AN INTERPROFESSIONAL APPROACH TO MANAGING MULTIDRUG-RESISTANT BACTERIAL INFECTIONS

Physician and Pharmacist Discussion

Question 1: Nav, In the monograph, you discuss the role of the pharmacist in managing MDR GNB and GPB infections. How do you as the pharmacist collaborate with infectious disease and other physicians to address issues that are relevant to these infections?

Navaneeth Narayanan, PharmD: First, to introduce myself, my name is Navaneeth Narayanan – I'm a clinical associate professor in the dept of Pharmacy Practice and Administration at the Rutgers Ernest Mario School of Pharmacy as well as an adjunct associate professor in the division of Infectious Diseases at the Rutgers Robert Wood Johnson Medical School. I practice as an infectious disease pharmacist at Robert Wood Johnson University Hospital in New Brunswick, New Jersey.

With respect to the question, I really work closely with the attending physicians as well as the fellows in the division of infectious diseases in many different areas ranging from clinical practice where I help participate in seeing consult patients, antimicrobial stewardship, setting policies and practices related to that, as well as research and education, which includes both but medicine as well as pharmacy trainees. I also work with non-ID physicians, as well. I can provide consultation to them on matters related to optimal antimicrobial therapy for their patients by giving expert insight into the pharmacology of different antimicrobials, as well as the clinical application. I also play a role, fortunately, in their medical education particularly through the lens of antimicrobial stewardship and helping ensure that the medical residents understand the appropriate use of antimicrobials in the hospital setting as well as in the outpatient setting. Overall, I really spend most of my time in my work day with the ID attendings as well as the fellows, more so than I even do with other pharmacists. The way I think about my position is that I work as a bridge between the pharmacy and the infectious disease division as well as the ID doctors that work in the community setting. So overall, I feel like there's a strong collaboration between myself and the different physicians in the hospital setting, whether that's an infectious disease physician or another specialty, and I think that my understanding of pharmacology and how to apply that in a clinical setting is really how I contribute and work collaboratively with these different physician groups.

Pinki Bhatt, MD: Just to introduce myself as well, my name is Pinki Bhatt. I'm an assistant professor of medicine in the division of infectious disease and allergy/immunology at Rutgers Robert Wood Johnson Medical School as well as an adjunct assistant professor at Rutgers Ernest Mario School of Pharmacy. In addition, I'm an associate program director of the Infectious Disease fellowship Program at the Robert Wood Johnson Medical School, as well, and in practice as an ID attending physician at the Robert Wood Johnson University Hospital in New Brunswick, New Jersey.

I think that collaboration between pharmacist and physician is very crucial right now, more than ever given the emerging number of multi drug resistant organisms. I've had the good fortune of working with several exceptional ID pharmacists over the years and I think their input brings a lot to the table. As an ID physician, I think if we were to have a question about an antimicrobial, majority of the time we would turn to an ID pharmacist. This is because they provide key information about drug toxicity, dosing and providing optimal use of antimicrobials (or stewardship) and regarding appropriate and targeted therapy. Having multidisciplinary collaboration between the physician and pharmacists regarding optimal use of

antimicrobials can also improve patient outcomes as it requires not only implementing appropriate antimicrobials for the patient, but also proper monitoring and de-escalation of antimicrobials when needed. In addition, pharmacists are well aware of new antimicrobials in the pipeline – so collaborating with pharmacists, especially during challenging cases, can be very beneficial.

Other ways that pharmacists and physicians collaborate regarding antimicrobial stewardship is working together to develop policies in the hospital depending on the patient population, using patient outcomes to assess effectiveness of antimicrobial policies within the system. ID physicians, whether they're clinical or microbiologists, also work very closely with pharmacists to ensure that appropriate microbial susceptibility tests are reported and to develop and distribute an empirical therapy guide based on these susceptibility patterns in the community and hospital. In addition to antimicrobial stewardship, I think collaboration between the physician and pharmacist is crucial to reduce transmission of infections and promote infection control at health care facilities and hospitals. This could include encouraging routine immunizations to hospital staff, promoting adherence to standard precautions, developing guidelines to decrease health care associated infections. I think that an additional benefit, most of all, of just having ID pharmacist educate physicians and physician-trainees on everything I listed above.

