Original Research Article

# Personal formulary for gonorrhea developed by residents of pharmacology

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## Abstract

**Introduction:** Incorporating P-drug concept in pharmacology curriculum can assist the students to learn principles of rational evaluation of available therapeutic options and form a well informed and rational decision concerning drug treatment for an individual patient. This study was designed to develop a personal formulary by senior residents and postgraduate students for the treatment of gonorrhea according to P-drug concept of Joshi and Jayawickramarajah.

**Materials and Methods:** Senior residents and junior residents (post graduate students) were taught about how to analyze and give score ($\alpha$) to drugs used for gonorrhea available in market with the help of various standard text books & journals available in the library, by internet and Current Index of Medical Specialties (CIMS). Scores were given to each four parameters (efficacy, safety, cost and convenience) from 1 to 10 for each drug. Each parameter had given a fractional numerical rating ($\beta$) according to the importance i.e. 0.4 for efficacy, 0.3 for safety, 0.2 for cost and 0.1 for convenience. Score ($\alpha$) was multiplied by fractional numerical rating ($\beta$) to get total score ($\gamma = \alpha \times \beta$). The drug with the highest score became the personal drug.

**Results:** Cephalosporin group had highest score (8.4). Treatment cost of Cefixime was lowest ($\Box$ 24.9) with respect to Ceftriaxone ($\Box$ 30.55) and Cefotaxime ($\Box$ 30.62) but the overall score was better for Ceftriaxone (score 7.2) so it was chosen as Personal drug for gonorrhea. Further personal formulary was developed for the P-drug ceftriaxone as a practical elaboration of the P-drug concept.

**Conclusions:** Teaching of P-drug concept to residents will be helpful in acquiring proper skills in the development of personal formulary and also helpful in promoting rational use of medicines.

**Keywords:** P-drug, Personal formulary, Rational uses of drugs, Prescription writing

## Introduction

With the increasing complexities of modern medicine, it has become necessary to work out a system by which patients are guaranteed the best in drug therapy. Selecting correct drugs for disease is not an easy task. It requires careful selection and repeated search for appropriate drugs. The individual physician does not have time to evaluate the flood of new drugs, drug combinations, and new dosage forms nor to determine the most advantageous drugs in any particular category. Instead they are influenced by various factors like efficacy, safety, cost, and availability of medicine during the process of drug selection. However, selection is not always done carefully as it is often based on previous experience or promotional campaigns by pharmaceutical companies.[1,2]

To bring order out of chaos and to limit the drugs available in a hospital to those that are necessary and the most effective in their field, development of P-Drug is necessary. The aim of personal formulary is to promote safe, effective, and economic prescribing.

The personal formulary is a practical elaboration of the Personal-drug concept, which is outlined in Part 2 of the WHO "Guide to Good Prescribing". Action program on Essential drugs.[3] In 2001, 'Teachers' Guide to Good Prescribing' was developed as a companion volume to help medical teachers to use the 'Guide to Good Prescribing' for teaching. Since Education is the cornerstone. It is a method of orienting students towards therapeutics and to expose them to a sequential decision-making process for developing prescribing skills.[4]

Extensive evidences suggest that education of both doctors and medical students can improve prescribing skills. They are conducted in small groups containing 10-12 students for 2 hrs. It consists of demonstration of animal experiments, prescription writing for common diseases and emergency conditions and problem-based learning. The post graduate students work as tutors and are involved in taking practical classes. However, we do not teach selection of P drug as per the method described by Joshi and Jayawickramarajah and "Guide for good prescribing" published by WHO.[5,6]

Rai has recommended inclusion of P-drug concept in the undergraduate pharmacology practical curriculum in India.[4] Indira Gandhi Institute of Medical Sciences, Patna, India is an autonomous organization to provide super specialty medical facilities in Bihar.

Gonorrhea is a bacterial sexually transmitted infection (STI) caused by Neisseria gonorrhoeae or gonococcus. Many people have no symptoms.[7] Men may have burning with urination, discharge from the penis, or testicular pain. Women may have burning with urination, vaginal discharge, vaginal bleeding between periods, or pelvic pain. Complications in women include pelvic inflammatory disease and in men

include inflammation of the epididymis. If untreated, gonorrhea can spread to joints or heart valves.[8]

This study was designed to develop a personal formulary by residents for the treatment of gonorrhea.

