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EVALUATION OF RATIONAL USAGE OF ANTIMICROBIAL AGENTS IN THE PAEDIATRIC DEPARTMENT AT TERTIARY TEACHING CARE HOSPITAL, GUJRAT

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ABSTRACT: Background: Prescription of drugs which needs to be continuously assessed and refined according to disease progression. It not only reflects the physician's knowledge about drugs but also know the pathophysiology of diseases and attitude towards rational prescribing. **Methods:** Retrospective study was carried out by collecting 350 prescriptions containing antimicrobial agents of the indoor patients admitted in the wards of Paediatric department at Sir Sayajirao General (SSG) Hospital, Vadodara. The data was collected by using case record form specially prepared for the study. **Results:** In our study, total 350 prescriptions containing 690 antimicrobial agents were prescribed during study period. Average number of antimicrobials per prescription was 1.97. 576(83.48%) and 114(16.52%) antimicrobials were prescribed by using generic name and trade name respectively. 599(86.81%) and 91(13.18%) antimicrobial agents were prescribed for parenteral administration as well as oral route respectively. 101(28.85%) prescriptions constitute single antimicrobial agents, while 249(71.14%) prescriptions contain either two or more than two antimicrobial agents. Among all prescriptions 3 % and 11% of them were without the age and address of the patients. Superscription was not mentioned in 47% of the prescriptions. Inscription, subscription and signature were inadequate in 18%, 11% and 22% of the prescriptions respectively. As per modified kunin's criteria, 72.17% of the patients received antimicrobial therapy appropriately in Paediatric department. **Conclusion:** Present study highlighted that large number of prescriptions did not conform to the pattern of typical prescription and lack in their rationality.

INTRODUCTION: Prescription order is an important transaction between the physician and the patient¹. It is an order for a scientific medication for a person at a particular time². It brings into focus the diagnostic acumen and therapeutic proficiency of the physician with instruction for palliation or restoration of the patient's health¹. It not only reflects the physician's knowledge of pharmacology and pathophysiology of diseases but also his / her skill in diagnosis and attitude towards selecting the most appropriate cost effective treatment¹.

The prescribing behaviour of the doctor depends upon the input from various sources like patients, academic literatures, professional colleagues, commercial publicity and government regulations. Various prescribing errors are result of ineffective use of these inputs and are very common in clinical practices³. The study of prescribing patient is a component of medical audit which seeks monitoring, evaluation and necessary modifications in the prescribing practice of the prescribers to achieve the rationale and cost effective medical care. Antimicrobials are among the most commonly prescribed drugs on worldwide basis.

Many a times desire of the physician to do something for the patient and to prescribe a "Pill for every ill" leads to over prescribing. Various studies indicate that out of total drugs prescribed, 28 to 42% of the drugs are antimicrobial agents.

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Around 50% of these prescriptions of antimicrobial agents are not needed, are inappropriate or are in wrong doses. The fear of physician whether he is missing any occult infection also makes him to use antibiotic “umbrella” for protecting him and his patient⁴. The extremely high efficacy of antimicrobial agents has proved to be a boon and curse. The double edged sword has now many more edges; the sharpest is the development of resistance to antimicrobial agents⁵.

With widespread use of antibiotics, the prevalence of resistance has increased⁶. The association of resistance with the use of antimicrobials agents has been documented both in patient⁷ and outpatient setting⁸. Wide spread irrational usage of antimicrobial agents and their shortage of supply in the government hospitals, low purchasing capacity of patients and incidence of antimicrobial resistance complicates the outcome of the therapies⁹. It was found out in some studies, link between rates of antimicrobial agent's prescription and resistance in the communities^{10,11}.

In general practice antimicrobial agent's usage is highest among children and approximately 70% of all the antimicrobial agents prescribed in children are for URTI¹². As in other developed countries the most frequent type of misuse is prescribing antimicrobial agents for infections, which are commonly caused by virus¹³. Moreover there seems to be a large variation between physicians in antimicrobial prescribing¹⁴.

Rational drug prescribing has been shown to reduce the cost of treatment, adverse drug reactions¹⁵. Despite advances in control of drug regulation and availability of drugs, the irrational drug prescribing is still worldwide concern. In the view of the emerging worldwide threat of bacterial resistance, there are increasing need to identify determinants and patterns of antimicrobial prescribing to identify where the clinical practice can be improved¹⁶.

