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ORIGINAL ARTICLE

Selecting The Cost Effective Antimicrobial : Quandary Of Medical Profession!

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ABSTRACT

Background: Antimicrobial costs vary tremendously. It is difficult to make a decision whilst selecting a cost-effective antimicrobial in clinical practice. Prescribing costly antimicrobials can have a negative impact on patient's compliance. **Aims:** a) To compare the average retail price of different antimicrobials available in oral and parenteral dosage forms and calculate the cost of one day therapy. 2) To select and justify the use of certain antimicrobials as the most cost-effective in common microbial infections. **Methods and materials:** Pricelist of available antimicrobial brands was procured from IDR official site. Average price of commonly available oral and parenteral brands of antimicrobials was calculated. Cost of one day therapy was also calculated. Difference between oral and parenteral cost was observed. **Results and discussion:** Study revealed that doxycycline and cotrimoxazole are the cheapest antimicrobials and ceftibuten is most expensive oral antimicrobial. Aztreonam is the most expensive parenteral antimicrobial in contrast to gentamicin which is the cheapest. A lot of take home messages and strategies are discussed. In general, parenteral dosage forms are more expensive than the oral dosage forms. The cost of one tablet is not directly proportional to the cost of therapy as the dosage of different antimicrobials vary. Long acting expensive drugs may ultimately end up being cheaper than the short acting counterparts. Costly antimicrobials need not be the better ones. Reducing the antimicrobial cost should remain our prime motive, and hence cost-effective antimicrobials should be selected, based on one's knowledge, so that the drug costs are reduced while maintaining good quality of care.

Key Words: Cost-effective antimicrobials, cost of therapy, oral and parenteral preparations.

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Introduction

The cost of antimicrobials varies widely. Not only different antimicrobials cost differently but the same antimicrobial prices may vary vastly from one brand to another.[1] Although newer drugs are usually more expensive than older drugs, they are sometimes more effective than their older counterparts in reducing illness, hospitalization or death.[2] The improvements in healthcare outcomes can

often justify the high costs.[3] Little information is available to doctors to determine which therapy works best[4] and very few studies have measured the cost benefits of new drugs.[2]

This study was undertaken to compare the average cost of one day therapy of various commonly available antimicrobials in general practice both for oral and parenteral use and to discuss the possible means of reduction of antimicrobial cost after duly comparing their price tags and considering their efficacy and safety in given conditions. The idea is to make physicians realize the importance of cost factor, as increased costs for better health outcomes can often have negative consequences – patients taking less than the recommended dose, saving medication for future use or taking a cheaper medicine of same chemical name, prescribed to the other person for a similar reason.[5],[6]

Methods

The pricelist of the available antimicrobial brands was procured from IDR official site called IDRMedCLIK@MedCLIK.com. Different and widely prescribed brands of commonly used oral and parenteral antimicrobials were selected for this study. The average price for each antimicrobial dose was calculated by taking up to 20 brands of each antimicrobial wherever possible. The prices considered for calculation were inclusive of local taxes. The total cost of one day therapy was then calculated from the average price considering the standard recommended dosage schedule. In case of parenteral dose, the lower range of the dose was considered for calculation.

Results

Our study reveals that of the commonly available oral antimicrobial preparations, ceftibuten (400 mg OD) is the costliest therapy followed by linezolid (600 mg BD), costing approximately Rs. 222/- and Rs. 155/- daily respectively [Table/Fig 1]. On the other hand, doxycycline and

cotrimoxazole are the cheapest drugs costing approximately Rs. 2.50 daily followed by tetracycline (Rs. 3.30 daily). Cefetamet pivoxil (3rd generation oral cephalosporin) costs Rs. 90/- daily (500 mg BD). Moxifloxacin (400 mg OD) is the costliest fluoroquinolone therapy (Rs 70/- per day) whereas clarithromycin (250 mg BD) is the most expensive macrolide (Rs. 50/- daily approximately). The cost of aminopenicillins is generally low but the amoxicillin cost increases many fold in combination with clavulanic acid (more than Rs. 60/- per day). Most of the fluoroquinolones (except moxifloxacin) cost around Rs. 5/- to Rs. 12/- daily. The cost of macrolides (except clarithromycin) varies between Rs. 12/- to Rs. 15/- daily