## Materials and Methods

This study was carried out in June 2017 in the Department of Pharmacology, IGIMS, Patna among the residents (senior residents and junior residents i.e. postgraduate students).

Personal formulary for gonorrhea was developed by using various standard text books, journals available in the library and on internet. Current Index of Medical Specialties (CIMS) was used to determine cost of drugs.[9]

Residents were taught about how to analyze and give score ($\alpha$) to drugs used for gonorrhea available in market. Four parameters according to P-drug concept of Joshi and Jayawickramarajah,[10] efficacy (0.4), safety (0.3), cost (0.2) and convenience (0.1) was taken into consideration for each group and their drugs.

1. **Efficacy** was derived according to the efficacy profile written in standard text books. Drug with more efficacy were given higher score.
2. **Safety** of a drug was described according to the side effect profile written in standard text books. Drug with more side effects were given lower score.
3. **Cost** was compared by taking average of costs of different brands written in Current Index of Medical Specialties (CIMS).
4. **Convenience** was compared according to the availability of drug, dosage form, dosage schedule, route of administration.[11-12]

Scores were given to each four parameters from 1 to 10 for each drug. Each parameter had given a fractional numerical rating ($\beta$) according to the importance i.e. 0.4 for efficacy, 0.3 for safety, 0.2 for cost and 0.1 for convenience. Score ($\alpha$) was multiplied by fractional numerical rating ($\beta$) to get total score ($\gamma = \alpha \times \beta$). Higher total score indicated a better value.[12]

The drug with the highest score became the personal drug choice. Next step was to verify suitability for selected P drug for particular patient. Then the senior residents and postgraduate wrote the prescription and kept a copy of personal drug description as a personal formulary.[10,13,14]

## Results

In this study personal formulary was developed by using parameters like efficacy, safety, cost and convenience according to Joshi and Jayawickramaraja. [10] Cephalosporin group had highest score (Table 1) and in this group ceftriaxone (score 7.2) had emerged as Personal formulary for gonorrhea (Table 2). The cost comparison of drugs was done by using CIMS10 (Table 3). The personal formulary was developed for the P-drug ceftriaxone as a practical elaboration of the P-drug concept, which is shown in (Table 4).

**Table 1:** Selection of personal formulary drug from drug group for gonorrhea

| Groups of drugs | Efficacy (0.4) | Safety (0.3) | Cost (0.2) | Convenience (0.1) | Total |
|---|---|---|---|---|---|
| Penicillin | 4 (0.16) | 5 (1.5) | 7 (1.4) | 3 (0.3) | 4.8 |
| Cephalosporin | 9 (3.6) | 8 (2.4) | 9 (1.8) | 6 (0.6) | 8.4 |
| Tetracyclines | 6 (2.4) | 6 (1.8) | 6 (1.2) | 5 (0.5) | 5.9 |
| Macrolides | 7 (2.8) | 8 (2.4) | 8 (1.6) | 8 (0.8) | 7.6 |
| Aminoglycosides | 8 (3.2) | 4 (1.2) | 2 (0.4) | 3 (0.3) | 5.2 |

**Table 2:** Selection of personal drug among cephalosporins for gonorrhea

| Drugs | Efficacy (0.4) | Safety (0.3) | Cost (0.2) | Convenience (0.1) | Total |
|---|---|---|---|---|---|
| Ceftriaxone | 8 (3.2) | 7 (2.1) | 7 (1.4) | 5 (0.5) | 7.2 |
| Cefixime | 6 (2.4) | 6 (1.8) | 8 (1.6) | 9 (0.9) | 6.7 |
| Cefotaxime | 6 (2.4) | 4 (2.4) | 7 (1.4) | 5 (0.5) | 6.7 |

