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ORIGINAL ARTICLE

Infection control team activity and recent antibiograms in the Kobe University Hospital

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The hospital infection control team (ICT) has a major role in suppressing or preventing infectious diseases. The purpose of this study was to investigate whether the work of the ICT had affected the antibiograms at the Kobe University Hospital in the past 3 years. The ICT's works are as follows: (1) to monitor whether physicians are instructed in the use of broad-spectrum antibiotics; (2) to check whether measures for preventing the occurrence or spread of infectious disease are performed along with appropriate standard precautions; (3) to provide rapid communication with physicians in bacteremia cases and (4) reporting the antibiograms in the hospital. In addition, we investigated changes in the antibiograms every 6 months based on all materials. There were 193 physician interventions in 2010 and 491 in 2011. The representative isolated bacteria included no additional bacteria with lower susceptibilities found over the past 1.5 years compared with the initial 1.5 years in the 3-year investigation period. The ratio for performing two sets of blood culture tests in all blood culture tests showed an upward tendency from 58.1% in 2009 to 71.1% in 2010 and 80.3% in 2011 ($r=0.995$, $P=0.063$, $b=0.089$). In conclusion, since the introduction of an expanded ICT role, our data showed an increased antibiotic susceptibilities in bacteria such as *Enteroccus faecalis* and the total amount of hand disinfectant agents tended to increase year by year, even though direct statistical analyses could not easily be performed. Further observation may be necessary for a definitive evaluation of ICT activities.
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INTRODUCTION

New ways of thinking about infection and infectious disease have recently spread. Traditionally in the field of infection and/or infectious disease, treatments were considered to be well established and research focused on the exploitation of antibiotics.[1] More recently, research has demonstrated that inappropriate use of antibiotics is the predominant factor in the spread of antimicrobial drug resistance.[2,3]

The control of hospital-acquired infections is a major priority for health-care organizations in developed countries, and evidence shows that an institutional approach is needed to reduce the incidence of infections.[4] An important part of the work of the infection control team (ICT) is the formulary restriction and pre-authorization of specified broad-spectrum antibiotics such as carbapenems.[5]

Many universities and general hospitals have now established ICTs, and their activity range has been wide.[5,6] In Japan, organized hospital infection control (IC) programs are widely implemented but are frequently under-resourced. Japan's fee-for-service payment system provides little incentive for hospitals to invest in IC. Without financial support for IC programs, hospital IC poses a heavy burden for Japanese health-care organizations.[7]

ICTs need to monitor the occurrence of infection and infectious disease, the causative bacteria and their antibiotic susceptibilities, and communicate this information with physicians. Another important role is to prevent the occurrence and spread of infection in the hospital

by ensuring instruction in skin disinfection, standard precautions and gown technique.[8] Also, physician intervention to ensure the appropriate selection and use of antibiotics, especially broad-spectrum antibiotics such as carbapenems, may be necessary to suppress the emergence of resistant strains.

In this study, we investigated how antibiotic use, the number of bacterial strains isolated and their antibiotic susceptibilities, and the use of disinfectant agents for hands in the hospital have changed since the ICT began to: (1) monitor if physicians are instructed in the use of broad-spectrum antibiotics; (2) check if measures for preventing the occurrence or spread of infectious disease are performed along with appropriate standard precautions; (3) provide rapid

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communication with physicians in cases of bacteremia and (4) report the antibiograms in the hospital.

MATERIALS AND METHODS

Bacteria

Bacteria were isolated from April 2009 to March 2012 in the 920-bed Kobe University Hospital from all materials including urine, sputum, blood, nasal secretions or pus. The isolated bacteria were from 10^5 or more colony forming units per ml in urine, one or more colony in 10 ml of blood, one or more colony in sputum, one or more colony in nasal secretions and one or more colonies in pus.

