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INSIDE

Perioperative Beta Blockers

ABSTRACT & COMMENTARY

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Dr. Crawford serves on the speaker's bureau for Pfizer.

This article originally appeared in the February 2009 issue of Clinical Cardiology Alert.

It was peer reviewed by Rakesh Mishra, MD. Dr. Mishra is Assistant Professor of Medicine, Weill Medical College, Cornell University. He reports no financial relationships relevant to this field of study.

Source: Bangalore S, et al. Perioperative beta blockers in patients having non-cardiac surgery: a meta-analysis. *Lancet*. 2008;372:1962-1976.

THE ACC/AHA GUIDELINES RECOMMEND PERIOPERATIVE BETA blockers for those already on them, patients undergoing vascular surgery, or those having intermediate- to high-risk surgery with established coronary heart disease, or at high risk of having it. However, recent studies have shown no beneficial effect of perioperative beta blockers and potential for harm. Thus, Bangalore et al conducted a meta-analysis of randomized, controlled trials of safety and efficacy outcomes of perioperative beta blockers assessed for 30 days post-non-cardiac surgery. The efficacy outcomes of interest were total mortality, cardiovascular mortality, myocardial infarction, stroke, and heart failure. The safety outcomes of interest were bronchospasm, bradycardia, and hypotension. The selection criteria were met by 33 trials out of 112 surveyed, and included over 12,000 patients. Beta-blocker therapy did not result in any significant reduction in total mortality, cardiovascular mortality, or heart failure, but did reduce myocardial infarction (OR = 0.65, 95% CI 0.54-0.79, NNT = 63). However, stroke was increased (OR = 2.0, 1.27-3.68, NNH = 293), as was bradycardia (NNH = 22) and hypotension, requiring therapy (NNH = 17); bronchospasm was not affected. An assessment of the trial methodology showed that only 13 had a low risk of bias. The beneficial results for myocardial infarction were driven by the 20 trials with a high risk of bias. Bangalore et al concluded that randomized trial data do not support the use of beta blockers preoperatively to prevent cardiovascular events in non-cardiac surgery patients.

Financial Disclosure

Hospital Medicine Alert's physician editor, Kenneth P. Steinberg, MD, has no relevant financial relationship related to the material presented in this issue.

Hospital Medicine Alert's physician editor, Kenneth P. Steinberg, MD, selected and reviewed the articles contained within this issue on February 10, 2009.

■ COMMENTARY

Although I am not a big fan of meta-analyses, this one was very carefully done and raises some interesting points. First, it exhibits how few excellent trials on this topic exist. Out of 112 reports of randomized, controlled trials of perioperative beta-blocker use with 30-day outcome data, only 33 met their quality inclusion criteria. Of those, only 13 were considered low risk for bias. The large, positive trial of Poldermans et al,[1] published in the *New England Journal of Medicine*, drove the positive data about outcomes with beta blockers, but was considered highly biased by Bangalore et al because many of the high-risk patients they studied should have been on beta blockers for other indications (eg, heart failure, post myocardial infarction); in the Poldermans study, myocardial infarction decreased 44%. Second, much of the negative data on beta blockers were driven by the POISE study,[2] which was considered low risk for bias. If POISE is eliminated, the reduction in myocardial infarction increases from 35% to 53% with beta blockers. Bangalore et al correctly point out that the doses of beta blockers used in POISE was eight times the equivalent dose of the agent used in the Poldermans study. Thus, some of the negative effects in POISE may have been due to giving such a large dose of beta blockers to beta-blocker naive patients. Third, sensitivity analyses showed that outcomes were better if beta blockers were titrated to a heart rate of < 75 beats/min and if they were administered for 24 hours or less. The latter is interesting since the largest percentage of perioperative events are thought to occur 48-120 hours after surgery.