[Table/Fig 2] compares the cost of parenteral antimicrobial preparations in common use. The cost of aztreonam (2 gm TDS) is approximately Rs. 2500/- daily followed by piperacillin (4 gm) and tazobactam (500 mg) combination, in TDS dosage schedule. Other costly parenteral antimicrobials include ceftiprome, teicoplanin, linezolid, piperacillin, ceftizoxime and netilmicin, all costing more than Rs. 500/- daily. Gentamicin is the least expensive parenteral antibiotic (Rs. 15/- daily) followed by ampicillin alone or in combination with cloxacillin. The cost of cefotaxime and lincomycin also turns out to be less than Rs. 100/- per day.

[Table/Fig 3] compares the oral and parenteral cost per day of a few antimicrobials where both forms are available. Generally the parenteral preparations are much more expensive than the oral forms. Parenteral cefuroxime costs six times more as compared to oral cefuroxime axetil.

Discussion

Which antimicrobial to use in practice is a matter of concern. Economical factors many a times prevents the practitioner to use a particular antimicrobial as he feels that the patient may not be able to afford the same.

Our study reveals that doxycycline and cotrimoxazole are the cheapest drugs to use. Unfortunately the current indications for these two antimicrobials are limited. The practitioner

Table/Fig 1: Comparative cost of one day therapy of commonly available oral antibiotics.

S no.	Name of the antibiotic	Dosage available	Number of brands studied	Average cost/tablet (Rs.)	Dosage schedule	Cost of therapy for 1 day (Rs.)
1.	Ampicillin	250mg	13	3.10	QID	12.40
2.	Ampicillin	500mg	13	6.12	QID	24.48
3.	Ampicillin+cloxacillin	250mg+250mg	20	3.67	QID	14.65
4.	Amoxycillin	250mg	20	3.75	TDS	11.25
5.	Amoxycillin	500mg	20	6.83	TDS	20.49
6.	Amoxycillin+cloxacillin	250mg+250mg	20	4.075	TDS	12.22
7.	Amoxycillin+clavulanic acid	250mg+125mg	20	25.29	TDS	75.87
8.	Amoxycillin+clavulanic acid	500mg+125mg	20	33.10	BD	66.20
9.	Cephalexin	500mg	20	10.73	QID	42.92
10.	Cefadroxil	500mg	15	7.45	BD	14.90
11.	Cefuroxime axetil	250mg	20	23.22	BD	46.44
12.	Cefixime	200mg	20	29.60	OD	29.60
13.	Cefdinir	300mg	7	32.87	BD	65.76
14.	Cefpodoxime proxetil	100mg	20	15.15	BD	30.31
15.	Cefetamet pivoxil	500mg	2	45.00	BD	90.00
16.	Ceftibuten	400mg	3	222.2	OD	222.2
17.	Ciprofloxacin	250mg	20	3.22	BD	6.44
18.	Ciprofloxacin	500mg	20	6.19	BD	12.38
19.	Lomefloxacin	400mg	13	11.14	OD	11.14
20.	Levofloxacin	500mg	20	6.25	OD	6.25
21.	Ofloxacin	200mg	20	6.57	OD	6.57
22.	Ofloxacin	400mg	20	11.27	OD	11.27
23.	Norfloxacin	400mg	20	2.73	BD	5.46
24.	Moxifloxacin	400mg	4	70.00	OD	70.00
25.	Pefloxacin	400mg	20	4.10	BD	8.20
26.	Cotrimoxazole	D.S.	15	1.35	BD	2.70
27.	Tetracycline	250mg	10	0.84	QID	3.36
28.	Doxycycline	100mg	20	2.45	OD	2.45
29.	Erythromycin	250mg	15	3.19	QID	12.76
30.	Roxithromycin	150mg	20	7.17	BD	14.34
31.	Clarithromycin	250mg	20	24.49	BD	48.98
32.	Azithromycin	500mg	20	15.31	OD	15.31
33.	Linezolid	600mg	8	77.78	BD	155.56

Table/Fig 2: Comparative cost of one day therapy of commonly parenteral available antibiotics.

