Original Article

Antimicrobial Utilization Study in a Neurology Setting

Namita Vilas Nasare[1], Ankit Bhardwaj[2], Vineeta Bablani[3], Renu Gupta[4], Suman Kushwaha[5], Sangeeta Sharma[6]

Background : Measuring antimicrobial consumption is necessary to understand the volume and patterns of use, to design appropriate interventions to reduce and rationalize its use.

Materials and Methods : The antimicrobial consumption in Neurology ICU and IPD were measured over a 5-year period using WHO Defined Daily Dose (DDD) methodology.

Results : There was an increasing trend in Antimicrobial Consumption (AMC) from 125.7 to 155.5 DDDs/100 days over 5 years with highest consumption in 2017-2018 (190.7 DDDs). The consumption of Watch group of antibiotics was higher than access group antibiotics both in ICU and IPD and constituted more than 75% of total antibiotic consumption.

Conclusions : The initiation of empiric therapy though may be necessary depending on the patients condition, however, duration of antibiotic therapy and reducing usage of prophylactic antibiotics for aspiration pneumonia and reducing consumption of Watch group of antibiotics were identified as stewardship opportunities. Feedback on AMC data and persuasive educational interventions to rationalize and reduce antimicrobial use are required.

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***Key words* : Defined Daily Dose, Antibiotic Resistance, Antimicrobial Resistance, Antimicrobial Use, Antimicrobial Consumption.**

Antimicrobial Resistance (AMR) has been recognized as a major public health problem with catastrophic consequences on human health, economy and food security[1]. Antimicrobial Use (AMU) is the key driver for AMR and has increased substantially globally, over past decades with nearly 30% of all hospital in-patients receiving antibiotics and out of it around 30-50% of all antibiotics prescribed are reported to be unnecessary, inappropriate or misused[2].

Antimicrobial Stewardship (AMS) is urgently required to rationalize antimicrobial use ie, reduce unnecessary use and promote appropriate usage when indicated in order to preserve these precious resources[1,2]. It is imperative that before initiation of any AMS activities, the magnitude of antibiotic consumption is measured to understand the extent and understand the causes of irrational prescribing so that interventions for reducing AMU can be designed accordingly[1]. The consumption data allows monitoring of trends and comparison across countries, regions, healthcare facilities as well as to inform policies, regulations and interventions for optimization of AMU. The Antimicrobial Consumption (AMC) data can also serve as benchmark for risk-adjusted inter and intra-facility use and to establish epidemiological association between antibiotic use and resistance over time[1].

Editor's Comment :

- Antimicrobial usage is the key driver for antimicrobial resistance; measuring antimicrobial consumption is necessary to reduce its use.
- The overall antimicrobial usage and initiation of antibiotics for empirical management may be necessary in Neurology settings but duration of antibiotics should be reduced.
- The reduced usage of Watch antibiotics, prophylactic therapy and timely de-escalation were identified as possible interventions towards further reducing antibiotic usage.

World Health Organization (WHO), Defined Daily Dose (DDD) methodology is an aggregate data collection method. The DDD is the assumed average maintenance dose per day for an antibiotic used for its main indication in adults. It allows identification of broad problem areas with drug use and data can be captured relatively easily[3,4].

Access, Watch, Reserve (AWaRe) categorization is a WHO tool to classify antibiotics into Access, Watch, Reserve category to target use of narrow-

Institute of Human Behaviour and Allied Sciences, Delhi 110095

[1]MSc (Pharmacology), Former Senior Resident, Department of Neuropsychopharmacology

[2]MBBS, MD, Former Senior Resident, Department of Neuropsycho Pharmacology

[3]MSc (Microbiology), Lab Assistant, Department of Neuropsycho Pharmacology

[4]MBBS, MD, Assistant Professor, Department of Microbiology and Corresponding Author

[5]MBBS, MD, DM (Neurology), Professor and Head, Department of Neurology

[6]MBBS, MD (Pharmacology), MBA, Professor and Head, Department of Neuropsycho Pharmacology

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spectrum antibiotics while reserving broad-spectrum antibiotics for "hardest to treat infections"[5]. 'Access' group are narrow-spectrum antibiotics which should be easily accessible as these are life-saving and have less potential for development of resistance. Access group antibiotics should be preferred over Watch and Reserve group. The 'Watch' group comprises broader spectrum antibiotics with higher potential for development of resistance and 'Reserve' group consists of last-resort antibiotics for targeted use in multidrug-resistant infections[5]. The DDD when linked with 'AWaRe' categorization reflects the pattern or quality of antimicrobial use.