So what do we do with this new data? It seems clear that if your patient is already on beta blockers for clear indication, he/she should stay on them. Those who should be on beta blockers for other reasons should be started on them early enough to titrate the dose to appropriate levels prior to surgery. All others should be considered on a case-by-case basis. For example, someone with known coronary artery disease, or who is highly likely to have it, and is undergoing high-risk surgery, may be an acceptable candidate, if he/she seems able to tolerate beta blockers. It is always ideal to have a few weeks to start therapy. The higher risk of beta-blocker complications in POISE was associated with the administration of high doses without titration just before surgery. This is probably not a good idea. Also, I agree with Bangalore et al that perioperative beta blockers should not be a practitioner performance measure until the issue is clarified further. ■

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Hospital Medicine Alert, ISSN 1931-9037, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

ASSOCIATE PUBLISHER: Russ Underwood.
MANAGING EDITOR: Leslie Hamlin.
DIRECTOR of MARKETING: Schandale Kornegay.

GST Registration Number: R128870672.
Periodicals Postage Paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Hospital Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $42. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

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Questions & Comments

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Rapid Response Team Did Not Reduce Hospital-wide Codes or Mortality

ABSTRACT & COMMENTARY

By David J. Pierson, MD

Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle

Dr. Pierson reports no financial relationships relevant to this field of study. This article originally appeared in the February 2009 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington. He reports no financial relationships relevant to this field of study.*

Synopsis: *With the largest cohort and longest follow-up yet reported, this prospective single-center study found that implementing a rapid response team*

reduced codes outside the ICU but had no effect on either hospital-wide code rates or overall patient mortality.

Source: Chan PS, et al. Hospital-wide code rates and mortality before and after implementation of a rapid response team. *JAMA* 2008;300:2506-2513.

CHAN ET AL PERFORMED A PROSPECTIVE BEFORE-AND-after cohort study of the effects of implementing a rapid response team (RRT) in a 404-bed tertiary-care academic hospital in Kansas City, MO. They tracked cardiac arrests (codes) both in and out of the ICU, as well as overall hospital mortality during two 20-month periods, January 2004 through August 2005 and January 2006 through August 2007. The intervention — implementation of a three-member ICU-based RRT and an extensive educational effort for ward staff — took place from September-December 2005. Patients were, thus, enrolled in the study during the same seasonal time periods before and after the intervention. The primary outcome measures were hospital-wide code rates and mortality. Chan et al undertook extensive measures to adjust for pre-intervention trends and to look for potential confounders that might affect the study variables.

The study included 24,193 patient admissions in the pre-RRT period and 24,978 patient admissions in the post-RRT period. There were clinically small but statistically significant differences in the two populations: Patients admitted during the post-intervention study interval were slightly older, more likely to be male, and more likely to be African-American, and the case-mix estimate was slightly higher. During post-intervention, there were 376 RRT activations: altered mental status (27%), tachycardia (23%), tachypnea (13%), hypotension (12%), and other a priori-determined triggers. Forty-six percent of RRT episodes resulted in transfer to a higher level of care (ICU 41%, telemetry 4%, operating room, or other procedure 1%).

After RRT implementation, non-ICU codes decreased (adjusted odds ratio [AOR], 0.59; 95% confidence interval [CI], 0.40-0.89) relative to ICU codes (AOR 0.95; 95% CI, 0.64-1.43; $p = 0.03$ for interaction), but there was no change in the rate of hospital-wide codes (AOR 0.76; 95% CI, 0.57-1.01). Hospital-wide mortality did not differ between the pre- and post-intervention periods (3.22 vs 3.09 per 100 admissions; AOR 0.95; 95% CI, 0.81-1.11; $p = 0.52$). A careful search for response team undertreatment or underuse that might have affected the mortality findings revealed very few instances.

■ COMMENTARY

This large, single-institution study showed that RRT implementation was not associated with reductions in hospital-wide code rates or mortality, although it did document a reduction in codes outside the ICU. One might suggest that, had they included just a few more patients, the small observed differences would have reached statistical significance. However, using post-hoc power calculations, Chan et al determined that, based on the differences observed, a pre-intervention and post-intervention population of 148,000 patients during each period would have been required to have 80% power to detect a 5% mortality reduction at the $p = 0.05$ level.