S. no.	Name of the antibiotic	Dosage available	Number of brands studied	Average cost/vial (Rs.)	Dosage schedule	Cost of therapy for 1 day (Rs.)
1.	Ampicillin	250mg	10	11.75	TDS	35.32
2.	Ampicillin	500mg	15	15.07	TDS	45.22
3.	Ampicillin+sulbactam	1gm+500mg	5	101.15	QID	404.60
4.	Ampicillin+cloxacillin	250mg+250mg	20	11.46	QID	45.85
5.	Carbenicillin	1gm	3	25.00	QID	100.00
6.	Piperacillin	2gm	5	210.33	TDS	631.00
7.	Piperacillin+tazobactam	4gm+500mg	15	649.12	TDS	1947.36
8.	Amoxicillin+clavulanic acid	1gm+200mg	20	163.71	BD	327.42
9.	Amoxicillin+clavulanic acid	250mg+50mg	8	53.67	TDS	161.00
10.	Ceftazidime	250mg	20	89.22	QID	356.91
11.	Ceftizoxime	1gm	4	310.50	BD	621.00
12.	Cefotaxime	1gm	20	385.54	BD	77.09
13.	Ceftriaxone	500mg	20	52.32	BD	104.65
14.	Ceftriaxone+sulbactam	1gm+500mg	10	128.50	OD	128.50
15.	Cefuroxime axetil	750mg	20	103.77	TDS	311.30
16.	Cefoperazone sodium	1gm	20	216.58	BD	433.16
17.	Cefpirome	1gm	10	393.70	BD	787.40
18.	Cefepime	1gm	9	184.70	BD	369.40
19.	Amikacin	500mg	20	51.30	BD	112.61
20.	Tobramycin sulphate	80mg	10	45.53	TDS	136.60
21.	Netilmicin	200mg	3	252.50	BD	55.00
22.	Gentamicin	80mg	8	7.74	BD	15.49
23.	Lincomycin	600mg	9	18.34	TDS	55.02
24.	Vancomycin	500mg	10	332.52	QID	1330.00
25.	Linezolid	600mg	4	326.68	BD	653.37
26.	Teicoplanin	200mg	3	667.50	OD	667.50
27.	Aztreonam	2gm	3	850.00	TDS	2550.00

Table/Fig 3 : Comparison of oral v/s parenteral costs.

S. no	Name of the antibiotic	Dosage	Cost of 1 day oral therapy (Rs.)	Cost of 1 day parenteral therapy (Rs.)
1.	Ampicillin	250mg	12.40	35.32
2.	Ampicillin	500mg	24.48	45.22
3.	Ampicillin+cloxacillin	250mg+250mg	14.65	45.85
4.	Amoxicillin+clavulanic acid	250mg(amoxicillin)	75.87	161.00
5.	Cefuroxime	250mg(O),750mg(P)	46.44	311.30
6.	Linezolid	600mg	155.56	653.37

therefore has no alternative but to prescribe costlier antimicrobials. Excellent knowledge of the spectrum of the antimicrobials and the possible organisms causing the infection are must to finally decide the antimicrobial.

The cost of one tablet is not directly proportional to the cost of therapy, as the dosage schedule is different for different antimicrobials. Thus although each tablet of cefuroxime axetil costs more than double the cost of cephalexin, the total cost of a day's

therapy of the former is just marginally higher than the latter. Similarly the average price of one lomefloxacin or ofloxacin tablet is more than thrice the average price of one capsule of amoxicillin 250 mg, but the cost of a day's therapy of all the three drugs is almost the same.

The choice of the antimicrobial in a given condition should primarily be influenced by the **ETC principles** i.e. efficacy, toxicity and cost, in this order[7]. If two agents are

equally effective but have significantly different adverse event profile, the safe agent should be selected. However, if efficacy and toxicity are relatively equal, cost should be considered, as prescribing a cheaper drug will vastly improve the patient's compliance.