The present study was conducted to measure antimicrobial consumption in Intensive Care Unit (ICU) and In-patient Department (IPD) of neurology over a 5-year period using DDD methodology, to understand the quality of prescribing using AWaRe categorization and make recommendations for appropriate AMS strategy(ies).

Materials and Methods

The data on antimicrobial consumption was collected retrospectively from Neurology Department (10 bedded Intensive Care Unit (ICU) and 34 bedded In-patient Department (IPD) of a Super-specialty Public Hospital from the indent records. The study was conducted after approval of Institutional Ethics Committee.

Defined Daily Dose (DDD) : The aggregated antimicrobial consumption (except for antitubercular drugs) was calculated year wise using the Anatomical Therapeutic Chemical (ATC) for (J01) DDD Index 2019, as per WHO Collaborating Centre for Drug Statistics Methodology, Oslo (Norway)using AMC tool version 19.1.1[3,4]. Bed occupancy data was collected from Medical Record Department.

Drug Utilization 90% (DU 90) : The average year wise DDD/bed days was arranged in descending order and cumulative DDD/1000 days (DID) calculated and expressed as Drug Utilization 90% (DU 90%).

Access, Watch, Reserve (AWaRe) : The quality of antimicrobial used was assessed by WHO AWaRe categorization method[5]. The antibiotics consumption by AWaRe category was calculated as the percentage consumption in each category.

Statistical analysis :

Data analysis was done using MS Excel and statistical measures like range, frequency, average, percentage, DU90% were calculated. Trend analysis was done using linear regression.

Results

The trends of total AMC in neuro ICU & IPD is shown in Fig 1. There was increasing trend in AMC over the years from 125.7 to 155.5 DDDs (R^2 = 0.317) with highest consumption in 2017-2018 (190.7 DDDs). The AMC was higher in ICU compared to IPD in all the years. Figs 2a and 2b depict the year wise antimicrobial consumption of antimicrobials (DU90) in neuro ICU and IPD respectively. The most consumed antimicrobial agents in ICU were ceftriaxone followed by metronidazole, piperacillin-tazobactam, meropenem whereas ceftriaxone, amoxycillin-clavulanic acid, metronidazole were most commonly consumed in IPD. Fig 3 depicts percentage consumption of antibiotics based on Access, Watch and Reserve categorization.

Discussion

This study analyzed the trends and pattern of antibiotic consumption in neurology setting. Although there are many reports of antibiotic use in ICU setting but this is the first study reporting AMC in neuro ICU and IPD, to the best of our knowledge. Intensive care settings are an appropriate focus area for AMS as a large proportion of antibiotics use, especially broad-spectrum and parenteral antibiotics occurs in these areas. It is important to study extent of use of antimicrobials in neuro settings as the profile of patients admitted here differs from other critical care setting.

We observed a rising trends in AMC over 5 years. The average DDDs of 5 years in Neurology ICU was quite high (116.3) but is comparable to total antibiotic consumption reported from several medical, surgical, and neurosurgical ICUs across India. A large variation has been reported in DDDs, globally, varying from 118.2