With this background, the present study was designed to evaluate the practice of rational prescription in patients (cases) admitted in various wards of Paediatric Department at Sir Sayajirao General Hospital, Vadodara. The data generated from this study would be helpful to communicate with the prescribers and

suggest the various lacunae observed to improve the prescribing practice. Thus it will ultimately benefit the patients with fewer incidences of adverse effects with minimal rise in resistant strain of bacteria and reduction in the cost of therapy.

MATERIAL AND METHOD:

Study setting: This retrospective study was carried out by collecting the prescriptions of indoor patients admitted in the wards of paediatric department at Sir Sayajirao General (SSG) Hospital, Vadodara to evaluate rational usage of antimicrobial agents from October 2005 to June 2006(09 months study). Total 350 prescriptions containing antimicrobial agents were collected from the hospital record section for the study. The patients who were admitted and received antimicrobial therapy were randomly selected and included in the study. Prescriptions were collected irrespective of the indications.

Study design: The data were collected by using case record form specially prepared for the study. The Case Record Form contains patient's information such as name, age, sex, address, date of admission, date of discharge, name of antimicrobial agents, dosage form, dose, frequency, route of administration, duration of treatment, use of anti-microbials for therapeutic or prophylactic purpose, complaints for which the consultation was sought, provisional/confirmed diagnosis, investigations, drug interactions, drug allergies, refill instructions. Patients taking other drugs for any existing diseases were not counted in the prescriptions. Only antimicrobial agents prescribed for any types of bacterial infections were included in the proforma.

The antimicrobial agents were divided into following major groups for the study (1) β -lactams = β -lactams (except cephalosporins) + vancomycin (2) cephalosporins (3) aminoglycosides (4) fluoroquinolones (5) sulfonamides (6) metronidazole and (7) macrolides.

Selection of indications:

A) For format of prescription -1) Patient's identity: Name and address of the patients. (2) Date on which the prescription was issued. (3) Superscription symbol: Rx meaning “take thou” or

“recipe”. (4) Inscription: This includes the name of drugs, dose, dosage forms, total amount of medication prescribed. (5) Subscription: The dispensing and compounding instructions to the pharmacist as regards to form and quantities to be dispensed or supplied. (6) Transcription or Signa: The direction to the patient for use of drugs. (7) Prescriber’s identity: Name, address and qualification.

B) Following basic drug use indicators were used in the study¹⁷

1. Total number of the antimicrobial agents prescribed irrespective of number of prescriptions.
2. Mean number of the antimicrobial agents per prescriptions.
3. Number of antimicrobial agents prescribed by generic vs. trade name.
4. Number of antimicrobial agents administered orally or parenterally.
5. Number of prescription with one or more than one antimicrobial agents.
6. Prescribing frequency of antimicrobial agents. Proportions of the different antimicrobial agents prescribed for different systems were calculated.

C) Analysis of rationality of administration of AMA was done by modified Kunin’s criteria¹⁸

- a. Agree with the use of therapy given as in the prescription. The treatment is appropriate in terms of choice of drug, dose, dosage regimen and duration of therapy.
- b. Agree with the use of therapy but a potentially fatal infection cannot be ruled out.
- c. Agree with the use of therapy but a different (usually less expensive and toxic) combination of therapy is preferred.
- d. Agree with the use of therapy but a modified dose, dosage regimen and duration would be recommended.
- e. Disagree with the use of therapy, administration is unjustified or unnecessary use of drugs.

Category I & II essentially indicate “Appropriate” therapy

Category III & IV indicate that there is some major deficiency in the choice or use of drugs by the doctor managing the problem.

These indicators are highly standardized in terms of their definition and facilitate the quick and reliable assessment of drug use in health care¹⁹.

Also Parameters like interactions (include drug-drug, drug-disease, food-drug interactions), Overprescribing (unnecessary use or duplication of drugs and dosage form as far as therapeutic or pharmacologic effect is concerned) and Banned drug formulations (which are banned by Drug Controller General of India) were checked.

Data were analyzed by using Microsoft excel sheet.

RESULTS:

A) Evaluation for format of prescription-:

Patient’s identity: Name, age and address of the patients were found in 95%, 97% and 89% of prescriptions respectively. Date of writing prescriptions were mentioned in all prescriptions.