**Table 3:** Cost of drugs/drug preparations available in india used in treatment of gonorrhea

| Drugs | Dose (mg) | Duration of treatment (in days) | Number of brands available in market | Range of cost of treatment (in Rupees, □) | Average cost of treatment (in Rupees, □) |
|---|---|---|---|---|---|
| Cephalosporins | | | | | |
| Ceftriaxone | 250mg | Single dose | 45 | □ 21.38 – 39.72 | □ 30.55 |
| Cefixime | 400mg | Single dose | 4 | □ 15.8 – 34 | □ 24.9 |
| Cefotaxime | 500mg | Single dose | 9 | □ 17.31 – 43.92 | □ 30.62 |
| Tetracyclines | | | | | |
| Doxycycline | 100mg | Twice daily for 7 days | 10 | □ 8.68 – 77 | □ 42.84 |
| Macrolides | | | | | |
| Azithromycin | 1g | Single dose | 2 | □ 36 – 36 | □ 36 |

| Aminoglycosides | | | | | |
|---|---|---|---|---|---|
| Spectinomycin | 2g | Single dose | 2 | ⬜ 200 – 200 | ⬜ 200 |
| Fluroquinolones | | | | | |
| Ciprofloxacin | 500mg | Single dose | 21 | ⬜ 3.47 – 9.95 | ⬜ 6.71 |

**Table 4:** Description of ceftriaxone as personal formulary for gonorrhea

| Inj 125, 250mg | | Antibiotic | | Ceftriaxone |
|---|---|---|---|---|

Dosage: Adult, 250mg i.m. single dose

**WHAT TO TELL THE PATIENT**

**Information:** ceftriaxone is an antibiotic
**Side effects:** Diarrhea, nausea, vomiting, abdominal discomfort, headache, transient hepatitis, eosinophilia, antibiotic associated colitis, bleeding disorders
**Contraindications:** cephalosporin hypersensitivity, porphyria, hypoalbuminaemia, acidosis, impaired bilirubin binding
**Instructions:**
**Warnings:** avoid in penicillin hypersensitivity, bleeding tendency, liver dysfunction
**Next appointment:**
**Follow up:**

## Discussion

Education is the cornerstone, given the extensive evidence that education of both doctors and medical students can improve prescribing.[15]

Incorporating P-drug concept in pharmacology curriculum can assist the students to learn principles of rational evaluation of available therapeutic options and form a well informed and rational decision concerning drug treatment for an individual patient. Training of students in pharmacology should be in such a way that they are able to prescribe rationally for common diseases, calculate dosages depending upon age and sex and prevailing health status of individuals, administer the drug through appropriate route and also identify adverse drug reactions and interactions.[16] There is a need of developing patient oriented problem-solving system of teaching in pharmacology in which students are oriented to learn rational use of drug by proper training.[17]

Rational use of drugs (RUD) entails that patients should receive medications appropriate to their specific clinical needs, proper dose and duration, with the lowest cost to them and their community.[18,19]

The above requirements will be fulfilled by the WHO Guide to Good Prescribing which gives medical students a normative model for therapeutic reasoning and prescribing and provides a six-step guide to the process of rational prescribing.[3,4]

Residents who teach the undergraduate students to develop a standard treatment for common disorders and develop a set of personal formularies by using National and International treatment guidelines, formularies, textbooks and other sources of drug information. The emphasis is that future doctors should master both steps of the drug-selection process, i.e. verification of suitability and alter the drug to individualize treatment.[19]

The first author Lalit Mohan had experience in teaching P drug concept in the Department of Pharmacology at the Manipal College of Medical Sciences (MCOMS), Pokhara, Nepal which concentrates on teaching rational use of medicines to medical students.

Drug/drug groups in gonorrhea are penicillin, cephalosporin, tetracycline, macrolides and aminoglycosides. The decision of which drug class to prescribe for a particular indication depends upon the availability of different medications, on the basis of efficacy, safety, suitability and cost of each class making the choice much easy.[20]

Ceftriaxone in a single injection of 250 mg provides sustained, high bactericidal levels in the blood. Extensive clinical experience indicates that ceftriaxone is safe and effective for the treatment of uncomplicated gonorrhea at all anatomic sites, curing 99.2% of uncomplicated urogenital and anorectal and 98.9% of pharyngeal infections.[21]

Aminoglycosides is generally less effective and slower in action than cephalosporin, while remaining groups are less efficacious. In safety considerations cephalosporin and macrolide have same safety profile. Followed by tetracycline which causes fatty liver, jaundice, Fanconi syndrome. Aminoglycosides are ototoxicity, nephrotoxicity, hypersensitivity reactions. Penicillin scored least in safety profile.