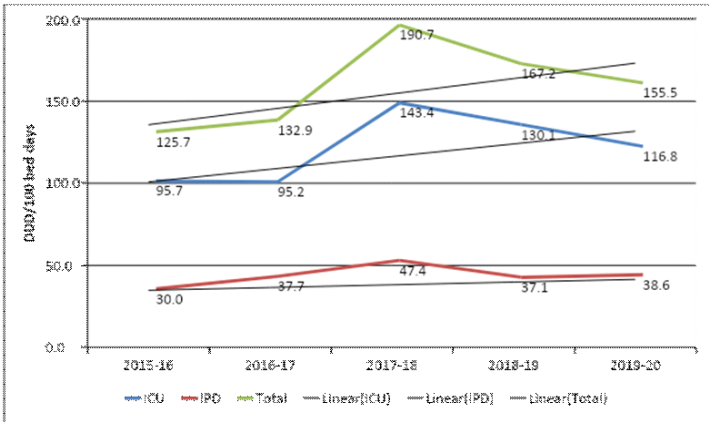

Fig 1 — Trends in total DDD of antimicrobials in neurology ICU and IPD over 5 years

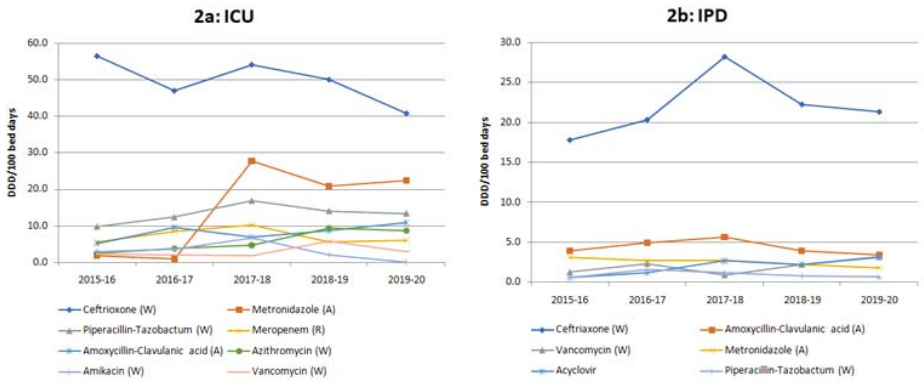

Fig 2 — Trends in DDD of antimicrobials (DU 90) in neurology ICU (2a) and IPD (2b) over 5 years (A: Access; W: Watch; R: Reserve)

to 560.11 DDDs, however a neurosurgical ICU in Gujarat, India reported DDDs as less as 52.8[6-10]. A large antibiotic surveillance study involving 35 ICUs in Germany reported DDD of 133 which is also more than our ICU[11]. These differences in the reported DDDs could be due to differences in the criticality and patient profile of the patients admitted in different settings. In the present study, the overall AMC consumption was three-fold higher in ICU compared to IPD with average DDD of 116.3 in ICU and 38.2 in IPD. Higher antimicrobial consumption in ICU can be justified in patients presenting with life-threatening infections requiring empirical broad-spectrum antibiotics within 1 hour of the suspicion of the infection.

The most consumed antimicrobial was ceftriaxone (a Watch group) in both ICU and IPD. In our setting, tubercular meningitis followed by acute meningoencephalitis, seizure disorders (status epilepticus), cerebrovascular accidents (stroke) are the most common clinical presentations. Ceftriaxone is commonly used empirically in critically ill patients on clinical suspicion of an infection to reduce morbidity, mortality and improve functional outcome[12]. The high consumption of ceftriaxone in IPD may also be justified as 14-28 days of therapy with antibiotics is required for completion of a course in a case of bacterial meningitis.