Superscription: Superscription (Rx) was not found in 47% of prescriptions. In many prescriptions it was replaced by the word ‘Adv’ indicating advice.

Inscription: All the prescriptions contain dosage form along with name of drugs, however dosage strength were absent in 18% of prescriptions.

Subscriptions: 11% of prescriptions were found to be with inadequate subscription. However, in our study, only those prescriptions were identified as having inadequate subscription in which it was very difficult for the pharmacist to ascertain the total amount of medication to be dispensed with.

Transcriptions or signature: Instructions to the patient were inadequate in 22% of the prescriptions. Directions regarding total amount of drug to be dispensed were inadequate in 23% of the prescriptions. However in these prescriptions latin words like o.d, t.d.s, q.d.s were written. Instructions regarding refilling of prescription were not given in all the cases.

Prescriber’s identity: Name and qualification of the prescriber were known in 100 % of the prescriptions. All the prescriptions were signed by prescriber.

B) Evaluation for rational drug therapy:

Total 350 prescriptions of the patients admitted in the wards of paediatric department were studied. Total numbers of antimicrobial agents prescribed in the wards were 690. Average number of antimicrobials per prescription was 1.97.

The results are summarized to study frequency of prescribing patterns of antimicrobial agents in different systems in accordance with diagnosis as well as prescribing frequency of antimicrobial agents by using table for the wards.

(A) Preference of antimicrobial agents:

During study period, highest numbers of antimicrobial agents prescribed were from aminoglycosides (233; 33.77%) while macrolides was the least (06; 0.87%) prescribed (**Table 1**). Among the total number of aminoglycosides prescribed, the highest were prescribed for respiratory tract infections (39.91%) and the lowest for soft tissue infections (1.29%) (**Table 1**). Also of among the total numbers of aminoglycosides prescribed amikacin (73.82%) and gentamicin (21.18%) were prescribed (**Table 2**).

TABLE 1: FREQUENCY OF PRESCRIBING PATTERNS OF ANTIMICROBIAL AGENTS IN DIFFERENT SYSTEMS IN ACCORDANCE WITH DIAGNOSIS IN PAEDIATRIC WARDS.

Antimicrobial Agents prescribed	Total Prescribed No(%)	RS No(%)	CNS No(%)	CVS No(%)	GIT No(%)	GUT No(%)	HBT No(%)	MISC No(%)	PROPH No(%)	Soft tissue No(%)
Aminoglycosides	233 (33.77)	93 (39.91)	27 (11.59)	08 (3.43)	15 (6.74)	08 (3.43)	05 (2.15)	66 (28.33)	08 (3.43)	03 (1.29)
β-lactams (exceptCP)+ Vancomycin	191 (27.68)	115 (60.20)	11 (5.75)	04 (2.09)	05 (2.61)	03 (1.57)	09 (4.71)	38 (19.9)	05 (2.61)	01 (0.52)
Cephalosporins	176 (25.51)	51 (28.98)	34 (19.91)	06 (3.41)	10 (5.68)	04 (2.27)	05 (2.84)	60 (34.1)	04 (2.27)	02 (1.34)
Fluoroquinolones	59 (8.55)	09 (15.25)	02 (3.39)	02 (3.39)	19 (32.20)	15 (25.42)	00 (0.0)	11 (18.64)	00 (0.0)	01 (1.69)
Metronidazole	15 (2.17)	04 (26.7)	00 (0.0)	00 (0.0)	04 (26.7)	01 (6.7)	01 (6.7)	05 (33.33)	00 (0.0)	00 (0.0)
Sulfonamides	11 (1.59)	03 (27.27)	00 (0.0)	00 (0.0)	04 (36.4)	00 (0.0)	01 (9.09)	01 (9.09)	00 (0.0)	02 (18.2)
Macrolides	06 (0.87)	03 (50)	00 (0.0)	01 (16.66)	00 (0.0)	01 (16.66)	00 (0.0)	01 (16.66)	00 (0.0)	00 (0.0)
Total	690 (100)	278 (40.3)	74 (10.72)	20 (2.89)	57 (8.26)	32 (4.63)	21 (3)	182 (26.37)	17 (2.46)	09 (1.3)

RS-Respiratory system; CNS-Central nervous system; CVS-Cardio vascular system; GIT-Gastrointestinal tract; HBT-Hepato biliary tract; GUT- Genitourinary tract; PROPH-Prophylaxis; MISC:-Miscellaneous including- Pyrexia of unknown origin, Malaria, Myasthenia gravis, Tetanus, Poisoning;CP- Cephalosporins.

