Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/critical-updates-treating-hospital-acquired-and-ventilator-associated-bacterial-pneumonia/11898/

Released: 10/23/2020
Valid until: 10/23/2021
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Critical Updates in Treating Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia

Announcer:
You're listening to CME on ReachMD. This activity, entitled "Critical Updates in Treating Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia," is provided by Prova Education and is supported by an independent educational grant from Merck.

Before starting this activity, please be sure to review the commercial support disclosure statements as well as the learning objectives.

Here is Dr. Keith Kaye

Dr. Kaye:
Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia, or HABP and VABP, are serious life-threatening infections that increase morbidity, mortality, and hospital costs. One of the things that we can do to improve outcome, is to implement effective empiric therapy; however, this isn't always so easy as we balance the risks of antimicrobial resistance due to unnecessary broad-spectrum prolonged antibiotic use with the need for effective therapy early on.

Today, we're going to discuss some important considerations with empiric therapy for HABP and VABP. This is CME on ReachMD, and I am Dr. Keith Kaye.

Dr. Kollef:
And I'm Dr. Marin Kollef.

Dr. Kaye:
So, let's dive right in. The choice of initial empiric therapy is often guided not only by national guidelines, but also by local guidelines and institutional antibiograms. When we consider issues around antimicrobial resistance, there are important factors that we should consider, several of which are host related. Dr. Kollef, I'm wondering if you can discuss some of these with us?

Dr. Kollef:
Yeah, I think that's really a critical issue, Keith. Even in the ICU last night, you know, this topic came up several times. And you know, when we're talking about patients and prescribing antibiotics, we need to really be considerate of what the local patient profile is, what our local susceptibility patterns are, but we also need to be aware of individual risk factors. And those risk factors certainly are important in assessing whether or not a patient might be at higher risk for having an MDR [multidrug-resistant] organism. Probably the most important risk factor is prior parenteral IV antibiotic therapy. I mean, we know that patients who receive prior parenteral antibiotic therapy within the prior 60 to 90 days are at higher risk for having subsequent colonization and infection with more drug-resistant organisms. We also need to think about risk factors for individual organisms. We know, for example, that an organism like *pseudomonas*, patients who have chronic lung disease, whether it's severe COPD, patients who have cystic fibrosis, interstitial lung disease, are going to be at a higher risk for having *pseudomonas* as a culprit pathogen. We also know that for *pseudomonas*, the presence of immune suppression increases the risk for that infection. Similarly, for MRSA [Methicillin-resistant *Staphylococcus aureus*], there are certain risk factors that we want to take into account, and that would include prior colonization with the organism or exposure to certain high-risk environments.

Dr. Kaye:
Those are really good points. I'll also add – you mentioned colonization and prior colonization with organisms like MRSA, and I'll just remind our listeners that, looking back at prior micro for your individual patient, you might find some very valuable information, maybe even respiratory tract cultures that can let you know whether or not your patients might be colonized or infected with a multidrug-resistant pathogen.

Dr. Kollef:
Now that we've reviewed the potential risk factors, Dr. Kaye, can you walk us through how you handle empiric therapy selection?

Dr. Kaye:
Yeah. When I'm thinking about empiric therapy, one of the major questions is: What's the likelihood that I'm dealing with a resistant pathogen, and what's the likelihood I need to provide coverage for that resistant pathogen? And there are two major considerations with these thought processes. The first is sort of epidemiologic risk factors or likelihood of a resistant pathogen, and you covered many of those issues just a moment ago. In addition to host factors, you want to look at your local antibiogram. You might even have a unit-specific antibiogram, which can often be helpful. You mentioned the importance of prior antibiotics, and all of these increase your knowledge as to whether or not these patients might truly have resistance risk factors. I think the other consideration that I always have is how sick is this patient? And if I don't provide adequate coverage, is this patient going to die or are they going to have a prolonged, severe ICU stay? Or do I have a little bit more wiggle room, and if I don't have it right on day one or two, might they be in the hospital an extra day longer, but maybe they aren't at that risk for severe outcome? So, the more acutely ill they are in terms of severe sepsis or fulminate and acute respiratory failure, the more likely I am to provide – regardless of their resistance risk factors, I'm more likely to provide a broad-spectrum coverage. And basically, the two broad agents that we consider are one, agents that are active against MRSA, which are typically vancomycin or linezolid in the ICU for pneumonia. And the second, which might even be a little bit more challenging, is the need for resistant *pseudomonas* coverage. And in those critically, severely ill patients with pneumonia, regardless of their resistance risk factors, you will want to provide double coverage for those patients.

Dr. Kollef:
Yeah, I think those are key issues. I mean, with critically ill patients, probably one of the most important determinates of outcome is the appropriate selection of antibiotics when they have a serious or life-threatening infection. And I think too often, you know, many clinicians work in environments where there are certain restrictions on antibiotics, often go-to drugs, then it really avoids or eliminates some of the thinking that should go into empiric antibiotic selection. But additionally, you know, we need to also think about the fact that antibiotics can promote resistance. And so, if we're starting out with a broad regimen, once we have our microbiology results, we need to think about de-escalating and really using the shortest course of therapy that's effective for the patient.

Dr. Kaye:
Well, Dr. Kollef, if someone isn't improving, or they're not behaving clinically, so to speak, or if you find out that you have a resistant pathogen that your initial therapy might not be covering, how do you approach sort of the next level of decision-making in those types of scenarios?

