Validation of a Cross-Infection Control Program in an Understaffed Intensive Care Unit

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ABSTRACT: **Background:** The authors describe a multifaceted cross-infection control program that was implemented to contain an epidemic of multidrug-resistant microorganisms (MRO) (carbapenem resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii*; extended spectrum β-lactamase producing *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter Cloacae,* and *Proteus mirabilis*; and methicillin-resistant *Staphylococcus aureus* and *Candida species*).

Objectives: To assess the effect of a control program on the incidence of cross-infection with MRO.

Methods: Clinical criteria triaged patients into a high-risk wing (HRW) or a low-risk wing (LRW). Strict infection control measures were enforced; violations led to group discussions (not recorded). Frequent cultures were obtained, and use of antibiotics was limited. Each quarter, the incidence of MRO isolation was reported to all staff members.

Results: Over a 6 year period, 1028 of 3113 patients were placed in the HRW. The incidence of MRO isolation within 48 hours of admission was 8.7% (HRW) vs. 1.91% (LRW) ($P < 0.001$). Acquired MRO infection density was 30.4 (HRW) vs. 15.6 (LRW) ($P < 0.009$). After the second year, the incidence of group discussions dropped from once or twice a month to once or twice a year.

Conclusions: These measures contained epidemics. Clinical criteria successfully triaged HRW from LRW patients and reduced cross-infection between the medical center wings. The quarterly reports of culture data were associated with improved staff compliance. MRO epidemic control with limited resources is feasible.

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KEY WORDS: bacteriological surveillance, intensive care unit, multidrug-resistant microorganisms (MRO) triage, cross-infections

Following a long-standing epidemic of cross-infection by multidrug-resistant microorganisms (MRO) in our multidisciplinary intensive care unit, we instituted a comprehensive cross-infection control program, which eventually controlled the epidemics. This paper describes the measures taken and their effects.

Epidemics of cross-infections by MRO can occur in any environment where broad spectrum antibiotics are often prescribed and frequent physical contact with the patients is often required [1-3]. However, in our case, the local epidemic spread over several years, and one or more MRO were isolated from virtually all patients who stayed in the unit for more than 5 days.

At the time, the intensive care unit (ICU) was divided into two wings, each wing contained a hall with five patient bays and a single bed isolation room. The bays in the halls were separated by cloth curtains. We first hypothesized that the cloth curtains separating each bed were the vector of cross-infection, and tried hanging newly washed and autoclaved curtains between admissions, but the epidemic continued. We next thought that cloth curtains were inadequate barriers and replaced them with vertical plaster of Paris and glass barriers. Again, the modifications did not reduce the rate of cross-infection.

The administration planned to construct a new unit, better designed for patient isolation, to be housed in a new surgical complex, but at the time, the foundations of the complex were just laid, and the new facility was several years away (the new facility was completed in November 2013).

In an attempt to reduce the rate of cross-infections in the interim, we implemented a comprehensive program that did not require staff increase or substantial structural changes. The program was developed by a team of nurses, intensivists, and infectious disease specialists. It was not a research project, but rather an emergency measure to reduce MRO infection rates. The protocol included prospectively planned periodic reviews, and we maintained bacteriological and epidemiological data.

The program successfully contained the epidemic. While some of the measures taken were particular to our unit, we think that many of the measures have universal applicability, and may be of interest to other units, particularly in areas with limited resources.

PATIENTS AND METHODS

SETTING

At the time of program initiation, the ICU was a 12 adult bed closed unit, belonging to the main teaching hospital of Ben-

Gurion University medical school. The unit admitted high acuity medical and surgical patients, usually requiring mechanical ventilation. The ICU was physically divided into two wings with a common utility space between them. Each wing contained a five-bed hall and one single patient room in the halls, the beds and equipment were separated by barriers that were made of glass (two-thirds high) and plaster of paris, with full height curtains in front. The nurse–patient ratio was one to two on evening and night shifts. On day shifts, two or three additional nurses were available. At least two physicians with certification in critical care medicine supervised care during the day. Their primary specialties were anesthesiology, internal medicine, or general surgery. Direct care was provided by two or more critical care medicine (CCM) fellows and a varying number of interns and residents on ICU rotation required by their specialty board.

