CHAPTER 10

Assessment of the efficacy of antibacterial agents

The committee for The Japanese Respiratory Society guidelines in management of respiratory infections

The Japanese Respiratory Society

Assessment of the efficacy of antibacterial agents


There are two major reasons for assessing the efficacy of antibacterial agents against hospital-acquired pneumonia (HAP). First, their efficacy must be assessed within two or three days after the initiation of antimicrobial therapy primarily to determine whether the regimen should be continued or modified, and second, to determine how long antimicrobial therapy should be administered, in other words, to determine the proper duration of antibacterial therapy. In any case, it is very difficult to assess the efficacy of antibacterial agents against HAP, and no response criteria have been presented even in the Guideline for hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies proposed by the American Thoracic Society (ATS). This is because the pathogenesis of HAP is greatly influenced by the underlying disorder(s).

When the choice of antibiotics is A*, B or H

The efficacy of antimicrobial therapy should be assessed on day 3 after the initiation of antimicrobial therapy, the same as in community-acquired pneumonia (CAP) in adults, and its efficacy should be assessed in accordance with the 'response criteria' proposed in the Guideline for diagnosis and treatment of community-acquired pneumonia.

When the choice of antibiotics is C

The efficacy of antimicrobial therapy should be assessed on day 2 after the initiation of antimicrobial therapy, or on day 3 at the latest, and its efficacy should be assessed in accordance with the 'response criteria' proposed in the Guideline for diagnosis and treatment of community-acquired pneumonia.

When the choice of antibiotics is D, E, F, or G

The efficacy of antimicrobial therapy should be assessed as soon as possible after the initiation of antimicrobial therapy, but since it takes several days before the response becomes evident, if the symptoms are obviously worse on day 2 or more after the initiation of antimicrobial therapy, an alternative antibiotic should be adopted. If there is 'no change', 'slight improvement', 'slight aggravation' or 'improvement', antimicrobial therapy should be continued, and its efficacy should be assessed daily until day 5 after the initiation of antimicrobial therapy. The final assessment must be made on day 5, and if there is no 'improvement' an alternative antibiotic should be adopted, taking Chapter 11 into thorough consideration.

INITIAL ASSESSMENT OF ANTIMICROBIAL THERAPY

(see Fig. 1 in Chapter 5)

Since pneumonia may be life-threatening when a severe underlying disorder is present, it is desirable to determine the efficacy of antimicrobial therapy as soon as possible, within one or two days after the initiation of antimicrobial therapy. On the other hand, it is difficult to achieve a 'response' if patients have an underlying disorder, and even if a 'response' is achieved, the onset of the 'response' may be delayed. We therefore propose these new guidelines for the management of HAP described below for patients with underlying disorders. However, as yet there is no evidence for this proposal.

*Capital letters refer to the letters in Figure 1, Chapter 5.
DURATION OF ANTIMICROBIAL THERAPY OR DECISION TO 'TERMINATE ANTIMICROBIAL THERAPY'

If patients have an underlying disorder, the 'response' may be rather limited, and the onset of 'response' is often delayed, making it difficult to decide on the proper duration of antimicrobial therapy. In such cases, the efficacy of antimicrobial therapy should be assessed in accordance with the 'response criteria' listed below, although there is no evidence for doing so.

When the choice of antibiotics is A and/or B

The efficacy of antimicrobial therapy should be assessed on day 3 after the initiation of antimicrobial therapy, the same as in CAP in adults.

When the choice of antibiotics is C and/or H

Generally, the efficacy of antimicrobial therapy should be assessed on day 3 after the initiation of antimicrobial therapy, the same as in CAP in adults. However, more careful and long-term administration of antimicrobial agents is required for the management of patients depending on the type of causative bacteria and underlying disorder(s).

