

# **RATIONAL USE OF MEDICINES IN CHILDREN**

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## **1. Introduction**

Irrational use of medicines is a major problem world wide. The World Health Organization estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately and that half of all patients fail to take them correctly, over use, under use or misuse resulting in wastage of scarce resources and serious health hazards. Implementing rational use of drugs in a country should start from the policy of rational importing and distribution of drugs. For this, health care administrators and politicians are responsible. Professionals should make their contribution. Improving the knowledge and attitudes of the prescribing doctors and dispensing professionals also play a major role. They should be provided with essential tools like books on drug doses and facilities to monitor their activities. Knowledge and attitude of the public is also important. Finally, to ensure implementing such a policy, clinical auditing, monitoring and a system of surveillance should be promoted.

## **2. Definition**

The rational use of medicines is defined as “patients receive medications appropriate to their clinical needs, in doses that meet their requirements, for an adequate period of time, and at the lowest cost to them and their country”. Please note this include non- pharmacological measures as well.

## **3. What is irrational use of medicines?**

A medicine is irrationally used if it is prescribed when there is little likelihood that it will have a beneficial effect or when the anticipated benefit is not worth the potential harm or the cost of the drug.

## **4. Possible reasons for irrational use of medicines**

The reasons are multifold, and some are given below:

- 4.1 Inadequate training in clinical pharmacology and basic principles underlying rational use of medicines.

- 4.2 Lack of continuing education, supervision and critical review of prescribing practices.
- 4.3 Biased and aggressive promotional activities by pharmaceutical industries and availability of many generic and brand preparations for a single medicine.
- 4.4 Patient load and their demand for relief.
- 4.5 Uncertain diagnosis or poor diagnostic facilities.
- 4.6 Reliance on prescriber's own limited favourable experience with a medicine regardless of scientific merit.
- 4.7 Lack of awareness about the cost of medicines, and about the impact of irrational prescribing on the health economics.
- 4.8 Competitive "private practice" where the practitioner wants to prescribe something "new and expensive" to attract the patients.
- 4.9 Less time spent on history taking, including previous medicines, clinical examination and not explaining to patients about the prescribed medicines.
- 4.10 Use of too many medicines (poly pharmacy) often in inadequate dose given for nonbacterial infections.
- 4.11 Lack of awareness of patients about the drugs they are taking. (Some prescribers use a coding system to name the drugs)
- 4.12 Self medication of prescription only medicines and non adherence to dosing regimes.
- 4.13 Some problems unique to the paediatric population. (lack of clinical trial data in children, off label use of medicines, lack of appropriate formulations)

## **5. Rational approach to therapeutics**

Medicines should only be prescribed when they are necessary, and in all cases the benefit of administering the medicine should be considered in relation to the risks involved. Bad prescribing habits lead to ineffective and unsafe treatments, exacerbations or prolongation of illnesses, distress and harm to the patient and high cost to the patient and the country.

## 6. The process of rational treatment

The following steps recommended by the World Health Organization will take the prescriber through the essential steps in rational approach to therapeutics.

### 6.1 Define the patient's problem

Prescriber should establish the diagnosis or identify and list the problems based on a detailed history (including medicines taken) examination and investigations. The list of problems usually represents the working diagnosis of the prescriber, and may differ from how the patient perceives the problem. Few examples of problems are; a disease/disorder, sign of an underlying disease, psychological or social problems, side effects of drugs, refill request (poly pharmacy), non – adherence to treatment, request for preventive treatment.

Case scenario: Aruni, 2 ½ year old girl who lost her mother in the Tsunami and presently living in a refugee camp with her father was admitted to your ward. She presented with abdominal pain, fever, vomiting and dysuria of two days duration, and was found to be febrile, very ill looking and with loin tenderness.

Inquiring into the past history revealed that Aruni had straining before micturition a few weeks before, and was seen by the doctor who visited the Refugee camp. The doctor has prescribed a white coloured tablet of which 1 ½ tablets were to be taken twice daily. After two days of starting treatment, the symptoms subsided and father had stopped the tablets.

One week later, she again developed dysuria and had increased frequency in passing urine. The same doctor saw the child again, and blamed the father for stopping the treatment early. He then prescribed yellow tablets of which ½ tablet was to be taken four times daily. While taking these drugs child developed vomiting and also passed yellow coloured urine. Father immediately stopped the treatment. On direct questioning, the father said that Aruni has been having constipation for last few months which he ignored.

