Original Article

THE IMPORTANCE OF THE EXAMINATION OF, EDUCATION ON, AND INFECTION CONTROL OF TUBERCULOSIS IN MEDICAL SCHOOL HOSPITALS IN JAPAN

Shuji KURANE and Shoji KUDOH

Abstract Since the incidence of tuberculosis (TB) has markedly decreased over the last half-century, dedicated TB hospitals in Japan have been reducing the beds or have been merging with other hospitals. In accordance with this situation, less than 30% of medical school hospitals (MSHs) have facilities for infectious TB patients. In the meantime, and contrary to the previous trend, elderly TB patients or those who have serious underlying diseases have been increasing. MSHs have therefore not only to take care of these patients, but at the same time they have to reform their TB education system in addition to upgrading TB infection control. To elucidate the current problem regarding TB in MSHs, the survey in the current study was performed for 80 MSHs in Japan in January 2002.

Two sets of questionnaires were prepared and delivered to doctors in these hospitals. One set mainly asked about the status of TB examination and education, and was aimed at doctors in the division of respiratory diseases of the department of internal medicine (Rs); and the other mainly asked about the status of TB infection control and was aimed at doctors in the divisions of infectious diseases, or whoever in charge of hospital infection control (Is). Response rates from Rs and Is were 75.0% (60/80) and 65.0% (52/80), respectively. Seventy-three point three percent (44/60) of Rs and 73.1% (38/52) of Is were working in hospitals without TB beds. Because of the current incidence of TB, the number of TB patients they examined in a year was small (35/60 of hospitals examined less than 20 TB patients in a year). Although there were some experienced doctors on TB in each hospital, most MSHs had only a small number of experienced nurses. Nevertheless, 89.3% of doctors in MSHs (a total of 100/112 Rs and Is) believed that they required TB rooms exclusively for TB patients who have some underlying diseases, and for TB education. Regarding the role of MSHs for TB patients care, the majority of doctors (70.5% of Rs and 68.4% of Is) considered MSHs should be able to offer treatment to TB patients with underlying complications.

As to the educational aspect, most medical schools (MSs) devoted little time to lectures on TB (the median was 1 to 1.5 hour); on the other hand, some MSs (31.8%: 14/44 of MSHs without TB rooms) included a clinical practices in TB hospitals for TB education, although its term was short.

Regarding TB infection control issues, most of the MSHs had active infection control committees in their hospitals and TB was thought to be one of the most important targets for these committees. About 40% (20/51) of these hospitals over the past few years had experienced nosocomial TB infection due in part to the so called "Doctor's delay". As one of the strategies to prevent nosocomial TB infection, special education sessions, not only for staff and residents but also students, were therefore performed in 60.8% (31/51) of MSHs. As to the evaluation of the tuberculin skin test (TST) status of medical students, the two-step TST was performed in 47.1% (24/51) of MSs (as most Japanese underwent their BCG vaccination in their childhood) and 54.9% (28/51) of MSs had a BCG revaccination policy for TST negative students.

Although steps toward reforms in TB issues in MSHs were slow, some minor progress had been made as compared with previous surveys performed by us and others. Even though the numbers of TB patients examined in MSHs have been smaller than before, MHSs still have to take care of some TB patients with some complications. A great deal of effort still needs to be expended to establish efficient and effective TB education and infection control systems. Even though many ideas have been put forward to improve the current situation, one of the most successful answers is to set up small number of special rooms, not only for TB patients but also for other airborne infectious diseases, in all MHSs. The other clue is to establish an intimate collaboration between MSHs and TB hospitals with regard to clinical TB education not only for medical students but also for medical staff.

Key words: Questionnaires, Medical school hospitals, Tuberculosis examination, Tuberculosis education, Tuberculosis infection control

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Original Article

USEFULNESS OF DIRECTLY OBSERVED THERAPY (DOT) DURING HOSPITALIZATION AS DOTS IN JAPANESE STYLE

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Atsuto YOSHIZAWA, Akihiko KAWANA, and Kouichiro KUDO

Abstract Many patients with smear positive tuberculosis were hospitalized during the initial phase of chemotherapy but DOT was not applied to patients with tuberculosis in Japan. We tried randomized clinical study to evaluate the usefulness of DOT during admission. 135 culture positive TB patients were administered by DOT and 124 culture positive TB patients were self-administered during admission. There was no significant difference between 2 groups in the clinical background factors, treatment and the incidence of adverse reactions. Treatment completion rate was 94.1% in DOT group and 87.9% in non-DOT group. Default rate was significantly lower in DOT group (4.4%) than in non-DOT group (11.3%). We concluded that "DOT during admission" was useful to improve the outcome of chemotherapy for tuberculosis and it is preferable to apply DOT throughout treatment course for patients with tuberculosis in Japan.