Chan et al discuss several possible reasons for their failure to demonstrate improved survival and reduced hospital-wide code rates after RRT implementation in their hospital. One is that the RRT tended to be called for patients who were not, in fact, about to code, and that those who did go on to cardiopulmonary arrest could not have been helped. Another is that patients triaged by the RRT to the ICU received heightened surveillance by unit staff, such that when they did arrest, preparations had been made and a hospital-wide code did not have to be called. A third is that many patients initially treated by the RRT were subsequently made DNR (do-not-resuscitate) as a result of that interaction. As Chan et al note, it may be that the RRT episode catalyzed end-of-life care discussions in patients that might not otherwise have taken place. However, based on the observed code case-fatality rates prior to implementing the RRT, Chan et al calculated that as many as 59 more hospital-wide codes would have occurred if the 73 RRT patients, who subsequently were made DNR, had not been seen by the RRT.

A fourth possible reason for the RRT's failure to improve hospital-wide mortality might be a higher prevalence of DNR status during the second part of the study. Data were not available to Chan et al on the numbers of patients designated DNR during the different study periods. Of course, it may also be that no reductions in hospital-wide code rates or mortality occurred after implementing the RRT because such teams do not in and of themselves actually affect these outcomes.

Following studies showing that many codes occur after hours of deterioration that could potentially have been detected and preventive actions taken, the Institute for Healthcare Improvement recommended that hospitals implement RRTs as one of the six strategies of the 100,000 Lives Campaign.[1] This de facto mandate sent hospitals scrambling nationwide to create, implement, and track the results of RRTs, and a number of before-and-after studies have concluded that these teams both

reduce the number of codes and save lives.[2] However, while the premise for RRTs appeared sound, the evidence base substantiating their effectiveness has been called into question.[3,4] Given the prevalence of medical error, practice variation, and poor adherence to evidence-based practice guidelines, there can be little doubt that better care results in better outcomes. However, this new study will hardly be reassuring to the advocates of RRTs as a means for improving overall quality of health care in hospitals. ■

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Posterior ECG Leads Improve the Detection of Left Circumflex Coronary Artery Occlusion

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

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Dr. Boyle reports no financial relationships relevant to this field of study. This article originally appeared in the February 2009 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Rakesh Mishra, MD.*

Source: Aqel RA, et al. Usefulness of three posterior chest leads for the detection of posterior wall acute myocardial infarction. *Am J Cardiol*. 2009;103:159-164.

OPTIMAL MANAGEMENT OF TRANSMURAL MYOCARDIAL infarction (MI) depends on rapid reperfusion of the occluded infarct artery. Therefore, accurate early diagnosis is the cornerstone of initial patient assessment in the emergency department. It is recommended that a standard 12-lead electrocardiogram (ECG) be performed within 10 minutes of presentation to diagnose ST-elevation MI, but diagnosis of infarction in the left circumflex coronary artery (LCCA) territory remains difficult. In a significant number of patients with LCCA occlusion, the standard 12-lead ECG may show no ST-elevation at all, and these patients may, therefore, not be referred for urgent reperfusion. Accordingly, Aqel et al performed a study to determine the utility of using three posterior chest leads to detect ischemia in the LCCA territory.

They studied 53 consecutive patients undergoing clinically indicated percutaneous coronary intervention (PCI) of the LCCA. Standard 12-lead ECGs were performed, and they also recorded tracings from three posterior leads, V7, V8 and V9, in the left posterior axillary line at the 5th interspace, at the left midscapular line at the 5th interspace, and at the left paraspinal border at the 5th interspace, respectively. They excluded patients with ST-elevation MI, previous coronary artery bypass surgery, and uninterpretable baseline ECGs. After the baseline 15-lead ECG was recorded, the angioplasty balloon was inflated in the LCCA for 120 seconds. The 15-lead ECG was performed after balloon inflation and then every 30 seconds. ECGs were analyzed by two cardiologists. Because there is controversy regarding the cut-off for ST-elevation in the posterior leads, with some advocating 1 mm and others suggesting 0.5 mm; Aqel et al analyzed their data using both cutoffs.

