



A Study on Optimal Duration of Antibiotic Therapy in Various Infectious Diseases

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ABSTRACT

Antimicrobials are a standout amongst the most usually prescribed medicines. However, they are often excessively and inappropriately used, which can lead to adverse effects (including fatality in a few cases) in individuals and the community as well. The duration of antimicrobial therapy needs to be sufficient to control the microbial infection and prevent relapse. The aim of this study is to estimate the duration of antimicrobial therapy in various infectious disease conditions and identify commonly prescribed antibiotics in infectious diseases. A Prospective Observational Study was conducted for one year (December 2013 - December 2014) on the patients diagnosed with infectious diseases of both sex and mean age of 39 ± 16.8 years in a super specialty hospital, Hanamakonda, Warangal, Andhra Pradesh, India. During the study period a total number of 2500 patients were reviewed, among them 752 patients were enrolled in the study who has met the inclusion criteria. Among the patients enrolled, 456 (60%) patients were males and 297 (48%) patients were females. In total, of collected 7 infectious diseases, the longer duration of antibiotic treatment was required to diseases like pancreatitis and malaria that is around 18 days followed by liver abscess of 13 days, typhoid fever of 11 days and gastroenteritis and pneumonia with 10 days each. The shortest duration of 9 days of antibiotic therapy is sufficient for UTI.

Keywords: Antibiotics, Infectious Disease, Duration of Antimicrobial Therapy.

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INTRODUCTION

Antibiotic use has been escalating steadily in recent years. In India, Antibiotic constitute 15.7% of the drug market (The largest therapy group)¹. Many studies of prescribing patterns suggests that antibiotics are often used in inappropriate ways which needs to be controlled. A few hospital- and city-based investigations of antibiotic use have proven that antibiotics are regularly prescribed in irrational or inappropriate ways in India resulting in the adverse outcome of antibiotic therapy. Moreover there is a threat of post-antibiotic era for the 21st Century – in which common infections and minor injuries can be fatal which emphasises the need for rational use of antibiotics². The duration of antibiotic therapy plays a key role in the rational use of antibiotics, so the duration of antibiotic therapy needs to be regulated properly to completely cure the bacterial infection and prevent its relapse. There have been relatively few studies determining the optimal treatment durations for infection. The data drawn from studies like this can help Professional organizations develop clinical practice guidelines to aid clinicians in choosing optimal treatment durations for individual patients. The optimal duration of antibiotic therapy is precise for many infections, such as for Urinary tract infections, Gastroenteritis, Liver abscess and Pneumonia, but in Practice the duration of therapy depends on clinical symptoms, the causative organism, whether source restriction is possible and the patient's response to therapy. On the other hand, for many syndromes associated with infections, there is no variation in outcome when antibiotics are used for reduced duration^{3,4,5}. Based on the expert opinion the recommended duration of therapy for most infections is 5–14 days, depending on the syndrome⁶. Several trials have proved that longer antibiotic therapy encourages the development or acquisition of antibiotic-resistant organisms. Longer presentation to antibiotics as well appears to have dangers and harms for the patient, such as increased risk of adverse effects like diarrhea, abdominal discomfort, hypersensitivity and vomiting, difficulties with adherence and Costly treatment for some antibiotics. For some infections, such as *Staphylococcus aureus* bacteraemia, enterococcal endocarditis, meningitis or tuberculosis, clear evidence favors prolonged treatment to prevent relapse. Nevertheless, it is recommended to concise the duration of therapy as far as possible, unless generally indicated, as this may lower the selection pressure (as the pipeline of newly discovered antibiotics is dried up) and help prevent resistance in the individual. In general, it is thought that short duration of antibiotic therapy results in similar outcomes to those of longer courses⁷. There is a typical confusion that resistance will develop if a recommended antibiotic course is not finished. Early discontinuance of anti-microbial treatment won't expand the danger

that resistance will augment. Restricting the duration of antimicrobial therapy is an important strategy for optimizing patient care and reducing the spread of antimicrobial resistance. It is additionally apparent that an overall approach to infection management includes a focus on selecting the right initial drug and dosing regimen for empiric therapy, and de-acceleration to a more specified drug regimen (or termination) based on subsequent clinical data and culture results. In addition to reducing resistance, other potential advantages of shorter antimicrobial courses incorporate lowered antimicrobial costs, reduced risk of superinfections such as *Clostridium difficile*-associated diarrhea, decreased risk of antimicrobial-related organ toxicity, and improved medication adherence.