Key words: DOT during hospitalization, Administration of drug, Completion rate, Default rate, DOTS

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Short Report

ACTIVITY OF CEPHEMS AND CARBAPENEMS AGAINST CLINICALLY ISOLATED *MYCOBACTERIUM ABSCESSUS*

[1]Kunihiko ITO, [2]Kenichi HASHIMOTO, and [2]Hideo OGATA

Abstract To screen effective useful drugs for disease due to *M. abscessus*, we determined MIC of 3 cephems [ceftazidime (CAZ), cefoxitin (CFX), flomoxef (FMOX)] and 3 carbapenems [imipenem (IPM), panipenem (PAPM), meropenem (MEPM)] for 8 strains of clinically isolated *M. abscessus* by micro-dilution method using MGIT system. In all the 8 strains, MICs of CAZ are higher than 32 μg/m*l*. MIC_{50}, MIC_{90}, MIC range of CFX are 32 μg/m*l*, >32 μg/m*l* and 16−>32 μg/m*l* respectively, and for FMOX, 16 μg/m*l*, 32 μg/m*l* and 16−32 μg/m*l*; for IPM, 8 μg/m*l*, 16 μg/m*l* and 8−16 μg/m*l*; for PAPM, 4 μg/m*l*, 16 μg/m*l* and 4−16 μg/m*l*; for MEPM, 8 μg/m*l*, 16 μg/m*l* and 8−16 μg/m*l*. From this study, it is concluded that FMOX, IPM, PAPM and MEPM can be clinically useful drugs in the treatment of the disease due to *M. abscessus*.

Key words: *M. abscessus*, Cephem, Carbapenem, Drug sensitivity, MIC, MGIT

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The 78th Annual Meeting President Lecture

PULMONARY *MYCOBACTERIUM KANSASII* INFECTION IN OKAYAMA, JAPAN

Toshiharu MATSUSHIMA

Abstract Our group discovered the first patient with pulmonary *M. kansasii* infection in Okayama Prefecture in 1976. The first case and another ten more patients over about eight years came exclusively from the southern seaside area of Kurashiki City (Mizushima Marine Industrial District and its vicinity). Thereafter, the cases of pulmonary *M. kansasii* infection have spread geographically and chronologically from the Mizushima district to neighboring areas in the prefecture. We considered the possibility of human-to-human transmission of *M. kansasii* by both the observed geographic spread and the existence of at least two occupational clusters (three welders working on the same line in the same factory building and nine workers in one ironworks), but we could not resolve several controversial problems.

Key words: *M. kansasii,* Non-tuberculous mycobacteriosis, Epidemiology, Okayama Prefecture, Mizushima Marine Industrial District

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The 78th Annual Meeting Lunch-Time Lecture

DEVELOPMENT OF NEW THERAPEUTIC METHOD FOR EMPYEMA

[1]Hiroyasu YOKOMISE, [1]Taku OKAMOTO, [1]Masashi GOTOH,
[1]Yasumichi YAMAMOTO, and [2]Yasuhiko TABATA

Abstract Objectives: We have investigated whether poly-lactic acid (PLA) sponge and fibroblast-growth-factor (FGF) released slowly from gelatin beads can induce fibrotic tissue in postpneumonectomy dead space.

Methods: Left pneumonectomy was performed in white Japanese rabbits. In the control group (N=5), left chest was closed without any treatment. In the PLA sponge group (N=5), PLA sponge and FGF (100 μg) released from gelatin beads were introduced into the left chest cavity.

Results: In the control group, herniation of the heart and right lung were observed without fibrotic material in the left chest cavity. In the PLA sponge group, dense fibrotic material was observed by chest CT scan 1 month after the operation. Pathological examinations revealed that PLA sponge and FGF did promote the organization of the fibrotic materials.