#### Box 1

#### Problems that require attention in managing Aruni

##### Identified problems

1. Urinary tract infection (UTI)
2. Constipation
3. Social problems

## 6.2 Specify the management objectives

It is essential to plan the management at the outset itself. Specifying the management objectives will prevent unnecessary drug use. If appropriate, it is a good idea to discuss the therapeutic (management in some instances) objectives with the patient and/or parents before the treatment is started.

### Box 2

#### Management objectives to treat problem 1 (UTI) identified in Aruni

##### Management objectives

1. Confirm the diagnosis of UTI
2. Treatment of current episode.
3. Prevention of further UTI.
4. Identify the underlying cause/s if possible and the consequences of UTI
5. Discuss and explain the treatment modalities with the father.

## 6.3 Selecting therapeutic strategies

Identify the treatment options to achieve the therapeutic objectives; four possible approaches to treatment are; information or advice; treatment without drugs (non-pharmacological treatment); treatment with a drug (pharmacological treatment); and referral. Often combinations of these approaches are required. Therapeutic (management) strategies to achieve the management objective 2 (treating the current episode) in Aruni are given in Box 3. Please note that you have to identify management strategies for each problem mentioned in Box 1 in this way. (E.g. constipation and social problems)

### Box 3

#### Management strategies to achieve the Objective 2 given in Box 2

##### Management Strategies

1. Information or advice
  - General information about UTI
2. Non-pharmacological
  - E.g. Increase fluid intake
3. Pharmacological
  - Appropriate antibacterial agents
4. Referral
  - e.g. Refer to a centre for further investigation if indicated

### 6.3.1 Non-pharmacological treatment

Often health problems can be resolved by non – pharmacological measures such as change in life style or diet, use of physiotherapy or exercise, or provision of adequate psychological support; these have the same importance as a prescription drug, and instruction must be written, explained and monitored in the same way.

### 6.3.2 Pharmacological treatment

This depends on the current problems, local health situation and currently available medicines in the said setting. Choosing the appropriate pharmacological treatment involves following steps

#### (a) Making an inventory of effective group of drugs

There are two ways to identify effective group of drugs; (1) looking at hospital, national or international treatment guidelines or the WHO/ national List of Essential Drugs, or (2) checking a good pharmacology reference book and determine which groups are listed for the therapeutic objective. Please note information provided by pharmaceutical industry is unreliable and biased towards its products. Box 4 illustrates the essential steps in making an inventory of effective groups in the case of Aruni’s UTI.

#### Box 4

#### Essential steps in making an inventory of effective groups in the case of Aruni’s UTI.

##### Steps in making an inventory of effective groups

1. Refer the national guidelines on managing UTI in children to make the inventory
2. Ascertain the availability of appropriate drugs in your institution from the inventory
3. Select the antibacterial agent group on the following points.

#### (b) Selecting the correct effective group from the above inventory

To compare groups of effective drugs, information on efficacy, safety, suitability and cost are needed. Reliable current strong evidence should support the efficacy claims. Safety of medicine is very important as adverse drug reactions top the list of iatrogenic diseases (see later). The cost of treatment and especially the cost/benefit

ratio of a drug or dosage form is a major selection criterion. Where two or more drugs appears to be similar, preference should be given to (i) the drugs which have been most thoroughly investigated; (ii) drugs with the most favorable pharmacokinetic properties; and (iii) drugs for which reliable local manufacturing facilities exist. Box 5 shows some criteria used in choosing the effective group to treat the UTI in Aruni

### Box 5

#### Some criteria used in choosing the effective group to treat the UTI in Aruni

- 1. Efficacy:** Aminoglycosides, cephalosporin, cotrimoxazole, nitrofurantoin and nalidixic acid & fluoroquinolones (ciprofloxacin) are proved to be effective in treating UTI empirically
- 2. Safety:** Use of ciprofloxacin is not recommended for infants, children, and teenagers under the age of 18 years since fluoroquinolones have been shown to cause bone development problems in young animals
- 3. Suitability:** Nitrofurantoin, and nalidixic acid are not suitable as they have poor tissue penetration and not effective in suspected upper UTI. Nitrofurantoin, nalidixic acid and cotrimoxazole are not suitable for managing Aruni as parenteral forms are not available.