Susceptibility testing

Antibiotic susceptibilities were tested and the results were interpreted and reported using the reference broth microdilution method, as described by the Clinical and Laboratory Standards Institute (CLSI) M7-A5 (2010; CLSI Document M100-S20). The MIC was defined as the lowest antimicrobial concentration that totally inhibited bacterial growth. Susceptibilities were evaluated by CLSI category. We tested bacterial strains against the following antimicrobial agents: ampicillin, piperacillin, amoxicillin–clavulanate combination, cefazolin, cefotiam, ceftriaxone, ceftazidime, cefmetazole, sulbactam/cefoperazone, imipenem, gentamicin, levofloxacin, sulfamethoxazole/trimethoprim and minocycline. Antibiogram data were analyzed every 6 months. We divided our 3 years of observation into the following six periods: 2009-1st, from April 2009 to September 2009; 2009-2nd, from October 2009 to March 2010; 2010-1st, from April 2010 to September 2010; 2010-2nd, from October 2010 to March 2011; 2011-1st, from April 2011 to September 2011; and 2011-2nd, from October 2011 to March 2012. For quality control, *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853 and *Enterococcus faecalis* ATCC 29212 were used.

ICT activity

Our ICT was activated in its current configuration at the beginning of 2009 and consists of physicians, nurses and specialized laboratory technicians for bacteriology, and specialized pharmacologists for antibiotics. The physicians and nurses are qualified in IC. The main activities and roles of the ICT are as follows: (1) intervention for the use of broad-spectrum antibiotics as described below in physician interventions, (2) recommending the use of disinfectant agents for hands, (3) rapidly reporting to and communicating with physicians on bacteremia cases (within 24 h), (4) reporting the antibiograms and the use of carbapenems in the hospital and (5) monitoring whether standard precaution measures were performed appropriately. We investigated how these works of the ICT affects antibiotic use, the number of bacterial strains isolated and their antibiotic susceptibilities over the past 3 years in the hospital, especially the comparison between the first 3 periods and the last 3 periods.

The amounts of hand disinfectant agents used in the hospital were calculated from the quantity shipped in the Department of Pharmacy from 2009 to 2012, totaled as the sum of chlorhexidine acetate with GOJO MHS (GOJO Japan K.K., Tokyo, Japan)

Physician interventions

Physician interventions were initiated in the current manner beginning in mid-2010, involving pharmacologists specialized in antibiotics and physicians qualified in IC under the management of the ICT. The main purpose was to examine the use of antibiotics and check for inappropriate use or performance of blood culture tests, and contacting physicians about the performance of blood culture tests if necessary. Broad-spectrum antibiotics were targeted, specifically anti-*Pseudomonas aeruginosa* drugs such as piperacillin, tazobactam/piperacillin, ceftazidime, cefepime, cefozopran, ciprofloxacin, pazufloxacin, amikacin, tobramycin and gentamicin, and carbapenems such as meropenem, biapenem, doripenem and panipenem/betamiprone. The team provides instructions and physician interventions on appropriate use, for instance, to avoid insufficient dosing or unnecessary use. The frequency of use of these antibiotics and the number of physician interventions were also investigated.

Statistical analyses

Statistical analysis was conducted using linear regression analysis with PASW Statistics 17.0 software packages (for Windows; SPSS Inc., Chicago, IL, USA). The trends in bacteria isolation rate and annual consumption of antimicrobial agents were analyzed for each month and the susceptibility of isolated strains to antimicrobial agents was analyzed for each period. Statistical significance was established at the 0.05 level.

RESULTS

Outcome of physician interventions

The current system of physician interventions started in July 2010 with meetings held roughly once a week. There were 24 meetings in 2010 (from July to December) and 47 in 2011 (from January to December). In 2010, 1974 patient cases were discussed for appropriate use of antibiotics, and 4098 patients were discussed in 2011. The number of physicians interventions performed in 2010 was 193 cases compared with 491 cases in 2011. The details of the interventions are shown in Table 1. In brief, recommendations for blood culture tests were the most common intervention, followed by de-escalation of antibiotics[9–11] and change of antibiotics (Table 1).

Blood culture tests

To recommend an exact diagnosis for bacteremia and check the antibiotic susceptibilities of causative bacteria, the ICT recommended two sets of blood culture tests in cases suspicious for bacteremia and this was the most frequent intervention for physicians (48% of total interventions in 2010 and 34% in 2011) as shown in Table 2. There were a total of 63 071 specimens including 19 557 specimens in blood culture tests during the study period (Table 2). The ratio of performing two sets of blood culture tests in all blood culture tests showed an upward tendency from 58.1% in 2009 to 71.1% in 2010 and 80.3% in 2011($r=0.995$, $P=0.063$, $b=0.089$). The isolation rate of organisms in blood culture tests was not significantly different, 12.6% in 2009 to 11.8% in 2010 and 10.0% in 2011 ($r=0.976$, $P=0.139$, $b=-0.733$).

