Acute Bacterial Skin and Skin Structure Infections: Advantages and Disadvantages of Early Discharge and Outpatient Parenteral Antibiotic Therapy

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Summary

Acute bacterial skin and skin structure infections (ABSSSI) can require long periods of antibiotic therapy. If an ABSSSI is treated while a person is in hospital, this may lead to an extended hospital stay of days or even weeks, even if the patient is in a stable enough medical condition to be discharged to their home environment. As such, inpatient treatment of an ABSSSI can incur high costs for the hospital and tie up beds that could be used for other patients. Michael Wilke from Inspiring-health GmbH, Munich, Germany, and the Medical School Hamburg, Germany, discussed with the EMJ how early discharge may be viable for patients who are medically stable and can either return to the hospital for daily treatment with intravenous (IV) infusions or are able to, reliably, take oral antibiotics. Also available are the long-acting antibiotics oritavancin and dalbavancin. The latter is administered only once via IV infusion. While the cost per dose of dalbavancin is more expensive than most oral or daily/twice daily IV antibiotic regimens, its use can facilitate early discharge, leading to reduced hospital stays and offset cost savings. Due to the administration schedule, the use of long-acting antibiotics circumvents issues with daily medication adherence.

INTRODUCTION

ABSSSI includes cellulitis/erysipelas, major cutaneous abscesses, and wound infections.[1] These are most often caused by Gram-positive *Staphylococcus aureus* (including methicillin-resistant *S. aureus* [MRSA]) and *Streptococci*, with fewer ABSSSI due to Gram-negative bacteria.[1] In the inpatient population, ABSSSI presents a large healthcare burden, including greater resource use and extended hospital stays.[2]

Wilke has extensive clinical and research experience in assessing and treating ABSSSI and analysing the health economics associated with such. Here, he discusses with EMJ the medical, quality of life, and economic issues associated with patients remaining in hospital for ABSSSI treatment; how those eligible for early discharge can be best identified; and the potential advantages of the long-acting antibiotic dalbavancin (marketed as Xydalba in Europe and Dalvance in the USA [Allergan Pharmaceuticals International Ltd, Dublin, Ireland]) within these realms.

CHALLENGES WITH PATIENTS REMAINING IN HOSPITAL TO TREAT AN ACUTE BACTERIAL SKIN AND SKIN STRUCTURE INFECTION

A number of issues can arise when a person with an ABSSSI is kept in hospital only for the treatment of such a condition, discussed Wilke. The first is that the nature of the infection, deep in the skin or soft tissue, can mean antibiotic therapy needs to be administered for a number of weeks. Another is that these patients may have comorbidities such as diabetes and bad microcirculation that are associated with a higher rate of ABSSSI.[3] A deep ABSSSI in such a patient means that they may be complex to treat with regard to antibiotic efficacy and safety. For instance, dose adjustment may be needed for antibiotics due to potential drug interactions with antidiabetic agents.[3]

A further problem is financial. In many countries, Wilke pointed out, payments for treatments and conditions are limited by health insurance companies covering only a set number of days, treatments, or amount of cost per condition. This means there can be instances where a person is staying in a hospital but costs are not reimbursed, incurring a loss of finances for the hospital.[4]

Also problematic, according to Wilke, is that in hospital, the patient is more at risk of picking up another infection and of passing on the infection they have, if it is transmissible.[5] Lastly, most patients do not like staying in hospital and would prefer to be in their home environment.

CHALLENGES WITH TREATING METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

MRSA can be a particularly challenging form of ABSSSI and it is vital when a patient presents with an ABSSSI that MRSA is considered, especially when it is purulent. This is carried out by careful consideration of signs and symptoms combined with specimen culture and susceptibility testing.[6] According to Wilke, the first challenge is that MRSA can survive for long periods on surfaces,[5] leading to a risk that it is transferred from a patient to the hospital environment and back to another patient. There is also the potential that the patient can carry MRSA out of hospital and into communal living settings, such as a nursing home.[7]

The next challenge, Wilke pointed out, is that there is a very limited armamentarium of drugs with proven efficacy against MRSA. Of these, all but two of them (IV dalbavancin and oral linezolid) must be administered via daily or twice daily IV infusion, and some, like vancomycin, necessitate therapeutic blood monitoring to ensure drug levels stay within the therapeutic range.[8]

IDENTIFYING PATIENTS WHO COULD BE SENT HOME FROM HOSPITAL WITH ANTIBIOTIC TREATMENT

According to Wilke, "one in three patients with an ABSSSI could be eligible for earlier discharge as a rule of thumb." Indeed, a multicentre, multicountry study of hospital inpatients with MRSA found that 37.9% could potentially be eligible for early discharge if eligibility criteria regarding infection and clinical stability were met.[9]

Wilke discussed how he and his colleagues have developed an algorithm that can be used by healthcare professionals at the bedside to assess if a person may potentially be discharged while still being treated for an ABSSSI. This algorithm can help point to an early discharge if no infection parameters are present, for example, laboratory detection of C-reactive protein, and/or if the infection is stable or slightly declining; the patient is clinically stable; there is no fever;

the patient is not in intensive care; they have not had surgery in the last 2 days or have any planned for the foreseeable future; wound dressings, if present, could be changed in the home setting; the patient does not have issues in taking oral medication (where applicable); and, in a healthcare professional's opinion, the patient would adhere to their medication regimen.