Their patients were recruited at a Veterans Affairs Medical Center, were all male, 63 ± 9 years of age, 47% were diabetic, 34% had prior MI, and 47% had prior PCI. The procedural indication was stable angina in 43%, unstable angina in 43%, and non-ST-elevation MI in 13%. Importantly, there were no collaterals to the distal LCCA territory observed in any patient. The site of balloon occlusion was ostial or proximal in all patients. The posterior leads showed more ST elevation than any of the standard 12 leads ($p < 0.0001$). Using a cutoff of 1 mm ST elevation in two contiguous leads, the use of posterior leads increased the detection of LCCA occlusion from 34% to 62%. Using a cutoff of 0.5 mm ST elevation in two contiguous leads, the use of posterior leads increased the detection of LCCA occlusion from 38% to 74%. If 0.5 mm is detected in any lead, the rate of detection of LCCA occlusion is increased from 47% to 77%. Aqel et al conclude that the 15-lead ECG identified more patients with posterior myocardial wall ischemia because of temporary balloon occlusion of the LCCA than the 12-lead ECG. This information may enhance the detection of posterior MI in the emergency department, and potentially facilitate early institution of reperfusion therapy.

■ **COMMENTARY**

This study is consistent with previous studies that have shown very poor sensitivity of standard 12-lead ECGs in detecting posterior MI due to LCCA occlusion. The data suggest that addition of the posterior leads to the standard 12 leads results in an approximate doubling of the diagnosis of LCCA occlusion. This is a rapid and inexpensive test that can be easily performed in the emergency room, and may enhance diagnosis of posterior ischemia in patients with an otherwise normal ECG. This may, in turn, facilitate earlier reperfusion in this patient cohort. Thus, the presence of a normal 12-lead ECG in patients whose symptoms are very suggestive of MI should prompt further investigation with extra ECG leads, or even an echocardiogram.

Several limitations of this study should be noted. First, the patients were all male, VA patients, and were predominantly Caucasian. Therefore, the results may not be applicable to all patient subgroups. Second, the balloon inflations were all ostial or proximal and, therefore, the sensitivity for ischemia caused by more distal LCCA occlusion may be lower than seen in this study. Third, the duration of ischemia was short, only two minutes. Although ECG changes usually occur early within this time frame, differences from clinical thrombotic occlusion of the LCCA with thrombus propagation over time may not be appreciated in this type of study. Despite these limitations, this study serves as a reminder that the standard 12-lead ECG has poor sensitivity for detecting LCCA occlusion, and that posterior leads may approximately double this sensitivity. ■

Benefits of a Dedicated ICU Clinical Pharmacist

ABSTRACT & COMMENTARY

By David J. Pierson, MD

This article originally appeared in the February 2009 issue of Critical Care Alert. *It was edited by William Thompson, MD.*

Synopsis: *In this large epidemiology study using a previous survey and 2004 Medicare data focusing on serious infections in the ICU, hospitals with dedicated ICU clinical pharmacists had lower ICU mortality rates, shorter ICU stays, and reduced charges.*

Source: MacLaren R, et al. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. *Crit Care Med* 2008;36:3184-3189.

In 2004, MACLAREN ET AL CONDUCTED A SURVEY OF US hospitals with ICUs to assess the prevalence and use of dedicated ICU clinical pharmacists.[1] That survey indicated that 62% of hospitals had clinical pharmacists with at least a portion of their full-time equivalent position specifically dedicated to direct involvement in patient care in the ICU rather than drug dispensing and other more traditional pharmacist roles. For the current paper, MacLaren et al used the results of that survey, along with ICD-9 diagnostic data, mortality, lengths of stay, total charges, drug charges, and laboratory charges obtained from the Expanded Modified Medicare Provider Analysis and Review (MEDPAR-Hospital-National) for the year 2004, to examine associations between having an ICU clinical pharmacist and those variables for three categories of ICU infections: nosocomial-acquired infections, community-acquired infections, and sepsis.