MATERIALS AND METHOD

A Prospective observational study was performed at a super specialty hospital, in Telangana region for a period of one year. All the patients who were admitted in the general medicine department of the hospital were reviewed on a daily basis and those who met our inclusion criteria: patients diagnosed with infectious diseases of both sex and mean age of 39 ± 16.8 years were included in the study. Patients with chronic diseases (SLE, Renal and hepatic failure, etc.), chronic infectious disease (HIV, TB). Patients who received antibiotics prophylactically were excluded from the study. All the necessary information from various resources like Patients case sheets, Physician's prescription (a copy of original prescription was used for data collection), Treatment charts and nurses notes was collected and documented. The data collected include demographic details (age, gender, address, occupation), past medical history, and past medication history, Laboratory reports Provisional and final diagnosis, Laboratory reports. The additional information is collected by interviewing healthcare professionals, Interviewing patients or patient care takers and any other relevant sources. The information collected above was documented in the designed data collection form, The patients who were not willing to participate in study were excluded and data collected from 752 prescriptions were analyzed for the indicators like duration of antibiotics in different disease conditions and selection of antibiotics for various disease conditions. The pattern of antibiotics prescription and utilization were observed and studied. The antibiotics used in various infectious diseases were compared for duration along with the choice and class of antibiotic.

RESULTS AND DISCUSSION

During our study period, 2500 patients were reviewed. Among them, 752 (30.08%) patients were enrolled into the study as per our study criteria. Among 752 patients, 456 (60.63%) were males

and 297 (39.49%) were females. Mean age of patients in our study site is 39 ± 16.8 . In the present study the high number of patients were found to be suffering from gastroenteritis constituting 237 (31.51%) of total patients followed by pancreatitis 109 (14.49%), liver abscess 104 (13.82%), typhoid fever 94(12.5%), UTI 84 (11.17%), pneumonia 74 (9.84%) and malaria 50 (6.64%) (Table 1). The Antibiotics chosen for the various infectious diseases were given in the Table2.

Table1: Distribution of males and females with different infectious diseases

Disease(ICD code)	Males N (%)	Females N (%)	Total	M: F
Gastroenteritis(K52.2)	109 (23.90)	128(43.09)	237(31.51)	0.85:1
Pancreatitis(K85.2)	94(20.61)	15(5.05)	109(14.49)	6.26:1
Liver abscess (K75.0)	99(21.71)	5(1.68)	104(13.82)	19.8:1
Typhoid fever(A01.0)	45(9.86)	50(16.83)	94(12.5)	0.9:1
Urinary tract infection (N39.0)	44(9.64)	40(13.46)	84(11.17)	1.1:1
Pneumonia(J18.9)	25(5.48)	49(16.49)	74(9.84)	0.5:1
Malaria(B54)	40(8.77)	10(3.36)	50(6.64)	4:1
Total	456	297	752	

Table 2: Selection of antibiotics for various infectious diseases

Antibiotics	Number of Patients receiving Parenteral therapy(%)	Number of Patients receiving oral therapy (%)
Gastroenteritis (237)		
FLQ + NIM	114 (48.10)	138(58.22)
CEPH	101(42.61)	74(31.22)
OTHERS	22(09.28)	25(10.54)
Pancreatitis (109)		
CEPH	53(48.62)	47(43.11)
CEPH + NIM	36(33.08)	-
NIM	-	21(19.22)
OTHERS	20(18.34)	41(37.61)
Liver Abscess(104)		
CEPH + NIM	52(50)	-
FLQ +NIM	24(23.07)	-
FLQ	-	39(37.5)
NIM	-	29(27.88)
OTHERS	28(26.92)	36(34.61)
Typhoid (94)		
CEPH	29(30.85)	23(24.46)
NIM	21(22.34)	23(24.46)
CEPH + FLQ	21(22.34)	-
FLQ	-	32(34.04)
OTHERS	23(24.46)	16(17.02)

