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Challenges Ahead of Studying Antibacterial Utilization in Hospitals: Limitations of Recommended Methods

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Inappropriate use of antibacterial medications in hospitals has confronted practitioners with difficult to treat infections caused by resistant microorganisms (1). Considering the vital role of these medications in patient care, it is important to study antibacterial utilization in hospitals and implement programs accordingly. Drug utilization studies could be conducted using individual level data (drug utilization evaluation) or aggregate data. Parallel use of different types of drug utilization studies would provide a more comprehensive picture from antibacterial use in hospital.

In order to conduct a reliable drug utilization study that enables us performing internal assessments and making meaningful comparisons with other studies, international methodological standards have been recommended. International drug classification system and standard unit of measurement are two main components of the recommended methodological standards for drug utilization studies by World Health Organization (WHO). Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) system was developed and recommended by WHO in 1981. This system has been maintained and updated by WHO Collaborating Centre for Drug Statistics Methodology based on the expert advice from members of WHO International Working Group for Drug Statistics Methodology (2).

Many studies were conducted using WHO ATC/DDD system and benefitted from its advantages (i.e. standardizing the recorded information, enable aggregating information, allowing meaningful comparisons). Nevertheless, researchers conducted antibacterial utilization studies in the hospitals faced some methodological challenges.

One of the challenges ahead of studying antibacterial utilization in the hospitals is emerged when DDDs are applied. DDD is the average daily maintenance dose of medication for its main therapeutic use in adults. DDDs for antibacterial were determined based on antibacterial use in moderate infections. However, severe infections are also treated in the hospital setting and DDD is potentially lower than the actual prescribed dose (PDD) in many cases. For instance, benzylpenicillin doses in the treatment of moderate to severe infections such as meningitis are higher than allocated DDD that is 3.6 g (6 MIU). Consequently, metrics that are calculated using DDD would overestimate the total consumption of antibacterial in the hospital. In other words, consumption data are higher when expressed in DDDs per 100 bed days compared to actual use. To overcome this limitation, other appropriate units of measurement should be considered in addition to WHO DDDs. Hospital-adjusted

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defined daily dose (haDDDs) has been recommended by researchers however, its adequacy needs to be confirmed in further studies. HaDDDs have been calculated and studied considering antibacterial use data in Norwegian hospitals (3). In this study, WHO DDDs were adjusted to recommended doses for hospitalized patients in guidelines. The relative occurrences of moderate and severe infections were also taken into account in the calculation of haDDDs.

Another challenging issue is selection of the best metric and indicator of antibacterial consumption in hospital. An appropriate metric should contain relevant denominator for the health context. DDDs per 1000 inhabitants per day, known as DID, has been frequently used to quantify medication consumption. However, DID is not an appropriate metric to quantify antibacterial use at the hospital level. Parallel use of DDDs per 100 bed days and DDDs per 100 admissions has been proposed in reporting hospital antibacterial use data as a standard approach. Using mentioned denominators, considering suggested precise definitions, would reflect variations in hospital clinical activity. European Surveillance of Antimicrobial Consumption (EASC) confirmed using both mentioned metrics in antibacterial use studies in hospitals. On the other hand, it has been recommended in the United States to use days of therapy (DOT) per 1000 patient days for measuring antibacterial use in hospitals. In order to calculate this metric, patient-level data would be required (4). Moreover, researchers should avoid variable definitions of metrics making comparisons difficult.

As the last note, a major obstacle to the studying antibacterial use in hospitals is lack of an international standard unit of measurement for drug use quantification in pediatric population. Using WHO DDDs to estimate antibacterial use in pediatric patients would confront the studies with major limitations. WHO DDDs were determined considering dosing in adult population. Without taking into account weight and age variations and corresponding dosing in children, estimations based on DDDs would be far from actual consumption in this population of patients. For example, antibacterial consumption in older children for whom medications were prescribed with inappropriately low doses might be estimated to be average. On the other hand, the consumption data from an adolescent ward would be much higher than that from a neonatal unit, making direct comparisons very difficult between hospitals with different patient case mix (number and types of patients treated by a hospital). A new algorithm has been proposed to make accurate estimations and comparisons of neonatal and pediatric antibiotic use in hospitals (5). However, this method needs to be validated in larger studies. Development of a standard international unit of measurement to quantify antibacterial use in children (e.g. simplified version of the adult DDD) is necessary.

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