Question 2: Thank you both for sharing your perspectives on engagement. Can you discuss how you use shared decision-making to take that next step in working with other HCPs to ensure infection control and prevention objectives can be met?

Pinki Bhatt, MD: Yes, I think there's an urgent need for improvements in surveillance to help optimize empirical therapy and drive antimicrobial stewardship and infection control measures. When it comes to antimicrobial stewardship, I think prevention is key and educating other health care providers is critical with respect to avoiding excessive use of antimicrobials and, really, working with antimicrobial stewardship. Elements of antimicrobial stewardship would include minimizing unnecessary antibiotic durations, using targeted therapy, so not broad spectrum if possible, avoiding treating asymptomatic bacteriuria, for example. Educating other health care providers regarding how and when to use stewardship on their patients is critical. Further details can regarding stewardship can be directed to the Infectious Disease Society of America (IDSA) and Society of Health Care Epidemiology of America guidelines.

Healthcare professionals are the first line defense against health care associated infections and transmission of multidrug resistant organisms, and so, following infection control measures is also very critical. I would recommend to refer to CDC guidelines for implementing infection control. Some ways to implement this would include maybe designing a system that eliminates risk and enables providers to successfully prevent infections. So that includes building a team, identifying the gaps in the hospital or health care facility, developing aims/goals based on those gaps, and then planning an evidence-based intervention in order to implement these interventions.

Like I mentioned earlier, education is so important. Educating other health care providers on how to minimize transmission of infections. So that would include hand hygiene, how to maintain indwelling lines or catheters, determining which patients require certain precautions, so like, standard, airborne, droplet, extended, etc., and being able to use PPE appropriately in those cases as well.

Navaneeth Narayanan, PharmD: I think from my perspective as an infectious disease pharmacist, antimicrobial stewardship is really the best example, from an administrative point-of-view, in terms of the cross-collaboration and the shared decision-making that happens among pharmacists and physicians, as

well as with other health care professionals. As recommended by CDC and IDSA, pharmacists and physicians are really supposed to be working together as leaders of this important program within any health care facility. So, there is really a lot of close collaboration and decisions that are usually made together given the complementary areas of knowledge and expertise between physicians and pharmacists. My personal experience really reflects this great collaboration that happens between physician colleagues and pharmacists. Additionally, pharmacists in the hospital setting can help other clinicians, especially non-ID clinicians, in choosing appropriate antibiotics by their understanding of the pharmacology and understanding of things like drug allergies as well as the proper dosing, which I think is not underscored enough in terms of its importance level when managing infections, and making sure we get the dose right to minimize relapses or reinfections or even the emergence of drug resistance that might happen in the future giving suboptimal doses.

Question 3: How do each of you integrate antimicrobial stewardship practices when managing patients with COVID-19 co-infection?

Navaneeth Narayanan, PharmD: I believe that antimicrobial stewardship principles and practices really apply in all settings and diseases and COVID-19 is really no different than any of those. Yes, it's a novel virus and it's a very complex disease. We're still trying to understand it fully, and this introduces a lot of uncertainty and I think the gut reaction for many clinicians is to "cover all the bases." And this includes the concern for bacterial co-infections. What we know so far about bacterial co-infection is that it happens at a relatively low rate in patients with COVID-19 in the hospital, but unfortunately the use of antibiotics seems to occur at a very high rate in these patients. And I think a lot of that, once again, comes from the unknowns of this disease state and the complexity and complications related to it. So clearly there's an imbalance here with the risk of secondary infections, which is relatively low based on the data that we have, and the use of antibiotics to empirically treat this potential complication, which is, unfortunately, relatively high. Remember, there's always a risk vs benefit here – so the benefits are thought to cover these co-infections, but because they're happening at a relatively low rate, the risks of overuse of antibiotics are probably even higher in terms of that balance between risk versus benefit. We just have to remember that overuse of antibiotics can lead to adverse effects as well as drug resistance which is a major problem in itself globally.