*AMINOGLYCOSIDE* is selected to treat the UTI in Aruni initially (before culture and ABST reports are available. The selection was based on the following merits:

- Proven efficacy
- Time tested,
- Safe in children,
- Easily available
- Cost effective
- Available in Essential Medicine List of Sri Lanka
- Good tissue penetration
- Parenteral forms are available
- Once daily administrations is adequate

### (c) Selecting the correct drug from the chosen group (P – drug)

The choice of P-drug should be based on evidence about maximal clinical benefits for the drug for a given indication with the minimum production of adverse reactions. The criteria used in choosing the effective group can be applied to choose the P- drug as well. *P drug is a prescriber's personal drug for a particular condition selected through the steps mentioned here.* Box 6 illustrates how a P – drug is selected to treat Aruni's UTI

#### Box 6

##### Selection of correct drug from aminoglycosides to treat UTI in Aruni

1. Available aminoglycosides are gentamicin, netilmicin, and amikacin.
2. Of these, GENTAMICIN is selected as it is time tested and cost – effective.

### (d) Selecting the active substance, dosage form, standard dosage schedule and standard duration of treatment

Choosing the dosage form, dosage schedule and duration are as equally as important as choosing the P – drug, and in paediatric population it is a must as many practical factors (taste, administration, etc.) impede effective treatment. See Box 7 in the case of UTI in Aruni

*Please note choosing a P – drug for some common therapeutic objectives can be done even before a patient presents. In this way, a prescriber can have his/her own P drug formulary.*

#### Box 7

##### Selecting the active substance, dosage form, standard dosage schedule and standard duration of treatment to treat the UTI in Aruni

1. **Active substance:** Gentamicin is the active substance.
2. **Route of administration:** Intravenous as it is not absorbed from GIT and the child is ill. Intramuscular route is not preferred as IM aminoglycosides are neurotoxic. Also note that IM injection is generally avoided in children as it is painful.
3. **Dosage schedule** – Single dose per day (Current evidence)
4. **Standard duration:** Continue until ABST is available to select suitable antibiotic. The standard duration is 7 days; however IV antibacterial agent can be followed by an effective oral antibacterial agent (from ABST reports) once Aruni is not ill, and able to swallow tablets.

#### **6.4 Verifying the suitability of the chosen pharmaceutical treatment for each patient**

The prescriber must check whether the active substance chosen, its dosage form, standard dosage schedule and standard duration of treatment are suitable for each patient. Verifying your P-drug is also suitable for the individual patient in front of you is probably the most important step in the process of rational prescribing. Review all the steps taken up to now

Please note; this guideline gives the outline of rational prescription in children using UTI as an example. Refer the National guidelines on management of UTI in children for details of management of UTI in children.

#### **6.5 Prescription writing**

Prescription is the link between the prescriber, the pharmacist, nurse and the patient so it is important for the successful management of the present medical condition. Please remember to (i) avoid shortened forms in the prescription, (ii) write the generic name of the drugs, (iii) take extra caution when decimals are written, and (iv) to write nanograms, and micrograms in full.

##### **A prescription should include:**

- Name, address, telephone of prescriber
- Date
- Generic name of the drug, strength
- Dosage form, total amount
- Label: instructions, warnings
- Name, address, age of patient
- Signature or initials of prescriber

#### **6.6 Give information, instructions and warnings**

This step is important to ensure patient's adherence to the treatment. On average 50% of patients do not take prescribed drugs correctly, take them irregularly or not at all. The most common reasons are that symptoms have ceased, side effects have occurred, the drug is not perceived as effective or the dosage schedule is complicated for patients, particularly for those who are in the extreme ages of life. Inform the patient about beneficial effects; warn about the side effects and how to deal with them.

The patient should be given a date for the next appointment so that the results of the treatment could be assessed. The WHO recommends six points to be included within the minimum information that should be given to the patient (see later). In the case of Aruni, failure to give information (about importance and duration of treatment, warning about side effects) has contributed to the current presentation.