CROSS-INFECTION PROPHYLAXIS PROTOCOL

The protocol consisted of six integrated components: physical isolation, generic infection control methods, restricted antibiotic prescription, bacteriological surveillance, close monitoring, and ongoing staff education.

PHYSICAL ISOLATION

On admission, patients were triaged by risk of harboring MRO according to the clinical criteria listed in Table 1. High risk patients were placed in one wing, designated as the high-risk wing (HRW). Patients who became colonized with an MRO during their stay were moved to the HRW as well. Other patients were placed in the second wing, designated as the low-risk wing (LRW). Each wing was staffed by a separate team of nurses, and movement between wings was discouraged.

GENERIC INFECTION CONTROL METHODS

Throughout the unit, each bay was equipped with a readily accessible supply of disposable caps, masks, gowns, and gloves. Dispensers of dyed 70% ethanol were placed on the bed rails and other readily available locations throughout the ICU. Plastic drawers for patient records and personal items were replaced daily, and taken for disinfection. Between patient contacts, caregivers were instructed to scrub with 70% alcohol and wear fresh disposable gloves and full-size aprons.

For patients in the HRW, additional precautions were taken. The bays were marked with a conspicuous contact isolation sign, and any patient contact required fresh operating room attire (caps, masks, sterile gowns, and gloves). In addition, the plastic drawers were discarded after the final disposition of the patient, and the bay was thoroughly decontaminated, using standard operating room procedures.

Table 1. Triage criteria

Positive culture of an MRO from any source within 14 days of ICU admission
Five or more days in the hospital prior to ICU admission
Exposure to broad-spectrum antibiotics for more than 5 days prior to ICU admission
Two or more contaminated operations for the same condition during the past month
Transfer from hospital wards endemic with MRO (mostly internal medicine)
Patients transferred from other hospitals after more than 24 hours
All transfers from nursing homes

MRO = multidrug-resistant microorganisms, ICU = intensive care unit

ANTIBIOTIC PRESCRIPTION

All decisions on antibiotic prescription were made on daily rounds with a designated infectious disease specialist, who was also available for phone consultations during off hours. If the latter was not available, all orders for antibiotics, except single dose prophylactic antibiotics before surgical interventions, required approval from the attending physician. The indications for empiric antibiotics were limited to patients with signs of systemic inflammatory response syndrome (SIRS) and high risk for sepsis, as judged by the ICU attending physician, usually in consultation with the infectious disease specialist.

ON-GOING STAFF EDUCATION

All ICU personnel were required to become familiar with the measures and underwent a 1 hour in-service instruction seminar led by an infection control nurse. Quarterly staff meetings included a short refresher as well as updated reports on the current rate of cross-infections. Rotating interns and residents had to complete the in-service training before commencing their ICU rotation.

MONITORING

The nurses assigned to a particular patient were responsible for enforcing contact isolation measures. In turn, nurse compliance was the responsibility of the nursing supervisor. In the event of a deviation, group discussions were held, but no disciplinary actions were taken, and deviations were not recorded.

BACTERIOLOGIC SURVEILLANCE

Routine bacteriological cultures from sputum, wounds, blood, urine, catheter tips, and potential sources of infection such as peritoneal fluid (when accessible) were obtained on admission and twice weekly until discharge. In patients with SIRS, additional cultures were obtained from potential sources. In the SIRS group, blood cultures were taken at fixed intervals each day and after each temperature spike. Patients with ventilator-associated pneumonia and negative cultures from tracheal aspirates underwent bronchoalveolar lavage.