Metronidazole, piperacillin-tazobactam, meropenem and amoxycillin-clavulanic acid were the next commonly prescribed broad spectrum empirical antimicrobials, in ICU similar to the pattern reported in previous studies[4-8]. These antimicrobials including ceftriaxone were prescribed prophylactically for suspected aspiration/acute aspiration pneumonitis in patients with status epilepticus, CVA (strokes, hemiparesis), multiple sclerosis affecting bulbar functions. Aspiration pneumonitis is most often a chemical injury requiring only supportive care without need to initiate antibiotics, but antibiotics are often prescribed in most patients in practice[13,14]. Our study reports high use of metronidazole in ICU. Metronidazole was used probably to provide a cover for anaerobes, however, there is limited evidence supporting role of anaerobes in aspiration pneumonia[13]. There is now sufficient evidence that neither prophylactic antimicrobial therapy nor metronidazole offers any clinical benefit for suspected aspiration/ acute aspiration pneumonitis. In fact, it may result in selection of antibiotic resistant strains requiring escalation of antibiotic therapy and adverse events such as *Clostridioides difficile* infection[13,14]. Empirical antibiotics with anaerobic coverage should be considered only in the presence of clinical risk factors for aspiration or presence of lung abscess, empyema, or necrotizing pneumonia[15].

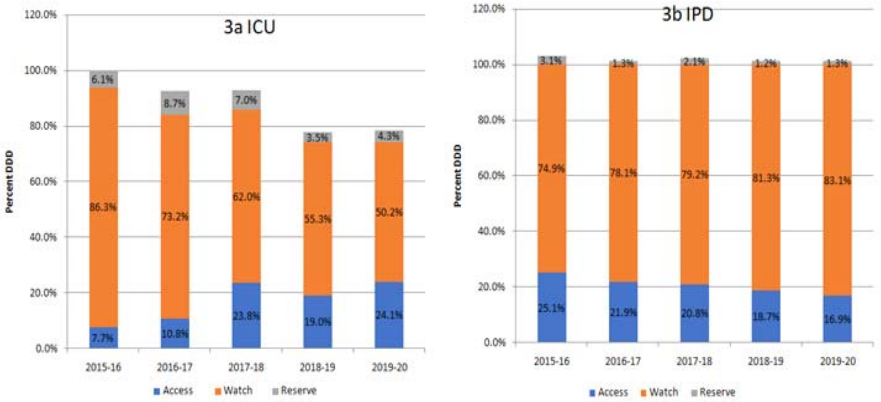

Fig 3 — Trends in percent antibiotic consumption according to Access, Watch and Reserve categorisation in ICU (3a) and IPD (3b)

WHO advocates that Access group of antibiotics should be preferred over Watch and Reserve group to improve access and should comprise 60% of the total antibiotic consumption[5]. However, in the present study, overall use of Access group antibiotics was ~20% in both ICU and IPD, whereas, Watch group antibiotics accounted for major proportion (>75%). Higher consumption of Watch group antibiotics in ICU could be because of its empirical use in life threatening infections as seen in Neuro ICU. In the present study though, AMC was lower in IPD but Watch group antibiotics comprised the major proportion. One of the reasons for high proportion could be failure to de-escalate the antibiotic started in ICU. Further, in ICU over the years, a gradual decline in consumption of Watch group antibiotics was observed without any change in consumption of Watch group in IPD.

The overall antimicrobial consumption and increasing trends require active intervention by providing feedback to the prescribers with targeted persuasive education programs to rationalize antimicrobial use and decrease overall consumption.

Limitations

DDD of anti-tubercular drugs has not been calculated as medicines for these patients are obtained directly from the DOTS centre. Further, DDD data should also be collated with the antimicrobial resistance data to guide antibiotic therapy in accordance with local antibiogram.

Conclusion

The overall extent and quality of antimicrobial use, initiation of empiric antibiotic therapy was appropriate and comparable to other published studies but there are opportunities to further reduce antimicrobial use particularly of Watch group antibiotics. AMS interventions such as feedback on AMC data and persuasive educational interventions, guidelines for management of common neuro-infections based on antibiogram, regular review and documentation of start and stop dates of antibiotics should be implemented. Regular audit of AMS actions such as de-escalation to narrower spectrum antibiotic or IV to oral switch after 48-72 hours can further help in timely de-escalation. To reduce the prophylactic antibiotics in aspiration pneumonia guidelines on prophylactic use of antibiotics for aspiration Pneumonia need to be developed. Cohort nursing training can reduce the incidence of aspiration reduction and thus reducing the antibiotic usage.

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