Conclusions: Fibrotic materials can be induced in the post-pneumonectomy dead space by PLA sponge and FGF released slowly from a gelatin sponge. New therapeutic method may be introduced near future by this concept, reduction of dead space with newly developed own fibrotic materials.

Key words: Empyema, Dead space, Regeneration, Slow releasing of growth factor

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The 78th Annual Meeting Evening Symposium

ROLE OF NEW QUINOLONES IN THE TREATMENT OF MYCOBACTERIOSIS

Chairpersons: [1]Akira WATANABE and [2]Yoshihito NIKI

Abstract New quinolones (NQs) have acquired potent antimicrobial activity against gram-positive cocci and penetrate well into organs when compared with old quinolones. Their indications were extended to the treatment of respiratory infection caused by gram-negative and gram-positive bacteria, and their possibility of an indication for the treatment of mycobacteriosis has been considered. Mycobacteriosis, against which NQs are expected to be effective, includes tuberculosis, which involves a problem of multiple-drug resistant bacteria, and atypical mycobacteriosis, for which there are few remedies. Since, there has been no established evaluation of NQs against mycobacteriosis, the purpose of the present evening symposium was to evaluate the role of NQs at present in the treatment of mycobacteriosis, as well as to present future prospects. Four speakers made presentations.

Dr. Chiaki Sano reported that STFX, GFLX, MXFX, and SPFX had a potent antibacterial activity against various acid-fast bacteria and were particularly effective against *M. tuberculosis*, *M. kansasii*, and *M. fortuitum*. Among these drugs, MXFX had a greater therapeutic effect in experimental mice model of a tuberculosis than SM when used concomitantly with INH+RPT. These results suggested that MXFX might become one of the first-line drugs, taking the place of SM. However, OFLX, SPFX, and STFX are not effective against MAC. Only MXFX exhibited a significant therapeutic effect when administered alone and potent therapeutic effect when used concomitantly with EB, in experimental mice model of MAC infection. These results suggested that 8-methoxy quinolone might be effective.

Dr. Yuka Sasaki reported the results of a questionnaire survey among national sanatoriums, as well as the current status of administration of NQs for the treatment of pulmonary tuberculosis based on the results of her study. The ATS recommended in 2002 that LVFX, MXFX, and GFLX be second-line drugs, which should be used alternatively only when first-line drugs cannot be used due to drug-resistant *M. tuberculosis* or adverse reactions. She reported that LVFX, MXFX, and GFLX were used in a similar manner also in Japan and that they achieved therapeutic results equivalent to those by first-line drugs. She stated that there were some urgent problems, for example, these drugs are not listed in the Tuberculosis Control Law of Japan or in health insurance, and no testing system for sensitivity to NQs has been established.

Dr. Atsuyuki Kurashima reported the results of a study conducted in other countries and his study on atypical acid-fast bacteria. He indicated the position of NQs in the treatment of pulmonary atypical mycobacteriosis. However, the significance of concomitant use of CPFX with RFP+EB in the treatment of MAC disease associated with AIDS has already been recognized. He was of the opinion that atypical acid-fast bacteria against which NQs were useful were *M. kansasii* and *M. fortuitum* alone at present and that NQs had a very limited effect in the treatment of pulmonary MAC infection, although there were only an insufficient number of studies on pulmonary MAC disease.

Dr. Koichi Wada reported on the advisability of administration of NQs in the treatment of mycobacteriosis as a whole and prospects for NQs. His conclusion was similar to those by the two former speakers: he stated that NQs are important for the treatment of tuberculosis as alternative drugs and that they should be used in sufficient doses when first-line drugs could not be used due to drug resistance or adverse reactions. He also stated that use of NQs, including duration of administration, should be discussed after the testing method for drug sensitivity has been established and that long-term use of NQs should be avoided in the treatment of atypical mycobacteriosis at present, although significant results have not been obtained in atypical acid-fast bacteria, mainly MAC.

In the last part of the symposium, an active discussion was held. Many opinions similar to those of the speakers were expressed also from the floor. Lastly, President Dr. Matsushima summarized the role of NQs in the treatment of mycobacteriosis at present and future prospects for NQs and confirmed the significance of having held the present symposium.

Key words: Mycobacteriosis, *Mycobacterium tuberculosis*, Atypical mycobacterium, New-quinolone agent

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