Bacterial isolation and antibiograms

A total of 13 010 specimens of all organisms were isolated. The isolation rate of each organism showed no variation during the study period (Table 2). The antibiotic susceptibilities of methicillin sensitive *S. aureus* (MSSA) and *E. faecalis*, *Enterobacteriae* including *E. coli*, extended spectrum β-lactamase (ESBL)-producing *E. coli*, *K. pneumoniae*, *Enterobacter cloacae* and *S. marcescens*, and *P. aeruginosa* in every year is shown in Tables 3, 4 and 5, respectively. Susceptibility rates of *E. faecalis* to ampicillin significantly increased from 99.2% in 2009 to 100% in 2010 and 2011 ($r=0.864$, $P=0.026$, $b=1.875$)

Table 1 Details of ICT interventions to physicians

	2010	*2011*
Intervention (case number)	193	491
Objective number for intervention	1947	4098
Details of intervention (%)		
Blood culture (appropriate) performance	48	34
Antibiotic de-escaration	10	14
Change of antibiotics	8	13
Cancelation of antibiotics	5	11
Dose-up of antibiotics	1	3
Others	28	25

Abbreviation: ICT, infection control team.

Table 2 Trends of blood culture and organism isolation rates at the Kobe University Hospital, 2009–2011

	2009	*2010*	*2011*	r	P-*value*	b
Number of the specimens	19635	20833	22603			
Number of blood culture specimens	5652	6483	7422			
Rate of two sets of blood culture (%)	58.1	71.1	80.3	0.995	0.063	0.089
Isolation rate of the organisms in blood culture (%)	12.6	11.8	10.0	0.976	0.139	−0.733
Number of all organism isolates	3978	4270	4762			
Isolation rate of each organism (%)						
Staphylococcus aureus (MSSA)	6.7	6.3	5.9	1.000	—	—
Enterococcus faecalis	5.5	6.1	5.7	0.327	0.788	1.071
Escherichia coli	10.1	9.0	8.7	0.950	0.203	−1.288
E. coli (ESBL)	1.5	1.5	2.4	0.866	0.333	1.667
Klebsiella pneumoniae	4.3	3.7	3.5	0.961	0.179	−2.308
Enterobacter cloacae	2.7	2.6	3.1	0.756	0.454	2.857
Serratia marcescens	2.0	1.3	1.6	0.569	0.614	−1.622
Pseudomonas aeruginosa	7.6	7.2	6.6	0.993	0.073	−1.974

Abbreviations: *b*, regression coefficient; ESBL, extended spectrum β-lactamaset; *r*, correlation coefficient.

Table 3 Antibiotics susceptibility of *Staphylococcus aureus* (MSSA) and *Enterococcus faecalis* at the Kobe University Hospital, 2009–2011

	Antibiotics susceptibility rate (%)								
Organism/antibiotic	*2009-1st*	*2009-2nd*	*2010-1st*	*2010-2nd*	*2011-1st*	*2011-2nd*	r	P-*value*	b
Staphylococcus aureus (MSSA)									
Tested number of isolates	141	152	172	268	157	201			
CEZ	100	96.8	100	100	99.2	100	0.397	0.436	0.278
CTM	NT	96.8	100	100	NT	100	0.795	0.205	0.406
IPM	100	96.8	83.4	100	100	100	0.130	0.806	0.018
GM	84.4	77.6	86.9	77.9	80.3	78.8	0.220	0.675	−0.052
LVFX	87.9	93.6	100	85.6	84.8	87.3	0.371	0.470	−0.057
CLDM	86.5	NT	NT	77.5	75.8	68.5	0.927	0.073	−0.122
MINO	96.5	NT	NT	97.7	97.7	94.5	0.226	0.774	−0.146
ST	100	NT	NT	100	99.2	100	0.478	0.522	−1.167
TEIC	100	100	100	100	100	100	—	—	—
VCM	100	100	100	100	100	100	—	—	—
Enterococcus faecalis									
Tested number of isolates	119	158	168	243	174	176			
PCG	92.2	97.7	NT	NT	97.5	100	0.699	0.301	2.447
ABPC	99.2	99.2	100	100	100	100	0.864	**0.026**	18.750
IPM	100	99.2	99.3	99.5	NT	NT	0.371	0.629	−6.053
LVFX	86.6	84.5	86.2	83.7	86.8	91.0	0.587	0.221	2.070
VCM	100	100	100	100	100	100	—	—	—