Our study revealed a lot of observations and take home messages:

1) Long acting expensive antimicrobials may ultimately end up being cheaper than the short acting counterpart. For example:

- Daily cost of once daily azithromycin is Rs. 15.32 in contrast to Rs. 12.76 of erythromycin given four times daily, however the total cost of azithromycin therapy (given for 3 days) is much less (Rs. 45.94) than the therapy cost of erythromycin (given for 5 days) which comes to more than Rs. 63/-.
- Although each tablet of ofloxacin is double the cost of ciprofloxacin, the total cost of ofloxacin 400 mg once daily (Rs. 11.27) is less than ciprofloxacin 500 mg BD (Rs. 12.38).
- The total cost of moxifloxacin therapy (400 mg OD) is much less than cefetamet pivoxil (500 mg BD), although the cost of one tablet of the former is Rs.25/- higher than the latter.
- Although the cost per dose of teicoplanin (200 mg OD) is Rs. 667/-, the total cost of one day therapy with vancomycin is Rs. 1330/- due to QID dosage.

2) Costly therapy need not always be a better therapy for treating any medical condition. For example:

- Commonly used time tested amoxicillin is much cheaper

and effective than many other antimicrobials.[8]

- It will be ridiculous to use the highly costly aztreonam for gram negative infections where aminoglycosides are equally effective. A possible chance of nephrotoxicity is not good enough excuse to routinely prescribe aztreonam which is five times costlier than the costliest aminoglycoside netilmicin and 165 times more expensive than the traditional and commonly used gentamicin.
- If *P. aeruginosa* is isolated, then piperacillin alone can be used with an aminoglycoside since in documented pseudomonas infection, tazobactam does not enhance the activity of piperacillin against this pathogen, but will increase the cost of therapy to great extent.[9]
- Cefpirome and cefepime are equally effective 4th generation cephalosporins[10],[11], but the cost of former is much more than latter.
- Cefuroxime axetil 250 mg BD (expensive; Rs. 46/- daily) is as effective as doxycycline 100 mg BD (Rs. 2.45 daily) in adults with acute exacerbation of chronic bronchitis.[12]
- Azithromycin or erythromycin could be cheaper and equally effective options as compared to high cost cephalexin and clarithromycin in acute streptococcal pharyngitis in children[13], and as compared to cefuroxime axetil, clarithromycin and co-amoxiclav in adults suffering from pneumonia.[14]
- It will be cost effective to use cotrimoxazole or amoxicillin in acute otitis media in children as

compared to co-amoxyclav or clarithromycin.[15]

- Levofloxacin 500mg OD (Rs. 6.25 daily) can be considered as a good effective choice for sinusitis[16] in adults as compared to widely prescribed co-amoxyclav (> Rs. 65/- daily), cefuroxime axetil (Rs. 46/- daily) or clarithromycin (approx. Rs. 50/- per day).
 - In life-threatening diabetic foot infection, even costliest parenteral antimicrobial aztreonam alone may not be enough to care the full spectrum of organisms. Piperacillin-tazobactam in combination with gentamicin would be cheaper and more effective therapy.[17]
 - Ciprofloxacin is safe, efficacious and cheap as compared to parenteral costly ceftriaxone in treating multidrug resistant typhoid fever (MDTRF) in children.[18] Although ciprofloxacin has a potential for arthropathogenicity, there is enough evidence to prove its safety in children with MDTRF.
- 3) Average cost per dose can be misleading in deciding the final cost of therapy in any condition. For example although one ampicillin parenteral dose (500 mg) is much cheaper (Rs. 15/-) than ceftriaxone alone (Rs. 52/-) or in combination with sulbactam (Rs. 125.5), for treating *S pneumoniae* pneumonia ampicillin will be much more expensive in the recommended dose of 1.5-2.0 gm every 6 hrly i.v.
- 4) Parenteral preparations are always costlier than oral. Thus, it would be advisable to use **I.V-PO switch** as early as clinically possible[19]. In case the same drug is not available in both the dosage forms, drugs with similar spectrum could be used for IV-PO

switch. For example, third generation cheaper oral agents like cefixime or cefpodoxime proxetil can be prescribed following ceftriaxone. Switching to oral antimicrobial therapy means not only lower antimicrobial costs but also fewer adverse effects and an earlier hospital discharge, thereby decreasing the patient's length of stay, too. New oral antimicrobials with high rates of absorption and good bioavailability now make it possible to reduce the costs by shortening the i.v. treatment period.[19]