UTI (84)		
CEPH + AG	40(47.61)	-
CEPH	16(19.04)	72(85.71)
FLQ + CEPH	-	12(14.28)
OTHERS	28(33.33)	-
Pneumonia (74)		
CEPH	32(43.24)	30(40.54)
PEN	19(25.67)	-
MCL	-	35(47.29)
OTHERS	23(31.08)	9(12.16)
Malaria (50)		
CEPH + ATS	23(46)	-
MFQ	18(36)	-
PMQ	-	50(100)
OTHERS	9(18)	-

In few patients just 1 antibiotic is prescribed to treat the disease while the others were treated with combination of antibiotics depending upon the severity of the disease. Most of the patients were treated with parenteral antibiotics while their stay in the hospital and oral therapy was advised during discharge (of the same class of antibiotic or another class).

FLQ: Fluoroquinolone, NIM: Nitroimidazole, CEPH: Cephalosporin, AG: Aminoglycoside, PEN: Penicillin, MCL: Macrolide, ATS: Artesunate, MFQ: Mefloquine, PMQ: Pimaquine

In our study site, males showed dominance in diseases like pancreatitis (6.26:1), liver abscess (19.8:1) and malaria due to social factors like alcoholism, occupation and frequent voyage. Pneumonia (0.5:1) was found mostly in women in our study site as many of them were diabetic. Gastroenteritis (0.85:1) was mostly observed in females as they are involved in household activities. All the other diseases like typhoid (0.9:1), Urinary tract infection (1.1:1) showed an equal proportion of males and females. In the present study, duration of antibiotic therapy for many of the infectious diseases is longer than that of required and standard duration of therapy. (Table 3) several studies, such as study conducted by Havey TC et al., a systematic review and meta-analysis on duration of antibiotic therapy for bacteremia and a study to compare clinical outcomes of receiving short (7-10 days) versus prolonged (>10 days) durations of antibiotic therapy for children with uncomplicated Gram-negative bacteraemia⁸ and a study conducted by sun hee park et al., have demonstrated that longer antibiotic therapy encourages the development or acquisition of antibiotic-resistant organisms⁹. In our study site on average a total of 10±1.32 and 11±1.2 days antibiotics were administered for treating gastroenteritis and

typhoid respectively, which is more than that of the duration stated in the standard regimen i.e 7 days. A study, Short-Course Azithromycin for the Treatment of Uncomplicated Typhoid Fever in Children and Adolescents¹⁰ showed that a 5-day course of Azithromycin was found to be an effective treatment for uncomplicated typhoid fever in children and adolescents. In our study most of the gastroenteritis patients received Fluoroquinolone + Nitroimidazole combination, 114 (48.10%) as parenteral therapy and 138 (58.22%) as oral therapy where as in typhoid 29 (30.85%) patients received cephalosporins parenterally and 23 (24.46%) patients orally and Nitroimidazole was also equally preferred, given in 21 (22.34%) patients parenterally and 23 (24.46%) patients orally. In our present study UTI patients received 9 ± 0.82 days of antibiotic therapy which is slightly more than that stated in standard regimen i.e 7 days but a short course (e.g. 3 days) is usually adequate for uncomplicated urinary-tract infections. There are few studies which are providing confirmation for this, for example Michael M *et al.*, 2002 conducted a systematic review of randomized controlled trials to compare the effectiveness of short course (2–4 days) with standard duration oral antibiotic treatment (7–14 days) for urinary tract infection (UTI) which finally concluded that a 2–4 day course of oral antibiotics is as effective as 7–14 days in eradicating lower tract UTI in children¹¹. Another example is Vogel T *et al.*, a double-blind randomized controlled trial interpreted that a 3-day course of antibiotic therapy is not inferior to a 7-day course for treatment of uncomplicated symptomatic UTI in older women, and that the shorter course is better tolerated¹². In our study most commonly prescribed antibiotic Combination for urinary tract infection is Cephalosporin and Aminoglycoside, given in 40 (47.61%) patients through intravenous route and in oral therapy cephalosporin alone is prescribed in 72 patients (85.71%). In our present study pneumonia patients received 10 ± 1.43 days of antibiotic therapy, which is higher than that mentioned in standard regimen and few studies. A study conducted by El Moussaoui *et al* compared outcomes for cases of mild to moderate-severe community acquired pneumonia¹³ i.e 7 days (14–21 days for severe infectious condition) adequate for Uncomplicated community-acquired pneumonia. Moreover prescribing patterns of longer duration of antibiotics for treating pneumonia may also cause antibiotic (penicillin)-resistant *Streptococcus pneumoniae* as mentioned in a study on Low dosage and long treatment duration of beta-lactam and its risk factors for carriage of penicillin-resistant *Streptococcus pneumoniae* *et al* conducted by Guillemot D^{7,4}. In our study site, most regularly prescribed Antibiotic for pneumonia is cephalosporin for both parenteral route and oral route, prescribed in 32 (43.24%) patients parenterally and in 30 (40.54%) patients orally. In our study when compared to many other infectious disease, liver abscess required long duration of