When the choice of antibiotics is D, E, F, or G

The duration of antimicrobial therapy is entirely at the discretion of the treating physician, who should make an appropriate decision based on the causative bacteria, status of the underlying disorder(s), and 'response' to antimicrobial therapy. If the patient's immune functions have deteriorated due to the underlying disorder(s), the causative bacteria may persist, leading to a relapse. For this reason, antimicrobial agents should be administrated for 14–21 days. On the other hand, a risk of emergence of resistant bacteria increases if antimicrobial agents are used for more than 14 days, and a risk of adverse drug reactions (in a dose-dependent manner) if aminoglycosides are used for more than 14 days. Therefore, antimicrobial agents should not be administered for more than two weeks without an appropriate reason.

CRITERIA FOR ASSESSMENT OF THE EFFICACY OF ANTIBACTERIAL AGENTS AGAINST HAP

As already mentioned in the Section on 'Diagnosis of Hospital-acquired Pneumonia', symptoms, physical findings, and clinical laboratory findings may be attributable to the underlying disorders themselves and it may be difficult to differentiate them from those attributable to HAP. Thus, there is only a limited amount of material available to assess the efficacy of antibacterial agents against HAP. Underlying disorders may also obscure pneumonia-related findings. In other words, it is difficult to assess the efficacy of antibacterial agents because of a lack of specific markers for efficacy assessment.

When the choice of antibiotics is A, B, C, H

Symptoms such as fever, cough, sputum and chest pain; laboratory findings such as leukocytosis, a positive CRP-response and accelerated ESR (erythrocyte sedimentation rate); and chest X-ray findings serve as response parameters for assessment of efficacy against HAP—the same as is usually true for pneumonia. Generally, the efficacy of antibacterial agents against HAP can be assessed based on the response criteria for CAP in adults.

When the choice of antibiotics is D, E, F, G

Some or all of the subjective and objective findings (mentioned above) cannot be used to assess the efficacy of antibacterial agents against HAP. Therefore, the patient's clinical course should be monitored based on the parameters that can be used as markers. Fever and chest X-ray findings are often helpful for this purpose. Care should be exercised in the efficacy assessment, which ultimately should be left to the discretion of the treating physician.

EFFICACY ASSESSMENT

Because of the inability to fully utilise response parameters, it is not as easy to assess the efficacy of antimicrobial therapy against HAP as objectively as it is against CAP. Moreover, it is rarely necessary to make an objective assessment of HAP. Therefore, the efficacy of antimicrobial therapy can be completely assessed clinically as follows:

1. Antimicrobial therapy is assessed as 'effective' if there is no relapse within one week of the termination of antimicrobial therapy and no requirement for post-therapy antibacterial drugs.
2. Antimicrobial therapy is assessed as 'slightly effective' if there is a relapse within one week of the termination of antimicrobial therapy even though no post-therapy antibacterial medications were required.
3. Antimicrobial therapy is assessed as 'ineffective' if post-therapy antibacterial medication is required.

Future investigation may be needed to address whether or not classification 2 'slightly effective' is necessary. It would be desirable to establish a protocol for each type of pneumonia if an objective assessment is needed for research and development of new antibacterial agents.
MONITORING OF RELAPSE

If the host’s immune functions have deteriorated, pathogenic bacteria often persist in the host, contributing to a relapse. It is therefore necessary to check for this. If a relapse of pneumonia occurs at the same site within one week after the termination of antimicrobial therapy and if the same pathogenic bacteria have caused it, it is proposed that the use of the term ‘recrudescence’ be used. This is slightly different from so-called ‘chupe’ in tuberculosis. It is suggested that the term ‘recrudescence’ be used because HAP is often recrudescent, and aspiration-pneumonia, in particular, is often recrudescent. ‘Recrudescence’ is distinguished from ‘recurrence’, which refers to an episode of pneumonia that occurs at a different site and time and is caused by different bacteria. Moreover, there is no evidence for choosing ‘one week’. In any case, it is necessary to check for ‘recrudescence’ and ‘recurrence’ in cases of HAP.

REFERENCES