MICROBIOLOGICAL METHODS

Blood cultures were processed using an automated blood culture system (Bactec 9240; Becton Dickinson, USA). Bacterial isolates

were identified according to routine bacteriological procedures; susceptibly testing to antibiotics was performed by the disk diffusion methods as described by Bauer et al. [4] and extended-spectrum beta-lactamases (ESBL) production was determined with an E-test ESBL strip (AB Biodisk, Solna, Sweden). *Clostridium difficile* toxins A and B were identified using an enzyme immunoassay (*C. difficile* tox A/B II, Techlab, USA).

STATISTICS

Data were analyzed using Epi Info™ version 6 (Centers for Disease Control, Atlanta, GA, USA). Differences between categorical variables were analyzed by two-tailed Fisher's exact test.

For cell values larger than Epi Info™ accepts, exact (Fisher's) 2-tailed probabilities of the null hypothesis were calculated as described by Lansgurd Fisher's Exact Test.

Continuous variables were compared using two-tailed analysis of variance (ANOVA) for normally distributed population, and Barlett's test was used for non-homogenous population. A two-tailed P value < 0.05 was considered statistically significant.

RESULTS

During the 5 year period (January 2002–December 2006) covered by this report, 3113 patients were admitted to the ICU of whom 1027 (33%) met or developed the criteria for admission or transfer to the HRW. Table 2 summarizes the distribution of demographic data and possible risk factors between the two wings. Age and gender, as well as Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were similar in the wings. Patients in the HRW were more often transferred from the operating room, had a primary pulmonary diagnosis and a longer time on the general ward.

Staff adherence to the protocol was mediocre initially, as indicated by the number of group discussions. Deviations were not recorded; however, the number of group discussions over protocol violations decreased gradually during the first year, from once or twice a week during the first 6 months, to once or twice over an entire year from the second year onward. The most common violation was failure of individual staff members to change aprons and caps between patient contacts and failure to wear full operating room attire for each patient contact in the HRW. The latter requirement had to be relaxed, and after the first 6 months full attire was only required for patients with known MRO infection. Failure to change gloves between patient contacts was rarely observed.

We obtained 55,615 cultures from all sources. Excluding duplicates, 3891 were positive. Gram negative organisms accounted for 2561/3891 (65.8%), gram positive organisms 861/3891 (22.1%), and fungal organisms 469/3891 (12.1%). 289/3891 (7.42%) of the positive cultures were taken before ICU admission.

Table 3 shows the distribution of positive cultures with MRO in samples taken before or within 48h of admission. 8.4% of the patients admitted to the HRW carried an MRO vs. only 1.9% of patients admitted to the LRW. The difference was highly significant (P < 0.00001), indicating that clinical criteria were successfully triaged patients to the appropriate wing.

Acquired infections by MRO were much more common in the HRW, even after adjusting for length of stay [Table 4]. The difference was most notable in carbapenem-resistant Acinetobacter and candida isolates. The exception was ESBL producing Proteus mirabilis, which showed a nearly equal incidence density between the wings.

DISCUSSION

This observational report demonstrates that the program was successful in triaging patients with high risk for harboring

Table 2. Patient characteristics by wing

	Low-risk wing N=2086	High-risk wing N=1027	*P* value
On ICU admission			
% Men	69.6%	64.3%	0.688
Age (years), mean years ± SD	55 ± 22.31	51 ± 21.22	0.364
Apache II score, mean ± SD	15.09 ± 7.88	16.19 ± 6.01	0.44
On daily antibiotics	16.1%	43%	0.002
Admitted from the emergency department	48.2%	17.9%	‹ 0.001
Transferred from the operating room	46.8%	53.2%	0.204
Primary pulmonary diagnosis	17.9%	28.6%	‹ 0.001
Trauma	26.8%	28.6%	0.629
General ward (days), mean ± SD	1 ± 1.65	3 ± 3.32	‹ 0.001
After ICU admission			
Operations or re-operations	8.9%	25%	0.021
Antibiotics	59.9%	89.5%	‹ 0.001
Antibiotic medication (days), mean ± SD	6 ± 5.86	15 ± 12.71	‹ 0.001
Ventilator use (days), mean ± SD	5 ± 5.64	8 ± 4.25	0.007
Central venous catheter (days), mean ± SD	5 ± 6.96	9 ± 5.48	0.007
Urinary catheter (days), mean ± SD	6 ± 7.79	10 ± 6.38	0.004
ICU (days), mean ± SD	4 ± 8.23	12 ± 13.73	‹ 0.001