The WHO Global Gonococcal Antimicrobial Surveillance Programme (WHO GASP), monitors trends in drug-resistant gonorrhea. WHO GASP data from 2009 to 2014 find widespread resistance to ciprofloxacin [97% of countries that reported data in that period found drug-resistant strains], increasing resistance to azithromycin [81%], and the emergence of resistance to the current last-resort treatment: the extended-spectrum cephalosporins

(ESCs) oral cefixime or injectable ceftriaxone [66%].[22] These comparative findings were helpful in allotting points (Table 1).[21,23] Subsequently we determined cost of individual drugs considering the lowest effective dose and develop range of cost and average cost and compared them. Fluroquinolones were cheapest with the highest score for this criterion and least was scored by aminoglycosides (Table 3). For convenience we compared availability of drug, dosage form, dosages schedule, routes of administration. Macrolide are given orally and got highest score.[24]

Cephalosporins as group got highest scores (Table 1). Whenever there are large choices of agents is available, for same class, similar considerations are involved. Thus, choosing a particular drug from a class for therapy is very important. So, we did comparison of individual agents in the cephalosporin group. Among cephalosporins, ceftriaxone exhibits maximum efficacy.[25]

Cefixime does not provide as high, nor as sustained, bactericidal blood levels as a 250-mg dose of ceftriaxone; further, it demonstrates limited efficacy. Ultimately after discussion and scoring of various parameters, ceftriaxone got highest score and emerged as personal formulary for gonorrhea (Table 2).[10,23] None of these injectable cephalosporins offer any advantage over ceftriaxone for urogenital infection. The incidence of side-effects was lowest in the ceftriaxone group.[24]

We verified the suitability of selected P drug for patient of gonorrhea by using a problem-solving exercise for example Sunil Kumar, aged 25 years is a businessman, is suffering from lower abdominal pain, Increased mucopurulent urethral discharge, dysuria (usually without urgency or frequency), fever, chills, nausea, and vomiting. On history he was not allergic to penicillin or cephalosporins. Verify of suitability for selected p drug for this condition and write the prescription for same?[13]

In this case ceftriaxone was selected as p-drug because it was suitable for this patient. It was effective, had appropriate bactericidal action for sustained period. After the selection of the P-drug, personal formulary was developed which includes information in the form of loose-leaf notebook, containing details about the effects of the drug, side effects, instructions, warnings & next appointment according to Guide for Good prescribing (Table 4).

There are many difficulties during teaching or developing personal formulary, like large number of brands and their variation in cost, comparing efficacy, comparing among class as large number of drugs belong to same class. Our study had limitations like the contribution in development of personal formulary was only from 3 SR and 4 PG students. The selection of drug for gonorrhea. It was not possible to exactly pinpoint ceftriaxone as a P-drug for gonorrhea. However, we reduced this bias by using group consensus or majority vote to give values. There are differences in opinion and argument over choice for particular disease and the whole purpose of exercise is

defeated by such argument. The basic motive of teaching P drug concept is that instead of memorizing, students can develop personal formulary after proper discussion and have known how to prescribe rather than what to prescribe which is the goal of WHO.[14] Application of the WHO method has improved the prescribing skills of undergraduate medical students.[26] Consequently, students are taught how to define their own P-drugs and are encouraged during their pharmacology teaching to develop a personal formulary.[2]

## Conclusion
The teaching of P-drug concept to PG students will help them acquire proper skills in the development of personal formulary. The ultimate aim is to expand this exercise further and transfer the skills to undergraduate medical students. The whole exercise will be helpful in promoting rational use of medicines.

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## Conflict of Interest
None.

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