Abbreviations: ABPC, ampicillin; *b*, regression coefficient; CEZ, cefazolin; CLDM, clindamycin; CTM, cefotiam; GM, gentamicin; IPM, ipipenem; LVFX, levofloxacin; MINO, minocycline; NT, not tested; PCG, penicillin G; *r*, correlation coefficient; ST, sulfamethoxazole/trimethoprim; TEIC, teicoplanin; VCM, vancomycin.
The bold value is statistically significant.

(Table 3), while those of ESBL-producing *E. coli* to amoxicillin–clavulanate combination significantly decreased from 67.6% in 2009-1st to 56.7% in 2011-2nd ($r = 0.961$, $P = 0.009$, $b = -0.195$) (Table 4). Except for them, there were no other strains with lower susceptibilities in the most recent 1.5 years in this 3-year investigation.

Analysis of amount of disinfectant agents used for hands

We checked the use of hand disinfectant agents to create an index for compliance for this standard precaution. The results are shown in Table 6. The total amount of disinfectant agents used for hands tended to increase year by year even though direct statistical analyses could not easily be performed.

DISCUSSION

The significance of IC and prevention has recently been broadly reconsidered after nosocomial infections, especially those involving resistant strains, became the focus of media reports on fatal cases or new resistant strains.[12–14] Our hospital established an ICT in 2000 consisting of only one physician and one to two nurses; in 2009, this was expanded to include several specialized laboratory technicians

Table 4 Antibiotics susceptibility of *Enterobacteriaceae* at the Kobe University Hospital, 2009–2011