TABLE2: PRESCRIBING FEQUENCY OF ANTIMICROBIAL AGENTS

Sr.No.	Antimicrobial agents	No. (%)	Sr.No	Antimicrobial agents	No. (%)
1)	Aminoglycosides			Cefipime	05(2.84)
	Amikacin	172(73.82)		Cefadroxyl	01(0.56)
	Gentamicin	61(21.18)		Ceftazidime	01(0.56)
2)	β-lactum(Except CP)+ vancomycin		4)	Fluroquinolones	
	Coamoxy-clav	70(36.65)		Ciprofloxacin	53(89.83)
	Amoxykid	29(15.18)		Ofloxacin	04(6.78)
	Ampicillin	41(21.47)		Gatifloxacin	01(1.69)
	Cloxacillin	2(1.05)		Norfloxacin	01(1.69)
	Tazobactum+Piperacillin	34(17.80)	5)	Metronidazole	
	Vancomycin	09(4.71)		Metronidazole	15(2.17)
	Crystalline penicillin	3(1.57)	6)	Sulfonamides	
	Meropenum	3(1.57)		Cotrimoxazole	11(1.59)
3)	Cephalosporins		7)	Macrolides	
	Cefotaxime	158(89.77)		erythromycin	6(0.87)
	Ceftriaxone	11(6.25)		Total	690(100)

Similarly, among the total numbers of antimicrobials prescribed from β -lactams group (191; 27.68%), highest numbers were prescribed for respiratory tract infections (60.20%) and the lowest for soft tissue infections (0.52%) (**Table 1**). From the β -lactam group, coamoxy-clav (36.65%) and ampicillin (21.47%) were prescribed more frequently, while cloxacillin (1.05%) was the least prescribed drug (**Table 2**).

From the cephalosporins (176; 25.51%), highest numbers were prescribed for miscellaneous conditions (34.1 %) followed by respiratory tract infection (28.98%) while the least (1.34%) were used for soft tissue infections (**Table 1**). Among the cephalosporins, cefotaxime (89.77%) was almost prescribed consistently, while cefadroxyl (0.56%) and ceftazidime (0.56%) were not prescribed frequently (**Table 2**).

From the total numbers of fluoroquinolones (59; 8.55%) prescribed, highest numbers were prescribed for gastrointestinal (32.20%) and genitourinary tract (25.42%) infections, while the lowest for soft tissue (1.69%) infections and none for either hepatobiliary diseases or for prophylactic purposes (**Table 1**). However among fluoroquinolones, ciprofloxacin (89.83%) was prescribed extensively, while surprisingly norfloxacin (1.69%) and gatifloxacin (1.69%) have very low preference in the prescriptions (**Table 2**).

Metronidazole, sulfonamides (cotrimoxazole) and macrolides (erythromycin) have very low frequency of prescription. All the three antimicrobials were prescribed for respiratory tract infections. However both metronidazole and cotrimoxazole were prescribed for gastrointestinal tract infections, while metronidazole was also prescribed for miscellaneous conditions (**Table 1**).

(B) Frequency of prescribing patterns of antimicrobial agents in accordance with diagnosis (**Table 1**): Highest numbers of antimicrobial agents were prescribed for respiratory tract infections (278, 40.3%) followed by for miscellaneous conditions (182; 26.37) and the infection involving central nervous system. Among the total numbers of antimicrobial prescribed for respiratory tract infections; the highest numbers were prescribed from β -lactam group followed by aminoglycosides

and cephalosporins (**Table1**). Similarly among the total numbers of antimicrobials prescribed for miscellaneous conditions, highest numbers were prescribed from aminoglycosides followed by cephalosporins and β -lactam group (**Table1**). However for soft tissue infections aminoglycoside, cephalosporins and sulfonamide were prescribed. (**Table1**).