antibiotic therapy (13 ± 1.9 days) similar to that of study results conducted by W. M. Wong et al., Sequential intravenous/oral antibiotic vs. continuous intravenous antibiotic in the treatment of pyogenic liver abscess¹⁴. Most often prescribed intravenous antibiotic combination in our study site is Cephalosporin along with Nitroimidazole 52 (50%) and fluoroquinolone alone is mostly prescribed for oral treatment in 39(37.5%) patients to treat liver abscess. In other diseases like, pancreatitis (18 ± 3.92 days) and malaria (18 ± 1.68 days along with prophylaxis) the treatment duration of antibiotics in our study site is more or less similar to the standard antibiotic therapy. In our study site the drug usually preferred for pancreatitis is a cephalosporin, it is given in 53 (48.62%) parenterally and 47(43.11%) orally. For malaria, the inpatients were mostly treated with combination of artesunate + cephalosporin 23 (46%) and the primaquine was the only antimicrobial drug chosen while discharge in total of 50 (100%) malarial patients.

Table 3: Total duration of antibiotic therapy

Disease	Parenteral therapy (Mean days \pm Sd)	Oral therapy (Mean days \pm Sd)	Total duration (Mean days \pm Sd)
Gastroenteritis (K52.2)	5 \pm 0.957427	5 \pm 0.547723	10 \pm 1.32
Pancreatitis (K85.2)	10 \pm 2.863564	8 \pm 2.302173	18 \pm 3.92
Liver abscess (K75.0)	6 \pm 1.581139	7 \pm 1.30384	13 \pm 1.9
Typhoid fever (A01.0)	5 \pm 1.407886	6 \pm 0.957427	11 \pm 1.2
UTI (N39.0)	4 \pm 0.957427	5 \pm 0.516398	9 \pm 0.82
Pneumonia (J18.9)	5 \pm 1.30384	5 \pm 1.632993	10 \pm 1.43
Malaria (B54)	5 \pm 1.643168	13	18 \pm 1.68

CONCLUSION

Antibiotics are one of the most commonly prescribed medicines in our study site, a super specialty hospital. The duration of antibiotic therapy is also most important aspect as that of selection, dose and route of administration. Majority of the patients in this study were male. Cephalosporins and fluoroquinolones were found to be the most commonly used antibiotics for the infectious diseases. Cephalosporins along with aminoglycosides and nitroimidazoles have also been frequently used. In our project diseases like pancreatitis (K85.2), malaria (B54) and liver abscess (K75.0) were found to require longer duration of antibiotic therapy (18,18 and 13 respectively) and the other diseases like Gastroenteritis (K52.2), Typhoid fever (A01.0), UTI (N39.0), Pneumonia (J18.9) can be cured with shorter duration (3-7days) of antibiotics without any relapse. Finally, there is a slight deviation of duration of practical antibiotic therapy to that of standard therapy. Many studies could also be carried out further to establish a practically possible optimal duration of antibiotic therapy.

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