	Antibiotics susceptibility rate (%)								
Organism/antibiotics	*2009-1st*	*2009-2nd*	*2010-1st*	*2010-2nd*	*2011-1st*	*2011-2nd*	r	P-*value*	b
Escherichia coli									
Tested number of isolates	199	214	213	331	281	239			
PIPC	64.5	66.1	60.5	56.6	60.4	66.8	0.180	0.733	−0.406
CTRX	NT	94.5	95.7	91.5	98.8	96.6	0.578	0.308	1.757
CAZ	96.5	88.5	91.9	96.7	98.0	94.1	0.588	0.219	1.372
SCPZ	NT	97.3	97.3	94.9	84.9	97.1	0.510	0.380	−0.782
IPM	99.5	100	100	100	99.6	100	0.138	0.794	5.273
GM	90.5	89.6	90.3	88.0	70.2	91.2	0.489	0.325	−0.540
AMK	99.5	100	99.5	100	98.0	99.5	0.569	0.239	−6.923
LVFX	80.5	71.6	71.9	78.8	79.6	74.6	0.098	0.853	0.221
E. coli (ESBL)									
Tested number of isolates	34	40	37	69	77	85			
A/C	67.6	63.6	NT	60.7	55.6	56.7	0.961	**0.009**	−0.195
CMZ	97.1	NT	100	98.4	98.6	100	0.659	0.227	0.462
SCPZ	NT	57.6	70.6	63.9	43.1	43.3	0.672	0.214	−0.045
IPM	100	100	100	100	100	100	—	—	—
GM	100	87.9	52.9	62.3	73.6	53.7	0.720	0.107	−0.034
AMK	100	100	100	100	100	95.5	0.574	0.234	−0.280
LVFX	26.5	21.2	23.5	26.2	26.4	20.9	0.068	0.898	−0.023
Klebsiella pneumoniae									
Tested number of isolates	88	89	84	144	113	143			
PIPC	39.8	56.9	54.9	56.0	43.8	53.2	0.603	0.205	0.029
CTRX	NT	100	100	98.4	100	100	0.109	0.861	0.125
CAZ	98.6	100	100	100	100	100	0.574	0.234	1.146
SCPZ	NT	100	98.6	94.4	100	100	0.158	0.799	0.054
IPM	98.9	100	100	100	99.0	100	0.084	0.874	0.139
GM	98.9	100	100	96.8	100	100	0.172	0.745	0.119
AMK	100	100	100	100	97.9	100	0.519	0.291	−0.543
LVFX	98.9	95.8	100	100	NT	98.4	0.365	0.546	0.181
Enterobacter cloacae									
Tested number of isolates	72	47	100	132	99	77			
PIPC	51.4	52.5	38.8	50.9	47.4	46.2	0.427	0.398	−0.076
CTRX	NT	55.0	46.3	50.9	48.7	47.7	0.707	0.182	−0.171
CAZ	54.2	52.5	80.0	51.9	NT	NT	0.469	0.531	0.020
SCPZ	NT	62.5	53.8	60.4	56.4	53.8	0.714	0.175	−0.149
IPM	97.2	97.5	100	99.1	100	98.5	0.684	0.134	0.508
GM	88.9	92.5	87.5	92.5	97.4	83.1	0.054	0.920	−0.010
AMK	100	97.5	100	100	100.0	100	0.519	0.291	0.456
LVFX	87.5	97.5	95.0	95.3	87.2	86.2	0.497	0.316	−0.089
Serratia marcescens									
Tested number of isolates	52	110	80	115	47	49			
PIPC	36.5	82.1	87.0	96.8	82.5	73.7	0.425	0.401	0.018
CTRX	NT	84.6	91.3	93.5	85.0	NT	0.047	0.953	0.008
CAZ	73.1	89.7	91.3	95.2	90.0	73.7	0.026	0.961	0.002
SCPZ	NT	89.7	100	98.4	100	81.6	0.122	0.845	−0.012
IPM	100	100	100	100	100	100	—	—	—
GM	78.8	97.4	100	100	100	97.4	0.590	0.218	0.063
AMK	98.1	97.4	100	100	97.5	100	0.359	0.485	0.247
LVFX	86.5	97.4	100	100	95.0	97.4	0.406	0.425	0.072

Abbreviations: AMK, amikacin; *b*, regression coefficient; CAZ, ceftazidime; CTRX, ceftriaxone; ESBL, extended spectrum β-lactamaset; GM, gentamicin; IPM, ipipenem; LVFX, levofloxacin; NT, not tested; PIPC, piperacillin; *r*, correlation coefficient; SCPZ, sulbactam/cefoperazone.
The bold value is statistically significant.

Table 5 Antibiotics susceptibility of *Pseudomonas aeruginosa* at the Kobe University Hospital, 2009–2011

	Antibiotics susceptibility rate (%)								
Organism/antibiotics	*2009-1st*	*2009-2nd*	*2010-1st*	*2010-2nd*	*2011-1st*	*2011-2nd*	r	P-*value*	b
Pseudomonas aeruginosa									
Tested number of isolates	184	185	286	376	255	273			
PIPC	88.0	94.0	95.2	92.7	86.8	94.1	0.036	0.947	−0.009
P/T	NT	NT	96.5	94.9	89.9	93.9	0.752	0.248	−0.155
CFPM	86.3	91.3	90.4	89.7	84.1	89.6	0.275	0.598	−0.089
SCPZ	NT	89.5	86.3	84.6	77.0	82.6	0.878	0.050	−0.155
IPM	79.9	83.3	84.7	82.8	70.9	77.8	0.620	0.189	−0.110
MEPM	85.7	88.0	81.3	86.8	85.5	78.7	0.591	0.217	−0.148
GM	79.9	93.0	88.7	91.8	88.0	88.0	0.190	0.718	0.037
AMK	94.0	84.0	NT	86.1	86.8	85.4	0.411	0.492	−0.105
LVFX	89.1	96.0	96.2	94.4	96.0	100	0.713	0.112	0.180
CPFX	90.3	80.7	79.9	83.1	83.3	84.6	0.203	0.700	−0.049
AZT	74.5	NT	NT	77.1	71.2	69.2	0.690	0.310	−0.192

Abbreviations: AMK, amikacin; AZT, aztoreonum; *b*, regression coefficient; CFPN, cefcapene; CPFZ, ciprofloxacin; GM, gentamicin; IPM, ipipenem; LVFX, levofloxacin; MEPM, meropenem; NT, not tested; PIPC, piperacillin; P/T, piperacillin/tazobactam; *r*, correlation coefficient; SCPZ, sulbactam/cefoperazone.