Out of the 690 antimicrobial agents prescribed, 576(83.48%) were prescribed by generic name while 114 (16.52%) were prescribed by trade name, 599(86.81%) and 91(13.18%) antimicrobial agents were prescribed for parenteral administration as well as oral route respectively, 101(28.86%) prescriptions constitute single antimicrobial agents, while 249(71.14%) prescriptions contain either two or more than two antimicrobial agents (**Table3**). Switch on therapy from parenteral to oral route were employed in 11% of prescriptions (**Table3**).

TABLE.3: PRESCRIPTION ANALYSIS

Total numbers of prescriptions	350
Total numbers of antimicrobial agents prescribed	690
Mean number of the antimicrobial agents per prescriptions	1.97
Antimicrobial administered by parenteral route	599(86.81)
Antimicrobial administered by oral route	91(13.18)
Antimicrobial agents prescribed by generic name	576(83.48)
Antimicrobial agents prescribed by trade name	114(16.52)
Numbers of prescriptions with one antimicrobial agents	101(28.86)
Numbers of prescriptions with more than one antimicrobial agents	249(71.14)
Switch on therapy from parenteral to oral route	11%

No interactions (drug-drug, drug-food, and drug-disease) and banned drug were found out during a study period. Over prescribing (14%) were found out during analysis like e.g. ciprofloxacin and tinidazole for diarrhoea, antibiotic for viral fever, viral hepatitis etc. In some cases, use of an antimicrobial was suddenly switched over to another antimicrobial after 1 or 2 days uses neglecting its duration make its inappropriate use. Duration of therapy was irrational in 11% prescriptions i.e. short in 8%, prolonged in 4% of the prescriptions. As per Kunin's modified

criteria, 72.17% of the patients received antimicrobial therapy appropriately while 27.83% inappropriately in Paediatric department (**Table 4**).

TABLE.4: ANALYSIS OF CASE SHEET FOR USE OF ANTIBIOTICS AS PER KUNIN'S CRITERIA.

Speciality	Appropriate			Subtotal
	I	II	III	
Paediatric Department	396(57.39%)	102(14.78%)		498(72.17%)
	Inappropriate			
	IV	V	VI	
	14(2.03%)	81(11.74%)	97(14.06%)	192(27.83%)
Total				690(100)

DISCUSSIONS: The results obtained after auditing of the prescriptions indicate that irrationality was found in prescription writing. Prescribers do not adhere to the ideal pattern of the prescription writing and these prescriptions are not explicit in their contents. Replacement of Rx sign with the word 'Advice' in large number of prescriptions is indicative of changing pattern of the prescriptions. Prescriber's identity and patient's information was all most present in all prescriptions. In many prescriptions latin words like o.d, t.d.s, q.d.s were used for direction, also dosage forms were incomplete, i.e. Tab, Inj, Cap were written. Uses of acronyms were not justifiable. Legibility of prescriptions were good, however clarity of instructions were inadequate in some cases.

In our study, it was found out that aminoglycosides were commonly prescribed antimicrobials followed by β -lactam group and cephalosporins. Amikacin, coamoxy-clav and cefotaxime were frequently prescribed. Wider use of amikacin observed in our study may be due to its broad antibacterial spectrum and drug of choice for the most cases of hospital acquired gram negative sepsis, as it is effective against organisms resistant to other conventionally used aminoglycosides (i.e. gentamicin, tobramycin).

Also physician's choice and easier availability in hospital pharmacy may also dictate a rather heavy use of a particular drug. Other factor contributing to the preferential uses of the above antimicrobial agents in the wards may be due to their low cost with better safety profile and ease of their availability from hospital pharmacy. A study carried out in eastern Nepal reported that, gentamicin, ampicillin, crystalline penicillin, cefotaxime were the most commonly prescribed²⁰.

Same research study was carried out in a tertiary hospital Bangladesh reported that ampicillin, gentamicin, amoxicillin, cloxacillin and ceftriaxone were prescribed frequently²¹. We observed the antimicrobial prescribing pattern which is in consonance with the studies carried out at these places. During study we have observed that, highest numbers of antimicrobial agents were prescribed for respiratory tract infections. Among them highest numbers were prescribed from β -lactam and aminoglycosides groups.

