Methods: Four guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation II instrument. Five topics were considered: indication for antibiotics, time until first antibiotic use, antibiotic therapy duration, appropriate antibiotics, and antibiotic use in abdominal trauma patients with hemorrhagic shock.

Results: Patients requiring surgery need preoperative prophylactic antibiotics. Patients who do not require surgery do not need antibiotics. Antibiotics should be administered as soon as possible after injury. In the absence of hollow viscus injury, no additional antibiotic doses are needed. If hollow viscus injury is repaired within 12 hours, antibiotics should be continued for ≤ 24 hours. If hollow viscus injury is repaired after 12 hours, antibiotics should be limited to 7 days. Antibiotics can be administered for ≥ 7 days if hollow viscus injury is incompletely repaired or clinical signs persist. Broad-spectrum aerobic and anaerobic coverage antibiotics are preferred as the initial antibiotics. Second-generation cephalosporins are the recommended initial antibiotics. Third-generation cephalosporins are alternative choices. For hemorrhagic shock, the antibiotic dose may be increased twofold or threefold and repeated after transfusion of every 10 units of blood until there is no further blood loss.

Conclusion: Although this guideline was drafted through adaptation of other guidelines, it may be meaningful in that it provides a consensus on the use of antibiotics in abdominal trauma patients in Korea.

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INTRODUCTION

Surgical site infection is a common complication after abdominal trauma and is associated with an increase in morbidity, mortality, and hospital stay, and the appropriate use of antibiotics for abdominal trauma is essential in decreasing surgical site infection. However, in the absence of a hollow-viscus injury, no additional antibiotics are warranted. In addition, the overuse of antibiotics is problematic, because systemic inflammatory response syndrome due to injury is often mistaken for infection in the acute phase. Therefore, it is essential for clinicians to have a guideline regarding antibiotic use in patients with abdominal trauma.

Since 2012, the Korean government has implemented a national trauma system including 17 level I trauma centers. Evidence-based protocol-driven care can ensure optimal comprehensive care for injured patients, but a lack of consensus regarding trauma management is problematic. In particular, there are limited data supporting the use of antibiotics for patients with abdominal trauma. Although the Eastern Association for the Surgery of Trauma (EAST) practice management guideline (PMG) was published in 2012, the recommendations were made only for patients with penetrating abdominal trauma [1]. Therefore, the Korean Society of Acute Care Surgery (KSACS) developed the Korean guideline for antibiotic use in abdominal trauma patients. The purpose of this guideline is to evaluate and adapt previous guidelines of antibiotic use in abdominal trauma through the guideline adaptation method using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument [2].

These guidelines target trauma patients with abdominal

injury, including abdominal penetrating injury as well as blunt injury, and were designed for trauma surgeons and emergency medicine doctors, who make the initial decision to administer antibiotics. Detailed information about antibiotic use will promote the understanding of infection prevention and control in trauma patients by other clinicians who work within multidisciplinary team settings, including infection specialists and nurses who care for trauma patients.

METHODS

Organization of the committee

In 2014, the KSACS appointed a task force to develop practice management guidelines. This task force included members of the clinical research committee, as well as general surgeons from regional trauma centers. The purpose of this project was to develop practice guidelines for antibiotic use in abdominal trauma patients.

Selection of key questions

The task force divided topics of consideration into 5 categories: indication for antibiotic use, time to first antibiotic use, duration of antibiotic therapy, appropriate antibiotics, and antibiotic use in abdominal trauma patients with hemorrhagic shock. Key questions to be addressed were formulated for each category. The selected key questions are listed in Table 1.

Literature search and quality assessment

The task force searched guidelines published until 2014 about antibiotic use for abdominal trauma patients through MEDLINE, Embase, and GIN (Guideline International Net-