Because of the nature of the databases used, the numbers of hospitals and patients, as well as of variables such as case mix, varied for each infection category. Of the 382 institutions responding to the original survey, 272 had Medicare patients with nosocomial infections; the corresponding numbers for community-acquired infections and sepsis were 265 and 276 hospitals, respectively. Numbers of patients in the different categories ranged from 8,927 (community-acquired infections) to 54,042 (sepsis). In each instance, the studied outcomes were better in hospitals with ICU clinical pharmacists than in institutions without pharmacists in this role. For nosocomial infections, community-acquired infections, and sepsis, respectively, hospital mortality rates with and without ICU clinical pharmacists were 14.61% vs 18.05%, 11.43% vs 13.28%, and 18.54% vs 19.43%, all statistically significant with p values of 0.008 or less. Compared to ICUs with clinical pharmacists, mortality rates in ICUs without them were 23.6% higher for nosocomial infections (386 extra deaths), 16.2% higher for community-acquired infections (74 extra deaths), and 4.8% higher for sepsis (211 extra deaths).

ICU lengths of stay were longer in hospitals without ICU pharmacists, by 7.9% (14,248 extra days), 5.9% (2855 extra days), and 8.1% (19,215 extra days) for the three infection categories, respectively (all differences significant; at least $p = 0.03$). ICUs that did not have dedicated clinical pharmacists had greater total Medicare billings: by 12% for nosocomial infections, by 11.9% for community-acquired infections, and by 12.9% for sepsis (all, $p < 0.001$). Differences for Medicare drug and laboratory

charges were similar. MacLaren et al conclude that, if these results "were extrapolated to all 933,638 Medicare patients in an ICU with the studied infections, the involvement of a clinical pharmacist could save 7409 patient lives, 390,921 ICU days, and $4,168,278,242 in total charges."

■ **COMMENTARY**

This study has some important limitations, the most important of which, in my opinion, relates to the 2004 survey[1] from which the participating institutions for the present investigation were selected. In that survey, only 382 (11.8%) of 3,238 US hospitals with ICUs (1034 ICUs) responded, and these institutions had some potentially relevant differences from the non-responding hospitals. Compared to the 88% of institutions that did not respond to the survey, more responding hospitals were not-for-profit, non-governmental hospitals, and fewer were in all the other categories (government, for-profit, and so on). In the responding hospitals, 52% of the ICUs were open (patient managed by private non-intensivist attending), 28% were transitional (patient co-managed by private attending and intensivist), and 20% were closed (patient managed by intensivist). Thus, whether the present study's results apply to a particular practice environment is unclear, and extrapolating the findings to include all US hospitals in 2009 — and especially MacLaren et al's generalizations about lives and money saved — seems pretty dubious.

Previous studies have shown that hospital mortality correlates inversely with the ratio of pharmacists to occupied beds, and that involving pharmacists directly in the care of ICU patients is associated with fewer adverse drug-related events, greater efficiency of care, and lower drug-related costs. Using hospitals with and without ICU pharmacists, as identified from a previous survey, the present study documents positive associations between having ICU clinical pharmacists and patient mortality, ICU length of stay, total charges, drug charges, and laboratory charges.

I think it is important to phrase this study's findings in this way, because MacLaren et al have not demonstrated that having an ICU pharmacist per se reduces mortality, length of stay, and charges. Whether they have dedicated ICU clinical pharmacists is likely only one of many ways in which the study hospitals differ. A number of aspects of the process of care in the ICU are similarly associated with improved patient outcomes. For example, hospitals with ICU pharmacists are probably also more likely also to have closed ICUs, trained intensivists, greater implementation of protocols and care bundles, multidisciplinary rounds, palliative care services, and other dedicated ICU personnel such as specialist respiratory therapists, nutritionists, and social workers.