The types of antibacterial used at each centre depend on many factors like the patient profile, type of infection, availability of antimicrobial, susceptibility patterns, the prescriber's awareness on rational antimicrobial use etc. Such statistics form an important index of ongoing antimicrobial audit as they indicate the changes in the pattern of usage accordance with the susceptibility patterns of bacteria. They also indicate the extent of use of newer antimicrobial agents.

Data analysis in our study showed that numbers of prescriptions with two or more than two antimicrobial agents is quite high as compared to those with single antimicrobial agent. Mean number of drugs per prescription was 1.97. This indicates a large numbers of prescriptions in our study were for multiple drugs. This may indicate empirical nature of therapy. A study carried out in Kathmandu valley reported that, a high percentage (93%) of patients were prescribed at least one antibiotic²².

These figures are quite opposite to our study. A study carried out by Marlies et al reported that 36% of the patients were prescribed at least one antibiotic²³. These reports are similar to our study. Prakash et al and Ansari et al found this number to

be 5.86 and 5.05 medicines per prescription respectively in their studies^{24, 25}. These figures are quite high as compared to our study.

In study, it was found out that 86.81% antimicrobial agents were prescribed for parenteral administration, while only 13.18% were for oral route in paediatric patients. A study carried out in Kathmandu valley showed that, 75% of antibiotics were given by injections²². These figures are somewhat similar to our study. The parenteral use of drugs in general and antibacterial in particular is important parameters to judge rationale drug use. Unnecessary use of parenteral antimicrobial adds to cost of therapy and also increases the risk of blood borne infections. In countries where disposable needles and syringes are scarce and the sterilization facilities are unsatisfactory, the administration of drugs by injection should be kept to the minimum required. Preference to parenteral route over oral route observed in our study could be due to study conducted in the indoor patients.

In our study observed that antimicrobial agents were prescribed more frequently by generic name (83.48%) as compared to trade name (16.52%). A study carried out by Nazima et al, showed that 77.61% of the drugs were prescribed by generic name, while remaining by trade name²⁶. These reports are similar to our study. These show that apparent control over the prescribing habits of the physicians for indoor patients at our hospital. The most probable reason for such prescribing may be due to easier availability of antimicrobial agents in our hospital pharmacy as well as proper communication between the prescribing physicians and the hospital authority.

As per Kunin's modified criteria, 72.17% of patients received antimicrobial therapy appropriately in the Paediatric department. This report is somewhat similar to reported by Deshmukh vs et al²⁷ was 66.2%. A study carried out by Pavani V et al, showed that 80% of patients received antimicrobial agents' appropriately²⁸. This report is different to our study.

In Paediatric department antimicrobial agents were used indiscriminately in patients of hepatosplenomegaly, viral hepatitis, pyrexia of unknown origin, epilepsy, viral hepatitis, herpes

simplex. There is no rationale for antimicrobial use in pyrexia of short duration (viral fever) without localizing signs except in toxic patients²⁹. Over prescribing was found only in 14% of the prescriptions, a figure far less than that reported by other Indian researchers³⁰. This may leads to unnecessary increase in cost of therapy which puts unnecessary burden on limited resources available. This not only exposes patients to avoidable adverse drug reactions but also to the problems of drug resistance.

Intravenous to oral switch therapy is inappropriate for critically ill patients who require intravenous antibiotic therapy and should not be considered in patients who have the inability to absorb drugs. These exceptions constitute a very small percentage of hospitalized patients for which intravenous to oral switch therapy is not ideal³¹. In present study switch on therapy was used in small number of patients' i.e. 11%. This report is similar to reported by Deshmukh vs et al²⁷ was 16.15%. Such type of studies provides necessary feedback to prescribing physicians and may prove useful to formulate antibiotic policy to policy makers.

CONCLUSIONS: It is concluded from the above study that irrationality was found in the prescription writing. This study highlights the problem of indiscriminate use of antimicrobial agents, duration of therapy and regarding proper format of prescriptions. Though irrationality was there but one of the positive finding was majority of antimicrobial drugs prescribed by using generic name at a satisfactory level. The results of study call for interventional strategies to promote rational drug therapy. More emphasis needs to be laid on teaching the art of writing a prescription to undergraduate and postgraduate medical students. A week's posting in clinical pharmacology and therapeutics if possible, should be taught over during internship and this period should be utilized in teaching prescription writing and rational drug therapy.

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