Table 1. Recommendation summary

Key question	Recommendation
Who is indicated for antibiotic therapy?	1. Patients requiring surgery should be administered preoperative prophylactic antibiotics. (1A) 2. Patients not requiring surgery should not be administered antibiotics. (1A)
When should antibiotics be started?	3. Antibiotics should be administered as soon as possible after injury. (1C)
How long should antibiotic therapy be administered in abdominal trauma?	4. In the absence of hollow viscus injury, no additional doses of antibiotics are needed. (1A) 5. If hollow viscus injury is repaired within 12 hours, antibiotics should be continued for no more than 24 hours. (1A) 6. If hollow viscus injury is repaired after 12 hours, antibiotics should be limited to 7 days. (2C) 7. Antibiotics can be administered for more than 7 days if hollow viscus injury is incompletely repaired or clinical signs persist. (2C)
What are the appropriate antibiotics?	8. Broad-spectrum aerobic and anaerobic coverage antibiotics are preferred as initial antibiotics. (1A) 9. Second generation cephalosporin are the recommended initial antibiotics. (1B) 10. Third generation cephalosporins can be an alternative choice. (2B)
How should antibiotic therapy be modified for patients with hemorrhagic shock?	11. In patients admitted with hemorrhagic shock, the administered dose of antibiotics may be increased twofold or threefold and repeated after transfusion of every 10 units of blood until there is no further blood loss. (2B)

work). The keywords used were antibiotics, intra-abdominal infection, intra-abdominal injury, trauma, panperitonitis, and abdominal trauma. Finally, four guidelines [1,3-5] were selected and assessed by the AGREE II instrument [2]. Nine committee members evaluated the quality of these guidelines according to 23 steps of the AGREE II instrument. In consensus meetings and using recommendations of these four guidelines, committee members developed new guidelines concerning each key question.

Strength of recommendations and grade of evidence

The GRADE system was adopted in the present guidelines after review and revision by the committee members. This system uses 2 basic levels of recommendation (strong and weak) and four levels of evidence (high-quality, moderate-quality, low-quality, or very low-quality) (Table 2) [6].

RESULTS

I. Who is indicated for antibiotic therapy?

Recommendations

1. Patients who require surgery should be administered preoperative prophylactic antibiotics. (1A)
2. Patients who do not require surgery should not be administered antibiotics. (1A)

Evidence summary

The 2012 EAST PMG was the only guideline to address whether antibiotic administration was necessary in patients with abdominal trauma [1]. The mortality rate was reported as 65%–70% in the 1910s when antibiotics were not used after abdominal surgery [7]. In 1998, the EAST PMG committee reviewed 39 articles and recommended that single broad-spectrum antibiotics should be used in patients with penetrating abdominal trauma, and no additional dose of prophylactic antibiotic was needed in the absence of viscus perforation. Because it was reported that use of antibiotics with anaerobic coverage reduced postoperative infections, the 2000 EAST PMG recommended that prophylactic antibiotics to cover anaerobic organisms should be administered to patients with penetrating abdominal injury [8,9]. The 2000 EAST PMG noted that there was no comparative blind study on whether to use antibiotics for penetrating abdominal wounds, because of ethical issues caused by high mortality and morbidity rates in patients who were not administered antibiotics [9]. Therefore, the use of antibiotics in patients with penetrating wounds is considered standard. Most previous studies of prophylactic antibiotics have targeted patients with penetrating injuries, and this seems to be the reason prophylactic antibiotics are used primarily in

Table 2. Strength of recommendations and quality of evidence

Definition	
Level of recommendation	
1	Strong recommendation
2	Weak recommendation
Quality of evidence	
A	RCT
B	Downgraded RCT or upgraded observational studies
C	Well-done observational studies with control RCTs
D	Downgraded controlled studies or expert opinion based on other evidence

RCT, randomized controlled trial.

patients undergoing surgery. However, emergency laparotomy is not always performed in patients with blunt trauma, and in these cases, antibiotics are not generally used. Therefore, there is no evidence concerning the use of prophylactic antibiotics for patients with abdominal blunt trauma who do not require surgery.

II. When should antibiotics be started?

Recommendation

Antibiotics should be administered as soon as possible after injury. (1C)