Pinki Bhatt, MD: I completely agree and I think in order to kind of add on to that, the data regarding the incidence of bacterial co-infections in patients infected with COVID-19 is very limited. However, a study that performed a systematic search of databases found that the overall percentage of patients with COVID-19 and bacterial infection was only 6.9% concluding that bacterial co-infections in hospitalized patients with COVID-19 is relatively infrequent.(Langford 2020) And other studies have also shown that approximately 70-80% of patients with COVID-19 receive antimicrobials at some point during hospitalization with most receiving antimicrobials despite having negative blood cultures.(Bhatt 2020; Rawson 2020) The citations to these studies can be referred to in the monograph (and are also listed at the bottom of the transcript page).

Basically, these studies, and what Nav also pointed out, is that a lot of this underscores the importance of antimicrobial stewardship during this unprecedented time. Given the scale of the pandemic, indiscriminate antimicrobial use will inevitably lead to other complications such as antimicrobial resistance, adverse drug reactions and infections such as *Clostridium difficile*. So, I think using this information helps me understand what a patient's risk for developing a secondary infection may be, in order to help me guide if empirical antibiotics are even needed. This is done via patient's clinical presentation, looking at their imaging and other diagnostic data to really understand if the antibiotics are needed. This in addition, gives

me a chance to educate other health care providers on importance of stewardship when treating patients with COVID-19.

Question 4: Pinki, what are your thoughts on the physician's role relative to infection control to prevent the transmission of multidrug resistant organisms?

Pinki Bhatt, MD: You know, I think as physicians we have a very important role in the hospital to help others prevent transmission of multidrug resistant organisms.

One, I think being a good role model when it comes to infection control is important in order to ensure that other providers are also following the necessary protocols in place. And that includes ensuring that appropriate PPE is utilized and worn, hand hygiene compliance upon entry and exit of patient rooms is done, etc.

Number two, I think physicians can play a key role in educating others to implement the set guidelines and protocol in place to prevent transmission of MDRO. Other ways physicians play a role were discussed earlier, but I would like to add the following: so, for example, from an administrative standpoint, a physician can make multidrug resistant organism prevention and control an organizational patient safety priority. Implementing multidisciplinary processed to monitor and improve health care personnel's adherence to the recommended infection control guidelines that are instituted at the facility, such as standard and contact precautions, can also be done.

Number three, identifying patients who are colonized or infected with MDRO and then notifying other healthcare personnel caring for the patient or facilities, especially if being transferred between facilities.

Number four, monitoring patient-care-unit trends of MDRO infections to really determine if these rates are decreasing and if any intervention is needed. Annual updates should also be conducted, which include changes in the prevalence/incidence of infection, action plans made to improve the adherence of infection control and to see if reduction of infections or transmission were seen.

Lastly, providing training and education to health care personnel regarding risks and prevention of multidrug resistant organism transmission is also very important when it comes to infection control.

Resources and References

Guidelines
Infectious Disease Society of America (IDSA): Tamma PD, Aitken SL, Bonomo RA, et al. Infectious Diseases Society of America Antimicrobial Resistant Treatment Guidance: Gram-Negative Bacterial Infections. Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America. 2020 Oct.

Society of Health Care Epidemiology of America Guidelines: Available at https://www.guidelinecentral.com/shop/antibiotic-stewardship-guidelines-pocket-card/. (Requires purchase)

Centers for Disease Control and Prevention. Core Elements of Antimicrobial Stewardship. Available at https://www.cdc.gov/antibiotic-use/core-elements/index.html.

COVID-19 References

Bhatt PJ, Shiau S, Brunetti L, et al. Risk factors and outcomes of hospitalized patients with severe COVID-19 and secondary bloodstream infections: a multicenter, case-control study. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2020;ciaa1748. Advance online publication. https://doi.org/10.1093/cid/ciaa1748.

Langford BJ, So M, Raybardhan S, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clinical Microbiology and Infection.* 2020;26(12):1622–1629.

Rawson TM, Moore LS, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020;ciaa530.