Having said that, I am convinced that MacLaren et al are justified in their recommendation that "hospitals should consider employing clinical ICU pharmacists." For decades, the institution in which I work has been fortunate to have specialist clinical pharmacists assigned to each of its main ICUs — including medical, trauma/surgical, and neurosurgical units. The presence of these experts on daily work rounds has improved adherence to clinical practice guidelines and unit protocols, facilitated matching of antibiotic therapy to local microbial susceptibility patterns, identified and prevented adverse drug reactions and interactions, and aided in efforts to prevent oversedation and drug withdrawal. And the educational impact of our ICU clinical pharmacists for physicians, nurses, and others on the staff has been immeasurable. ■

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MRSA VAP: Vancomycin or Linezolid?

ABSTRACT & COMMENTARY

By Andrew M. Luks, MD

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Dr. Luks reports no financial relationship to this field of study.

This article originally appeared in the February 2009 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD.*

Synopsis: *This open-label, multicenter trial showed that treatment of MRSA ventilator-associated pneumonia with linezolid was associated with non-statistically significant improvements in microbiologic cure, clinical cure, survival, duration of mechanical ventilation, and ICU length of stay when compared to therapy with vancomycin.*

Source: Wunderink RG, et al. Early microbiological response to linezolid vs vancomycin in ventilator-associated pneumonia due to methicillin-resistant *Staphylococcus aureus*. *Chest*. 2008;134:1200-1207.

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) is a common cause of ventilator-associated

pneumonia (VAP). Several studies have shown that linezolid is associated with higher clinical cure and survival rates when compared with vancomycin in the treatment of MRSA nosocomial pneumonia.[1,2] Wunderink et al sought to build on these data and determine if treatment with linezolid was also associated with a faster microbiologic response than vancomycin for patients with MRSA VAP.

They conducted a prospective, randomized, open-label, multicenter study at 36 sites over a three-year period. Patients were eligible for inclusion if they were ≥ 18 years of age with suspected VAP based on the presence of purulent sputum, fever or hypothermia, hypotension, or leukocytosis, leukopenia, or bandemia. Patients had to have been in the hospital > 5 days, have been on mechanical ventilation for at least 48 hours, and be expected to need mechanical ventilation for at least 72 hours following enrollment. Patients were excluded if they had received antimicrobial agents with activity against the patient's MRSA isolate for ≥ 48 hours prior to enrollment. Bronchoalveolar lavage (BAL) was performed anywhere from 24-72 hours post-study enrollment, and patients were deemed to have MRSA VAP if the quantitative culture yielded > 10^4 cfu/mL of the organism.

Patients were randomized to receive linezolid 600 mg IV every 12 hours or vancomycin 1 g every 12 hours for 7-14 days. Seventy-two to 96 hours later, a repeat BAL was performed from the same lung subsegment as in the initial collection. After four days or following the second bronchoscopy, patients receiving linezolid could be switched to oral therapy (600 mg every 12 hours). Patients were withdrawn from the study due to non-compliance or protocol violations, if it was deemed medically necessary, or if the baseline quantitative cultures yielded < 10^4 cfu/mL for MRSA. Using intention-to-treat analysis, the authors examined differences in microbiologic cure rates between linezolid- and vancomycin-treated patients with microbiologic cure defined as a repeat BAL containing < 10^2 cfu/mL for MRSA. Secondary outcomes included clinical outcome, mortality, the duration of mechanical ventilation, and hospital and ICU length of stay.