Evidence summary

The only practice guideline to address the best timing of antibiotics administration was the 2012 EAST PMG [1]. Burke et al. [10] and Alexander et al. [11] performed animal research on the relationship between the timing of antibiotic administration and the incidence of staphylococcus infection, and reported that the therapeutic effect was greatest in the group administered antibiotics within 3 hours of the bacterial injection, especially when a therapeutic blood antibacterial level was reached before bacterial injection. This became the backbone study for the proposition that the earliest antimicrobial administration is the most effective to prevent surgical site infection. Fullen et al. [12] retrospectively analyzed 295 patients with abdominal penetrating injury to confirm the correlation between the occurrence of skin and intra-abdominal abscess and the timing of antimicrobial administration (preoperative, intraoperative, and postoperative groups), and showed that the preoperative group had a significantly lower infection rate than the other two groups (7% vs. 33% and 30%, respectively). Although there have been no other studies about this issue in abdominal trauma patients, the application of the same principle of antibiotic use is notable, and various studies

have reported that the early administration of antibiotics for complex and open extremity injuries reduced infectious complications [13]. Therefore, if emergent abdominal surgery is necessary, antibiotics should be administered preoperatively. In patients with intra-abdominal infection due to abdominal trauma, antibiotics should be started as soon as possible with identification of the contamination [4,5].

III. How long should antibiotic therapy be administered in abdominal trauma?

Recommendations

1. In the absence of hollow viscus injury, no additional doses of antibiotics are needed. (1A)
2. If hollow viscus injury is repaired within 12 hours, antibiotics should be continued for no more than 24 hours. (1A)
3. If hollow viscus injury is repaired after 12 hours, antibiotics should be limited to 7 days. (2C)
4. Antibiotics can be used for more than 7 days if hollow viscus injury is incompletely repaired or clinical signs persist in patients with traumatic abdominal injury. (2C)

Evidence summary

The EAST PMG committee reviewed articles from 1976 to 1997, and published PMG for prophylactic antibiotic use in penetrating abdominal trauma in 1998 [9]. Among these articles, Fabian et al. [14] reported a randomized controlled study that enrolled 515 patients in 1992, and showed that there was no major infection among 280 patients without hollow viscus perforation in spite of the preoperative single administration of prophylactic antibiotics. This study became the evidence that single prophylactic antibiotics should be used in abdominal trauma without viscus injury.

A number of studies have assessed the duration of antibiotic use, and the 1998 EAST PMG recommended that prophylactic antibiotics for penetrating abdominal injury should be used within 24 hours in the presence of hollow viscus injury [9,14-16]. Later, Kirton et al. [17] compared a 24-hour course and a 5-day course of ampicillin/sulbactam in a prospective randomized double-blind placebo-controlled study. It was confirmed that there was no significant difference in the infection rate between the 2 groups, and this became additional evidence of antibiotic use within 24 hours. The 2012 EAST guideline was updated with further research [1]. The guidelines for the prevention of infections associated with combat-related injury was published by the Infectious Disease Society of America (IDSA) and Surgical Infection Society (SIS) in 2011, and recommended that antibiotics be administered in penetrating abdominal injury with suspected or known viscus injury and soilage for 24 hours after prompt definitive washout [3,14,18].

According to the 2010 IDSA-SIS guideline for complicated

intra-abdominal infection, if hollow viscus injury caused by penetrating, blunt, and iatrogenic trauma is repaired within 12 hours, antibiotics should be administered within 24 hours, and if the injury is repaired after 12 hours, antibiotics could be administered during 4–7 days [4,19,20]. These results indicate that short-term antibiotic use is not appropriate in patients with infection beyond the initial site or in patients with a large amount of intra-abdominal infected fluid; instead of considering prophylactic antibiotic treatment for these patients, they should be treated with antibiotics according to established peritonitis treatment [20].

IV. What are the appropriate antibiotics?

Recommendations

1. Broad-spectrum aerobic and anaerobic coverage antibiotics are preferred as initial antibiotics. (1A)
2. Second generation cephalosporins are recommended as initial antibiotics. (1B)
3. Third generation cephalosporins are alternative choices. (2B)

Evidence summary

Several guidelines for prophylactic antibiotic use in patients with abdominal injury have emphasized broad-spectrum antibiotics to cover aerobic and anaerobic organisms [1,3,8]. In a randomized controlled trial in 1973, the kanamycin/cephalothin and the kanamycin/clindamycin regimens were compared. The kanamycin/clindamycin group, in which clindamycin was used for coverage of anaerobic bacteria, had a significantly lower infection rate than the kanamycin/cephalothin group (10% vs. 27%). This difference was caused by infection rates by anaerobic bacteria, which occurred in 2% of the clindamycin group and 21% of the cephalothin group [8]. The guidelines for the prevention of infections associated with combat-related injury recommended that the selected antibiotics should be effective for all predictable bacteria, able to cover all wound sites, and have a narrow spectrum [3]. Colon injury has the highest intra-abdominal infection rate, and anaerobic bacteria is most frequently isolated, which is identified 1,000–10,000 times more frequently than aerobic organisms [15].

