The concept of personal drugs in the undergraduate pharmacology practical curriculum

It is very important to incorporate clinically relevant practicals into the undergraduate pharmacology practical (UGPP) curriculum.[1] Various medical colleges in the state of Gujarat have included clinical practicals in their UGPP curriculum.[2] Rai has recommended the inclusion of the 'P-drug' concept in the UGPP curriculum.[3]

The conference of experts on the rational use of drugs, convened by the World Health Organization in Nairobi in 1985, stated that: *"Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community."* This goal can be achieved by acquiring knowledge of the principles of rational drug usage during undergraduate training. This correspondence emphasizes the importance of this concept.

What is a P-drug?[4]

The drugs you are going to prescribe regularly and with which you will become familiar are called P(ersonal)-drugs. The P-drug concept includes the name of a drug, dosage form, dosage schedule and duration of treatment for a specified condition. Due to varying availability and cost of drugs, different national formularies and essential drug lists, medical culture and individual interpretation of information, P-drugs differ from country to country and between doctors.

There are four reasons that indicate why a P-drug should never be the one that has been suggested or dictated by clinical teachers, senior colleagues or by sales representatives: a) the latest and the most expensive drug is not necessarily the best, the safest or the most cost-effective, b) by developing one's own set of P-drugs, one can learn to handle pharmacological concepts and drug-related data in an effective manner, c) by compiling one's own set of P-drugs, one can prescribe alternatives when the P-drug cannot be used and d) one has the final responsibility for his / her patient's well being, which he / she cannot pass on to others. While physicians can and should draw on expert opinion and consensus guidelines, they should always think for themselves.

Example for selecting a P-drug for acute amoebic dysentery

Amoebiasis is one of the common infections encountered in clinical practice and it is relatively easy to understand the pathophysiology as well as the treatment of amoebiasis. Therefore, we have selected the example of acute amoebic dysentery and analyzed it in consultation with standard textbooks of pharmacology.[5-8]

Exercise

A 50 year-old male patient complains of bloody, mucoid stools and abdominal pain. There is no history of alcohol abuse. You have diagnosed it as a case of acute amoebic dysentery. Choose an appropriate drug and mention its dosage schedule and duration of treatment.

Answer

The process of choosing a P-drug can be divided into five steps:[4]

1. Define the diagnosis
2. Specify the therapeutic objective
3. Make an inventory of effective groups of drugs
4. Choose an effective group according to criteria
5. Choose a P-drug

Step 1: Define the diagnosis

Amoebiasis is a protozoal infection caused by the ingestion of amoebic cysts of *Entamoeba histolytica* in contaminated food or water. The cysts transform into trophozoites in the intestine, which either live on the surface of colonic mucosa or invade it. On the mucosal surface, the cysts remain as commensals, passing into the stools (luminal cycle) and serve to propagate the disease. If they invade the mucosa, they form amoebic ulcers and cause acute dysentery (characterized by the presence of blood and mucus in the stools) or chronic intestinal amoebiasis (characterized by vague abdominal pain, amoeboma).

In some instances, trophozoites also invade extraintestinal tissues, mainly liver and less commonly the brain, where they produce amoebic abscess and systemic disease. Some individuals harbor the parasites (carriers) without developing overt disease but the cysts are present in their feces and they can infect others.

Step 2: Specify the therapeutic objective

As amoebiasis is transmitted by the fecal-oral route and poor hygienie plays a major role in the spread of the disease; avoidance of contaminated food and water as well as proper sanitation can help in prevention of transmission of the disease. But in this example, we will discuss drug treatment only. Here, the specific therapeutic objectives would be to treat the signs and symptoms, eradicate the disease and prevent transmission of the disease and further complications.

Step 3: Make an inventory of effective groups of drugs

Efficacy is the first criterion for any group of drugs.[4] In this case, the drugs must have antiamoebic activity. There are five groups with such an effect:

1. Nitroimidazoles [*e.g*, metronidazole, tinidazole,

secnidazole, satranidazole ornidazole]
2. Alkaloids [*e.g*, emetine, dehydroemetine]
3. Amide [*e.g*, diloxanide furoate]
4. 8-Hydroxyquinolines [*e.g*, iodochlorohydroxyquin, diiodohydroxyquin]
5. Antibiotics [*e.g*, tetracyclines, paromomycin]

Step 4: Choose an effective group according to criteria

An effective group should be selected according to criteria of efficacy, safety, suitability and cost of treatment.[4] These criteria are listed in Table 1.