Dr. Kollef:
Yeah, I think there are two parts to that, you know. The first part is the individual, where you've started them on an empiric antibiotic regimen, they're clearly not responding, and then the micro results come back indicating that the organism is not susceptible to the empiric regimen. That type of inadequate treatment, that's been associated in multiple studies with a higher risk of mortality for patients with serious infections and patients in the ICU. And obviously one has to broaden the antibiotic regimen based on the susceptibilities of the pathogen. Having said that, the more ideal strategy would be to try and get that appropriate therapy on board from the beginning. That's really going to be based on your local susceptibility patterns and the risk factors that that patient may possess. The other issue is that, you know, there are times, particularly in the ICU, where we present the patient with an antibiotic and the organism is susceptible to it, but the patient's not responding. And that may have to do with dosing considerations, whether or not the patient has augmented renal function and may be clearing the drug at a higher rate. So it really becomes more of a complex issue within the ICU and – particularly when we're dealing with patients who have life-threatening infections, and we really need to take into account that empiric therapy.

Dr. Kaye:
For those just tuning in, you're listening to CME on ReachMD, and I'm Dr. Keith Kaye. And here with me today is Dr. Marin Kollef. We're just about to discuss the role of newer antimicrobials and other novel agents in treating HABP and VABP.

Dr. Kollef:
So, let's transition into the newer antimicrobials and novel agents.

Dr. Kaye:

So, this is an exciting time in the arena of newer agents that have received FDA indications for the treatment of HABP and VABP. These newer agents all offer some degree of enhanced activity against resistant pathogens. The first that we'll discuss is *imipenem-cilastatin*-relebactam, which combines imipenem, which is an old but well-known and trusted carbapenem, with a novel beta-lactamase inhibitor, relebactam, which can inhibit ESBLs as well as KPC.

Imipenem-relebactam was compared to piperacillin/tazobactam for the treatment of HABP and VABP and was noninferior. Outcomes were very similar between these two antibiotics.

There are also some antibiotics over the past few years that have been approved that deserve mention. One is ceftazidime-avibactam, which combines an old, third-generation cephalosporin ceftazidime with a novel, pretty broad-spectrum beta-lactamase inhibitor, avibactam. Another agent is ceftolozane tazobactam, which now we see an old beta-lactamase inhibitor, tazobactam, which we know in the past is, and currently is coupled to piperacillin, but it's a novel cephalosporin. And another antibiotic that deserves mention, although it does not have the HABP/VABP indication yet, is cefiderocol, which is a novel, broad-spectrum siderophore cephalosporin. This agent should be reviewed by FDA, and might be considered or will be considered at least for a pneumonia indication in the not too distant future. I will say that the safety profile of all the newer agents that I've mentioned, all were relatively safe. They compared favorably with their sort of tried and true trusted comparator antimicrobial. So, it's a growing list, and it's an exciting time to be in the ICU and in ID.

I think at this point I am going to ask Dr. Kollef another question. We know that COVID-19 is raging havoc not only in the US, but you know, across most of the world. What sort of new challenges has this brought to you in the ICU, particularly with regards to HABP and VABP?

Dr. Kollef:
Yeah, that's a great question, Keith. I don't know that I've seen an increase in resistance yet, but there is a concern for that in part because I think there's a tendency – and I've seen it here and I've spoken out against it – that when patients come up from the emergency room with respiratory failure due to COVID, they're often treated with very broad-spectrum antibiotics. And, I've spent a lot of time de-escalating and stopping antibiotics, but I think it's been sort of a global trend. And obviously, more antibiotic use, more parenteral antibiotic use, will undoubtedly breed more resistance over time. The main thing that I've seen with this pandemic is that there's just more fertile ground for these types of infections. Patients are on the ventilator for longer periods of time with COVID, and obviously the thing that really increases the likelihood for having a nosocomial infection is spending more time on the ventilator. And if you're being treated with antibiotics, you're more likely to subsequently develop an infection with an antibiotic-resistant organism. But the fact that these patients are on the ventilator, and many times for weeks or more, that really is what's predisposing them to becoming infected with more antibiotic-resistant organisms. So I don't know that I'm seeing any trends in terms of more resistance, but I do think we're seeing more patients who are on the ventilator for longer periods of time, and that simply will drive up the numbers of infections with MDR organisms.

Dr. Kaye:
Yeah, we've had a similar experience at Michigan and elsewhere with other colleagues I've talked to. During times, particularly when there are surges in COVID-19 cases, the frequency of those acutely and then chronically ill patients who spend long times in the ICU, as you're saying, with antibiotic exposures, you're simply seeing more of those types of patients at times. So you might see more resistant pathogens, but maybe not proportionately so, but just a raw number.

Well, I want to thank you, Dr. Kollef. This has been a fascinating conversation. If you had one sort of take-home message or an additional thought that you'd like to share with our audience, what would it be?

Dr. Kollef:
We've got to really try and get the most appropriate therapy to that patient when they initially present with that serious infection. So we really need to take into account, you know, the local microbiology that we're dealing with, the patient-specific risk factors, and even if it means starting broader, we also need to be considerate of the fact that we've got that stewardship role that we have to fulfill.

Dr. Kaye:
Yeah. I think that's a really good point. And I agree. I think a lot of the stewardship and resistance issues arise not necessarily with empiric therapy, but it's not acting upon or de-escalating or stopping that unnecessarily broad-spectrum empiric therapy on day – when it's no longer empiric – when you're on day 2, 3, or 4 and you actually have some more clinical and microbiologic data. So I want to thank Dr. Kollef, and it's been wonderful speaking with you today.

Dr. Kollef:
Same here. Thank you very much, Keith.

Announcer:

You have been listening to CME on ReachMD. This activity was provided by Prova Education and is supported by an independent educational grant from Merck. To receive your free CME credit, be sure to complete the post-test and evaluation at reachmd.com/Prova. This is CME on ReachMD. Be Part of the Knowledge.