Escherichia coli is the most common anaerobic bacteria, and it and *Bacteroides fragilis* occupy 20%–30% of stool weight. These 2 organisms are the most common sources of surgical site infection after colon surgery. Condon et al. [21] reported that the rate of surgical site infection was 39%, because the first generation cephalosporin used as prophylactic antibiotic was not effective against anaerobic bacteria such as *B. fragilis*. For this reason, exclusive use of first generation cephalosporins is not effective as prophylactic antibiotic, and antibiotics to cover anaerobic bacteria are essential in cases of colon injury.

Hofstetter et al. [22] compared the combination of aminoglycoside, ampicillin, and clindamycin with cefoxitin alone in 119 patients who underwent abdominal surgery due to traumatic injury, and reported that the rates of surgical site infection were similar in both groups (12% vs. 13%), indicating that the exclusive use of second generation cephalosporin was possible in these patients. The 2012 Surviving Sepsis Campaign guideline recommended that empiric broad-spectrum antibiotics should be generally administered to patients with severe sepsis, and combination antibiotic therapy could also be used [23]. However, compared with mono-antibiotic therapy, combination therapy in severe trauma patients had no additional benefit in the mortality rate and increased the risk of antibiotic resistance [18]. The risk of infection increased in an 'S' shape depending on the degree of injury in severe trauma patients, and longer use of prophylactic antibiotics might be required in these patients [24]. Additionally, mono-therapy with ertapenem, which was approved by U.S. Food and Drug Administration, had the same or superior efficacy in elective colon surgery compared to other combination therapy [25]. Moxifloxacin also showed equivalent efficacy with other combination therapies in patients with complicated intra-abdominal infection [26]. In addition, several meta-analyses comparing combination therapy with aminoglycosides and mono-therapy with beta lactam antibiotics reported that the addition of aminoglycoside had no additional benefit [15].

Although there have been no one-to-one comparative studies between second generation and third generation cephalosporins, when third generation cephalosporin was used, the rate of surgical site infection in elective colon surgery was 8%–19%. In addition, second generation cephalosporins were recommended as preoperative antibiotics for elective colon surgery [27], and as the basic antibiotic in combination therapy for complicated intra-abdominal infection [4,19]. If resistance to first or second generation cephalosporins increases gradually in hospitals, use of third generation cephalosporins is recommended. However, antibiotic resistance due to the general use of third and fourth generation cephalosporins should be seriously considered [28]. Prophylactic antibiotics should be selected according to the prevalence of antibiotic resistance in respective hospitals.

V. How should antibiotic therapy be modified for patients with hemorrhagic shock?

Recommendation

1. In patients admitted with hemorrhagic shock, the administered dose of antibiotics may be increased twofold or threefold and repeated after transfusion of every 10 units of blood until there is no further blood loss. (2B)

Evidence summary

Because of vasoconstriction and decrease of antibiotic transportation to peripheral tissues in patients with hemorrhagic shock, administration of an additional dose of prophylactic antibiotic is recommended [1]. In a study of 150 patients with abdominal trauma, Ericsson et al. [16] concluded that the use of high-dose amikacin significantly reduced infection in patients with a large amount of hemorrhage, and the infection rate was increased in trauma patients with a subtherapeutic blood level of antibiotics. This was the only study with a recommendation about antibiotic use in hemorrhagic shock, so the recommendation level is only 2B. The guidelines for the prevention of infections associated with combat-related injury in 2011 recommended that prophylactic antibiotics should be administered again in patients who undergo large transfusions (1,500–2,000 mL of hemorrhage) regardless of the timing of first administration [3]. However, that guideline was supported by not studies of spine and hip trauma rather than abdominal trauma [29,30]. Therefore, more evaluation will be needed to apply this recommendation to the present guideline, because of insufficient evidence in abdominal trauma patients.

CONCLUSION

This guideline will be updated by the clinical research committee of the KSACS every 5 years. Although this guideline was made by adaptation of other guidelines, it may be meaningful in that it provides a consensus on the use of antibiotics in abdominal trauma patients in Korea.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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