Efficacy

The drug should work as soon as possible (the therapeutic

Table 1

Comparison between the drug groups used in acute amoebic dysentery

Efficacy	Safety	Suitability
Nitroimidazoles		
➢ *Pharmacodynamics* Amoebicidal action ➢ *Pharmacokinetics* Complete absorption from small intestine Wide distribution Metabolism in the liver Urinary excretion Plasma half life (8-29 hours)	➢ *Side effects* Relatively frequent, but non-serious in nature Nausea, anorexia, metallic taste, abdominal pain (most common) Headache, glossitis, dryness of mouth, transient neutropenia (less frequent) Neurotoxic effects like vertigo, dizziness, numbness of extremities (on prolonged use)	➢ *Contraindications* Neurological disorders, blood dyscrasias, 1st trimester of pregnancy, chronic alcoholism ➢ *Drug interactions* With alcohol, warfarin, lithium, phenobarbitone, rifampicin
Alkaloids		
➢ *Pharmacodynamics* Potent and directly acting amoebicides ➢ *Pharmacokinetics* Administration by S.C./I.M. injections, Can't be given orally (vomiting) Very slowly excreted in urine	➢ *Side effects* Highly toxic Frequent nausea, vomiting Abdominal cramps, diarrhoea, Weakness and stiffness of muscles Hypotension, tachycardia, ECG changes and myocarditis (most serious) Cumulative toxicity on prolonged use	➢ *Contraindications* Presence of cardiac/renal disease, Pregnancy
Amide		
➢ *Pharmacodynamics* Highly effective luminal amoebicide Because of poor tissue amoebicidal action, it is preferably a luminal amoebicide and less effective in invasive amoebic dysentery However, it has produced high cure rates in mild intestinal amoebiasis	➢ *Side effects* Very well tolerated Flatulence (only side effect) Occasional nausea, itching and rarely urticaria	
8-Hydroxyquinolines		
➢ *Pharmacodynamics* Kill the cysts forming trophozoites in the intestine Do not have tissue amoebicidal action, not very effective in acute amoebic dysentery	➢ *Side effects* Well tolerable Nausea, transient loose and green stools, pruritus Iodism (due to chronic iodine overload) Neuropathic syndrome: subacute myelo-optic neuropathy (SMON)	➢ Not recommended during pregnancy and for children
Antibiotics		
➢ *Pharmacodynamics* 1. Tetracyclines: Direct inhibition of amoebae only at high concentration	➢ *Side effects* Epigastric pain, nausea, vomiting, diarrhoea (irritant effets) Dose related toxicity: Liver and kidney damage, phototoxicity, adverse effects on teeth and bones, antianabolic, Hypersensitivity, Superinfections	➢ Should not be used during pregnancy, lactation and in children
2. Paromomycin: Antiamoebic action	➢ *Side effects* Rare with oral doses but include abdominal pain and cramping, epigastric pain, nausea, vomiting, steatorrhoea, diarrhoea, rash, headache Same risks of nephrotoxicity and ototoxicity seen with other aminoglycosides (parenteral route)	

S.C.-subcutaneous, I.M.-intramuscular

Table 2

Comparison between drugs within the group of nitroimidazoloes

	Efficacy	*Safety*	*Suitability*	*Cost of treatment*
Metronidazole	No difference	No difference	No difference	Rs. 6.75*
Tinidazole	No difference	No difference	No difference	Rs. 12.65*
Secnidazole	No difference	No difference	No difference	Rs. 26.40**
Ornidazole	No difference	No difference	No difference	Rs. 39.00*
Satranidazole	No difference	Better tolerability, absence of neurological and disulfiram-like reactions	Can be preferred in patients with susceptible neurological symptoms	Rs. 40.00*

*Five days' treatment, **Single dose

objective). Therefore, both pharmacodynamics as well as pharmacokinetics of a drug should be considered during its selection for a specific condition.[4] Among the five groups, nitroimidazoles and alkaloids are very efficacious for acute amoebic dysentery while the remaining groups are less efficacious. The mean effective concentration for most susceptible protozoa (≤ 8 µg/ml) is achieved within 0.25-4 hours with a single dose of metronidazole 500 mg.

Safety

All drug groups have side effects; alkaloids are highly toxic drugs while there is a greater chance of side effects with the antibiotic group as compared to the nitroimidazole group.

Suitability

This is usually linked to an individual and hence, is not considered during compilation of a list of P-drugs.[4] In this case, oral nitroimidadazoles should be preferred as alkaloids are administered by the parenteral route.

Cost of treatment

There is a greater link of prices with individual drug products than with drug groups.[4] The nitroimidazole group is selected as a first choice for this case. Cost of treatment[9] with each agent of this group is listed in Table 2.

Step 5: Choose a P-drug

Choose an active substance and a dosage form

There is not much difference in efficacy and safety of the five drugs in the nitroimidazole group. With regard to suitability, the five drugs hardly differ in contraindications and possible drug interactions. However, better tolerability (no nausea, vomiting or metallic taste), absence of neurological and disulfiram-like reactions are claimed with satranidazole as compared to other substances in this group. This means that the ultimate choice depends on cost. In this case, metronidazole is the cheapest active agent. This should be followed by a luminal amoebicide to prevent carrier state (diloxanide furoate is the rational choice for this).

Choose a standard dosage schedule

For acute intestinal amoebiasis, metronidazole 400 mg three times a day is sufficient (plasma half-life of metronidazole is eight hours).

Choose a standard duration of treatment

Duration of treatment for acute intestinal amoebiasis is usually 5-7 days with 400 mg metronidazole.

For this case, metronidazole (oral route) would be the P-drug listed in one's personal formulary, *i.e*, Tablet metronidazole 400 mg three times a day for five days followed by Tablet Diloxanide furoate 500 mg three times a day for 10 days.

To conclude, awareness among undergraduates about the rational use of drugs can be increased by inclusion of similar exercises for various clinical conditions (*e.g*, mild-to-moderate hypertension, acute bronchial asthma, peptic ulcer etc.) in the UGPP curriculum.

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