From 1950s through the 1970s, the cost of the antimicrobial and its administration didn't seem to have much effect on the prescribing habits of doctors.[20] But owing to the present day escalation in antimicrobial prices and in addition, the expense of hospitalization, it is an important issue to consider the cost of antimicrobial administration. Certain points should be kept in mind:

- i) It is seen that most of the prescribed medicines belong to 'branded' category and this adds to the cost of therapy.[21] Generic preparations should be ordered for hospital use whenever possible, as they are usually cheaper.[22]
- ii) The more frequently the antimicrobial is given, the more expensive it is to administer it, in terms of personnel time, iv material used and so on. Therefore, henceforth the hospitals should opt for drugs with less frequent dosing intervals to minimize the impact of the cost of the i.v route. [20] Rather the greatest component of cost is often the hospital stay itself. Thus hospital antimicrobials policy should be formulated to treat infections effectively with the most appropriate cost-effective drug, to minimize the impact on hospital resources and to have the greatest

- potential impact on overall treatment cost.
- iii) Multiple antimicrobials can be generally more expensive than monotherapy.[20] However in some settings two antimicrobials can be cheaper than one. For example the use of piperacillin plus gentamicin is less expensive than piperacillin-tazobactam.
 - iv) Oral therapy is more cost-effective although iv antimicrobials are usually preferred in severe infections.
 - v) For empirical therapy bactericidal agents with broad spectrum will be more cost effective.
 - vi) If possible, agents with known serious or 'costly' adverse effects should be avoided and alternative 'safe' drugs with similar efficacy should be prescribed which could be less expensive.
 - vii) Antimicrobials with poor tissue penetration should be avoided. For example, use of cefuroxime in meningitis is not recommended because it will simply add to the cost without therapeutic benefit.[10],[11].
 - viii) It is a good habit to consider pharmacokinetic/ pharmacodynamic parameters i.e. effect of food, CSF entry, drug interaction, etc. before selecting an antimicrobial, to prevent an error in choice.
 - ix) Knowledge of the local resistance pattern is essential while choosing the antimicrobial, as sensitivity can vary from place to place. This is specially important in severe infections and intensive care units.[23]

The question of which medicines work best at the lowest cost has become more and more important as costs have increased beyond the capacity of the takers. The **Agency for Healthcare Research and Quality (AHRQ)** has done lots of research regarding increased prescription costs of

antimicrobials.[24] The impact of their research is as follows:

- a) ***Expensive antimicrobials do not always have better outcomes***: Some studies reveal that older antimicrobials like amoxicillin provide better treatment outcomes than newer antimicrobials for children with acute otitis media.[25] Another study concluded that there was no difference in outcomes between out patients with Community Acquired Pneumonia (CAP) who were treated with less expensive as well as more expensive antimicrobials.[26]
- b) ***New expensive antimicrobials can reduce overall costs***: In some instances newer and more expensive antimicrobials can lead to cost benefits. A study opines [27],[28], that new antimicrobials may be more effective, have fewer side effects and report better quality of care than older antimicrobials. They may also lower the overall cost by lessening the need for other health care services.
- c) ***Outpatient antimicrobial treatment can be effective and reduce cost of therapy***: AHRQ research has documented that some antimicrobial treatments offered as an outpatient basis give the same outcomes as given on an inpatient basis at lower cost. Treating women with PID as outpatient could save 500 million dollars a year.[29]
- d) ***Preventive antimicrobial therapy can be cost effective***: AHRQ research has shown that antimicrobials like cotrimoxazole or aerosol pentamidine can help to prevent *Pneumocystis carinii* pneumonia (PCP) in HIV patients and can reduce the capital cost or admission in Intensive Care Unit (ICU).[30]

Cost of antimicrobials is a matter of concern. Physicians should take appropriate

measures and make the best use of their knowledge to select the most cost effective antimicrobial. Practicing pediatricians should realize that the doses and the cost therein mentioned in this study pertain to adult population; however the same could be extrapolated for use in children. Efforts should be made at all levels to identify antimicrobial therapies that can lower health care costs while maintaining quality of care.

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