Table 6 Analysis of used amount of disinfectant agents for hands

	2009	*2010*	*2011*	*2012*
GOJO MHS (L)	309 630	467 910	525 630	568 320
Chlorhexidine acetate (L)	106 000	232 000	247 000	391 000
Total (L)	415 630	699 910	772 630	959 320

for bacteriology, specialized pharmacologists for antibiotics, and physicians specialized in infection control and infectious diseases.

One of the roles of the ICT has been generally recognized as suppression of nosocomial infection, and to accomplish this goal the ICT reports the current status of bacteria isolated in the hospital, especially focusing on resistant strains such as ESBL-producing bacteria, as well as preventive measures used for suppressing the spread of infection such as instruction in hand disinfection.[15–17] Our results show that the antibiogram of ESBL-producing *E. coli* resistant to amoxicillin–clavulanate combination decreased from 2009-1st to 2011-2nd. In addition, the isolated ratio of ESBL-producing *E. coli in all E. coli* tended to increase in the past three periods (20.8% in 2010-2nd, 27.4% in 2011-1st and 35.6% in 2011-2nd) compared to the previous three periods (17.1% in 2009-1st, 18.7% in 2009-2nd and 17.4% in 2010-1st), and the susceptibility of ESBL-producing *E. coli* to levofloxacin was 20.9–26.5% (Table 4). The ratio of ESBL-producing *E. coli* isolation was higher than that seen in European studies (11%)[18] and the susceptibilities to levofloxacin were similar to other studies from Japan.[19] These facts provide significant data for preventing further increases in the isolation of resistant strains in hospitals and further decreases in antibiotic susceptibilities, two of the essential tasks of the ICT.

To limit the emergence of resistant strains or inhibit infection as soon as possible, physician interventions are also necessary in cases of inappropriate use of antibiotics,[20,21] especially the unnecessary use of a broad-spectrum antibiotics and/or insufficient dosing over a long duration which may cause the emergence of resistant strains but not suppress infection.[22,23] Our interventions involve reporting the total antibiotic use, the bacterial strains isolated and their antibiotic susceptibilities. The data showed that after ICT intervention, antibiotic use changed to appropriate dosages or to antibiotics with a narrow spectrum for the targeted bacteria (data not shown).

Our most frequent ICT intervention was the recommendation of two sets of blood culture tests to improve the diagnosis of bacteremia and help select appropriate antibiotic therapies based on the antimicrobial susceptibility results of the causative bacteria.[24,25] As mentioned above for the guideline, a single set of blood culture tests may result in bacterial contamination and this might decrease the significance of the test and lead to inappropriate antibiotic use.

Our future task is to expand the role of the ICT hospital-wide. For this purpose, we will establish committees and hold conferences on topics of IC, infectious disease or antibiotics for all the workers in the hospital, not just physicians, including nurses, clinical technologists and pharmacologists, as well as physicians whose specialties are not as closely involved with infectious disease prevention or IC. Our mission is to promote the concept that IC requires the participation of all the workers in the hospital.

We would like to emphasize the limitations of our work. First, it is not easy to quantify the direct relationship between ICT activity and changes in the antibiograms from the statistical analyses. Second, the observation period is too short to draw definite conclusions. These limitations should be overcome by the quantification of ICT activity and statistical evaluation over a longer duration of observation.

In conclusion, since the introduction of an expanded ICT role, our results showed increased antibiotic susceptibilities in bacteria such as *E. faecalis* and the total amount of hand disinfectant agents tended to increase year by year even though direct statistical analyses could not be easily performed. Further observation may be necessary for a definitive evaluation of ICT activities.

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