ECONOMIC AND PATIENT QUALITY OF LIFE IMPACTS OF EARLIER HOSPITAL DISCHARGE

Being able to treat an ABSSSI in the home setting has been shown to reduce healthcare-associated costs and increase patient quality of life.[2,10] Wilke discussed how this raises the probability that a patient can be discharged within the insurance-covered length of stay for their medical condition (in countries where this applies), so that costs are at least covered, or losses are minimalised.

Also, he continued, "if a patient is discharged earlier from the hospital, the beds are free to treat a new patient." This cuts down on waiting times and, in economic terms, means more revenue can be generated per patient. Additionally, most patients, Wilke discussed, "do not appreciate being in hospital, where there are people in the room and there is no privacy." Most, he continued, "are happier in their home environment. You can organise your day as you want, not like the hospital staff wants to. In hospital, you can't just go out for a walk."

If a patient is discharged and needs to come back into the hospital for outpatient parenteral antibiotic therapy (OPAT), they are at least, Wilke highlighted, "back in life again. For instance, they can go to a restaurant and meet their children."

POTENTIAL CHALLENGES ASSOCIATED WITH DISCHARGING A PATIENT RECEIVING ANTIBIOTIC THERAPY

In many countries, treatment can be carried out via an OPAT programme where the patient attends an outpatient clinic daily or twice daily for IV antibiotics. However, while this therapy may be advantageous for people who live locally, another issue, explained Wilke, is that "if the patient does not live nearby, they might have to travel 100 km on a daily basis, which might counter the effect of being at home again." Treatment-related complications associated with IV antibiotic administration may include venous access issues, drug-related side effects, skin rash, and nephrotoxicity. If detected in the OPAT setting, such issues may lead to rehospitalisation.[10]

Although oral drug therapy may be the solution when the infection is amenable to such and a patient can take drugs orally, a challenge here, Wilke discussed, is that "current oral drug therapy with linezolid for MRSA has a limit of 28 days but some patients need treatment longer than this, so then they have to switch to another drug and go back into IV treatment."

One challenge associated with discharging a patient while they are still being treated for an infection is, according to Wilke, that "you have to track the patient and make sure that your anti-infective regimen is perpetuated." Indeed, compliance with taking a course of antibiotics is an ongoing problem in healthcare.[11,12] "Many won't take them at all after discharge," he explained and discussed how even studies using smart pill bottles with electronic sensors combined with self-report questionnaires, so the patient knows they are being monitored, show non-adherence to a drug regimen.[12]

TREATMENT WITH DALBAVANCIN

Dalbavancin is a long-acting lipoglycopeptide antibiotic used for Gram-positive bacteria such as *Streptococci* and MRSA.[13-16] With a terminal half-life of 15.5 days, the administration is a single 1,500 mg dose or a 1,000 mg dose on Day 0 and 500 mg on Day 7, administered as a 30-minute IV infusion.[15,16]

According to Wilke, dalbavancin "has advantages and a disadvantage. One advantage is that you can administer it then send the patient home as it's so long-acting." This, he explained, means that a single infusion can be given on the morning of discharge. Another advantage Wilke highlighted is that "the long half-time of dalbavancin can avoid all issues of adherence and compliance when taking antibiotics." A third advantage is that dalbavancin has a generally favourable side effect profile.[13-16]

Dalbavancin is, though, very expensive per dose. However, Wilke pointed out that while a drug such as vancomycin is much cheaper, the costs of having to remain in hospital while being treated are also very high. With vancomycin, therapeutic drug monitoring is also needed, adding to the costs that include healthcare staff and general hospital care.

A case data analysis by Wilke and colleagues found that administration of a single dose of dalbavancin in patients with an ABSSSI had the potential to reduce the length of hospital stay by 6.45 days and healthcare costs by 2,865 EUR.[4]

CONCLUSION

Treatment of ABSSSI can include many weeks of antibiotic therapy, which may mean a person has to remain in hospital even when otherwise fit for discharge. The advent of OPAT or home therapy means that eligible patients can be discharged, leading to large savings and freeing up hospital beds. However, typical IV therapy necessitates a once or twice daily return to the hospital for drug administration if oral medication is not indicated. The use of dalbavancin, though expensive, can mean a patient can be discharged from the hospital early and is advantageous in the realm of therapy adherence.

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