ICU = intensive care unit, SD = standard deviation, Apache II = Acute Physiology and Chronic Health Evaluation II

Table 3. Cultures obtained before admission or within 48 hours

	LRW (n=2086)	HRW (n=1027)	Total (3113)	Isolates/100 admissions	*P* value	Odds ratio (L/H)	Confidence interval	
				LRW	HRW			
Candida	18	31	49	0.86	3.02	‹ 0.0001	0.28	0.15-0.52
ESBL	13	23	36	0.62	2.24	‹ 0.0001	0.27	0.13-0.57
MRSA	3	21	24	0.14	2.04	‹ 0.0000	0.07	0.02-0.24
CR	6	11	17	0.29	1.07	‹ 0.006	0.27	0.09-0.78
Total	40	86	126	1.92	8.37	‹ 0.0000	0.21	0.14-0.32

MRSA = methicillin resistant *Staphylococcus aureus*; ESBL= extended spectrum β-lactamase producing *Klebsiella pneumoniae*, Enterobacter, excluding *Proteus mirabilis*; CR= Carbapenem resistant *Pseudomonas aeruginosa* or *Acinetobacter baumannii*; LRW = low-risk wing; HRW = high-risk wing

P values are exact 2-sided probabilities of the null hypothesis

Table 4. Acquired microorganism by wing

	LRW (n=2086)	HRW (n=1027)	LRW AID (8386 days)	HRW AID (11369 days)	*P* value
Candida	64	156	7.63	13.72	‹ 0.0002
MRSA	18	50	2.15	4.40	‹ 0.036
ESBL	16	53	1.91	4.66	‹ 0.015
ESBL-PM	6	10	0.72	0.88	= 0.3631
CR	27	118	3.22	10.38	‹ 0.0001
total	131	387	15.62	34.04	‹ 0.009

AID = acquired infection density (infections per 1000 exposure days); LRW = low-risk wing; HRW = high-risk wing; ESBL= extended spectrum β-lactamase producing *Klebsiella pneumoniae*, Enterobacter, excluding *Proteus mirabilis*; ESBL-PM = ESBL with *Proteus mirabilis*; CR = Carbapenem resistant *Acinetobacter baumannii* and *Escherichia coli*

P values are exact 2 sided probabilities of the null hypothesis for AID

MRO to the HRW wing, and except for *P. mirabilis,* reduced the rate of cross-infection between the wings. The patient triage method [Table 2] was based on well-known risk factors [5,6,7] for MRO infections, and proved effective: 84.4% of the patients who harbored index microorganisms on admission were triaged to the HRW directly; only 7% of them had a known positive culture before the ICU transfer.

Patients admitted to the LRW had a significantly shorter length of stay. This observation may suggest that the higher incidence of infection by MRO in the HRW was due to longer exposure time. However, as shown in Table 4, acquired incidence density (incidence per 1000 patient days) was still much higher for all MRO except *P. Mirabilis*.

STUDY LIMITATIONS

This study has several limitations. We initiated the program as an interim solution for a pressing clinical problem, and therefore no control data are available. After moving to the new facility, the physical conditions changed, and the program was discontinued. The data are relatively old, but publication was delayed for risk management concerns. Consequently, the data presented here do not prove that the program reduced the rate of cross-infection within the HRW.

Although candida species were more frequent in the HRW, clinical infections with *Candida sp.* relate to the use of broad-spectrum antibiotics, and to reduced host-defense mechanisms [8,9]. Compared to patients placed in the LRW, patients in the HRW required more aggressive and longer antibiotic treatment; therefore, cross-infection is not a likely cause of systemic candidiasis, and we did not attribute the reduced rate of systemic candidiasis to the program.