Wunderink et al identified only 50 patients (30 linezolid and 20 vancomycin) who had a MRSA concentration of 10^4 cfu/mL on the baseline BAL sample. Of these patients, only 23 linezolid patients and 19 vancomycin patients underwent follow-up BAL at 72-96 hours. Patients treated with linezolid had a non-statistically significantly higher microbiologic cure rate than patients treated with vancomycin (56.5% vs 47.4%). None of the 10 linezolid patients with microbiologic treatment failure died, as compared with five of 10 patients with microbiologic failure in the vancomycin group. Regarding the secondary outcomes, patients treated with linezolid had higher clinical response rate (66.7% vs 52.9%), greater survival at the end of the study (86.7% vs 70%), fewer days on mechanical ventilation (10.4 days vs 14.3 days), shorter hospitalization (18.8 days vs 20.1 days), and shorter ICU length of stay (12.2 days vs 16.2 days), but none of these differences reached statistical significance. The incidence of treatment-related adverse events was similar between the two groups.

■ COMMENTARY

Vancomycin has long been the standard treatment for MRSA VAP. While it is generally effective in this regard, the entire course of therapy must be administered intravenously, which usually mandates central or PICC line placement. Linezolid offers a potential advantage in this respect, as an oral form of the medication is available and patients can be switched to this route after several days on the intravenous form. Clinical use of the medication is not as widespread as is vancomycin, however, and one plausible reason might be the lack of randomized, prospective trials establishing its efficacy relative to vancomycin for VAP. The earlier studies of these two agents all examined patients with nosocomial pneumonia, not just patients with VAP, and several were retrospective in nature.

By focusing on patients with VAP and collecting data in a prospective manner, this study attempts to address these issues and puts forth some intriguing results. However, the study has some methodological issues, the most important of which is the very low number of patients who completed the study protocol. Given the prevalence of MRSA and of VAP, it is unclear how a multicenter study conducted at 36 sites over a three-year period could only enroll 50 patients. As a result, the study was clearly underpowered, and none of the results reached statistical significance. The study was also open-label, although blinding a study in which the dose and frequency of administration of one of the medications must be adjusted based on drug-levels is admittedly difficult. It is also not clear to me that Wunderink et al's definition of microbiologic cure (repeat BAL with < 10^2 cfu/mL at 72-96 hours) is a valid endpoint that has any correlation with meaningful clinical outcomes.

Finally, it is noteworthy that the lead author, who is also the lead author on several other studies comparing linezolid with vancomycin, is a paid consultant for Pfizer, Inc., the maker of linezolid, while all but two of the other authors are either employees of or consultants to the company. In fact, there are surprisingly few studies in the literature comparing these two agents in adults

that are not authored by the lead author in this study, and one of the few studies in adults for which he is not an author has similar issues with relationships between the paper's authors and linezolid's manufacturer.[3]

The question of which medication is the better option for patients with MRSA VAP is an important one. The existing literature suggests that linezolid may be as effective as, if not more effective than, vancomycin, but before we make wholesale changes in our practice and adopt linezolid as the treatment of choice for this problem, we need larger, prospective trials conducted with less influence from the company with a stake in the outcome of the study. ■

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CME Questions

1. **In the meta-analysis of randomized, controlled trials of perioperative beta blockers by Bangalore et al, the use of perioperative beta blockers resulted in:**
   a. a reduction in total mortality.
   b. a reduction in heart failure.
   c. a reduction in myocardial infarction.
   d. All of the above

2. **In the study by MacLaren et al, compared to hospitals that did not use ICU clinical pharmacists dedicated to direct patient care, hospitals that utilized the pharmacists experienced:**
   a. lower hospital mortality.
   b. lower overall Medicare charges.
   c. longer lengths of ICU stay
   d. All of the above

3. **In the report by Chan et al, implementation of a rapid response team led to which of the following?**
   a. A reduction in non-ICU codes.
   b. A reduction in hospital-wide codes.
   c. A reduction in rates of intubation for respiratory failure.
   d. A reduction in hospital mortality.

Answers: 1. (c); 2. (d); 3. (a)

CME Objectives

The objectives of *Hospital Medicine Alert* are to:

• review pertinent safety, infection control, and quality improvement practices;

• discuss diagnosis and treatment of acute illness in the hospital setting; and

• review current data on diagnostic and therapeutic modalities for common inpatient problems. ■