Similarly, point estimates of infection by *P. mirabilis* were significantly higher in the HRW. However, after we adjusted for length of stay, the difference disappeared. Since *P. mirabilis* infections relate to the use of urinary catheters [10] its incidence is expected to correlate with length of stay rather than the prevalence of cross-infection.

Better ICU design and a higher nurse–patient ratio are also effective in reducing the rate of cross-infection [15]. However, a general shortage of qualified nurses and the economic circumstances in our locality generally precluded these measures. Our program was based on the well-established observation that the vectors of transmission of MRO are mostly healthcare workers or contaminated equipment in the patient's immediate environment [16]. MRO are usually transmitted from patients already colonized at the time of admission [17,18,20] due to the frequent need for staff and equipment to move from patient to patient. In crowded units such as ours, some cross-infection is inevitable, and may account for the higher rate of MRO isolation in the HRW. However, as demonstrated here, it is possible to reduce the incidence of cross-infection by isolating HRW from LRW patients.

The clinical efficacy of routine bacteriological surveillance in preventing cross-infection has been questioned [12] and several studies failed to show benefit [13], perhaps because culture and antibiotic susceptibility results may take up to 10 days to present [14]. It is therefore likely that routine surveillance does not affect the outcome of individual patients [21]. We therefore believe that the observed benefit on staff compliance was probably not due to the frequent cultures, but to the quarterly reports of their results to the whole staff. It is likely that the encouraging reports improved compliance with the sometimes burdensome demands of the program.

There is indirect evidence that as the program progressed staff compliance increased. To enhance voluntary compliance, we did not record protocol violations; but the incidence of group discussions was greatly reduced after the first year. While this observation may be a manifestation of the Hawthorne Effect [22], it may also indicate that compliance became an established routine.

The regular bacteriological reports probably enhanced the subjective feeling of the nursing staff that the measures successfully reduced the incidence of cross-infections, at least between the wings. While some of the measures described here are particular to our ICU, many have general applicability. The data presented here suggests that strict infection control methods can reduce the rate of cross-infection at least between the wings. Bacteriological surveillance by itself may not reduce the rate of cross-infections, but the quarterly reports of their results to the entire staff provide encouraging feedback and appear to sustain compliance. Under austere conditions, a program such as the one presented here may reduce the incidence of cross-infection with MRO in the ICU at a reasonable cost.

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Capsule

DNA damage linked to fitness loss in aging

Loss of metabolic function is associated with physical decline and diseases associated with aging. Park et al. provided evidence for a link between accumulated DNA damage and such metabolic dysfunction. Activity of the DNA-dependent protein kinase (DNA-PK), which is activated in response to DNA damage, was increased in skeletal muscle of older mice. DNA-PK phosphorylates HSP90α, a chaperone protein that protects the activity of a key metabolic regulator, called adenosine monophosphate, activated protein kinase. A small-molecule inhibitor of DNA-PK improved the physical fitness of young obese mice and older mice. Whether such benefits can be provided without the deleterious effects of inhibited DNA repair, such as cancer, remains to be explored.

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Capsule

Differentiating myeloid cells

Hematopoietic stem cells are a common progenitor of adaptive and innate immune cells. However, the precise factors that guide differentiation down these disparate pathways remain unclear, in part because of difficulties in working with small numbers of precursor cells. Lee and colleagues solved this problem for myeloid lineage cells by immortalizing murine myeloid progenitors with conditionally over-expressed Hoxb8 and labeling these cells with a Ccr2/ Cx_3cr1 dual reporter. They found through a small-molecule library screen and confirmatory in vivo validation that the mTORC1-S6K1-Myc pathway regulates myeloid differentiation. Disrupting this pathway in progenitor cells results in a lack of monocytes and neutrophils. Hence, the mTORC1-S6K1-Myc pathway functions as a checkpoint in terminal myeloid differentiation.

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