### **6.7 Monitor (? Stop) treatment**

The purpose of monitoring is to check whether the treatment has solved the patient's problem. In practice monitoring targets at 2 aspects; is the treatment effective? Are there any side effects? History taking, physical examination and laboratory tests will usually provide the necessary information for monitoring. For Aruni, follow up investigations have to be arranged, and prophylactic antibacterial therapy may have to be continued until the investigations are done (Please refer the National guidelines on management of UTI in children for details of management of UTI in children)

### **Recommendations**

1. Protocol committee should continue to function assisting paediatric care givers in following rational prescription in children. All the protocols should include audit indicators e.g. How many patients had the diagnosis confirmed before commencement of antibiotics ?
2. The guidelines should be continuously updated and “marketed”.
3. Paediatric care givers, administrators, policy makers have to ensure that these guidelines should be implemented. Adequate resources should be provided.
4. The culture of Audit should be embedded in paediatric practice.  
(See Appendix 5)
5. Establish programmes to improve public awareness about the commonly used drugs and management policies of common conditions.
6. Colleagues and other professionals should contribute and participate at the level of import and distribution of drugs giving special attention to paediatric needs.

7. Uniform patient information leaflets for specific conditions should be printed and available in all the hospitals.
8. Prescription sheets should be designed with adequate space and columns to ensure that it is possible for doctors to implement what we recommend in this document.
9. Drug dose books should be made available for everybody. Make it essential to have one at the registration.
10. Nurses and pharmacists should be incorporated into rational use of drugs system of everybody playing a role and taking responsibility. (prescription to be signed by the nurse before administering drugs)

## Appendix 1

Minimal information – leaflets should be printed for selected conditions. Protocol committees should prepare them along with the protocol. e.g. asthma, epilepsy, diarrhoea, nutrition, RTI, dengue, viral fever,

Minimum information that should be given to the patient

1. Effects of the drug
2. Side effects
3. Instructions
4. Warnings
5. Future consultations
6. Everything clear?

## Appendix 2

### Adverse drug reactions in children

The WHO defines ADR “a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function”. No one can argue about the vital role medicinal products play in influencing morbidity and mortality in all age groups; however no drug is totally devoid of risk. For all medicines there is a trade-off between the benefits and the potential for harm. **The harm can be minimized by ensuring that medicines of good quality, safety and efficacy are prescribed and used rationally.** Children form a highly heterogeneous group in which drug pharmacokinetics and pharmacodynamics together with physiological development vary significantly with age, thereby placing them at a possible increased risk ADRs.

In order to prevent or reduce harm to patients and thus improve public health, mechanisms for evaluating and monitoring the safety of medicines in clinical use must be in place. In practice, this means having a well-organized pharmacovigilance system. The WHO defines “pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine related problems”. Monitoring the safety of medicines after marketing is one of the important functions of pharmacovigilance (postmarketing pharmacovigilance).

In Sri Lanka, the National ADR monitoring centre (Info\_Vig), based in the Department of Pharmacology, Faculty of Medicine, Colombo coordinates the pharmacovigilant activities for the Ministry of Health. Individual Adverse Drug Reaction (ADR) reports completed by health professionals can help the National ADR Monitoring Centre and the Drug Regulatory Authority to take necessary actions regarding the safety of drugs used in Sri Lanka.

**What to report?** Any suspected reactions, drug interactions, quality failures or congenital malformations associated with the following;

- All therapeutic agents including those taken for self medication (Over The Counter medications)
- Vaccines
- Herbal products
- Blood products
- X-ray contrast media,
- Dental or surgical materials
- Devices (e.g.; inhalers, intrauterine devices)
- Contact lens fluid
- Cosmetics

**Where to report?**

Postal address: Info\_Vig, Department of Pharmacology, Faculty of Medicine  
PO Box 271, Kynsey Road, Colombo 8

Telephone: 2695300 Ext 315/410, or direct 5677244

Fax: 2691581 Attn Department of Pharmacology

E mail address: info\_vig@yahoo.com

**How to report?** Please see the attached form. You can photocopy the form

### **Appendix 3**

#### **Off label medicines/ prescriptions for children**

Many medicines that are given to children are not licensed for the particular indication, age of the child, suitable formulation, or route of administration. However doctors are forced to use those medicines in children. If not possible effective treatment would be denied to children. This type of use of medicines in children (licensed medicines used outside the conditions of the license) is known as “off label use”. Rarely certain medicines that are given to children have not received a license for any indication – called “unlicensed use”.

**Unlicensed use:** The medicines administered to children, which have no license at all for human administration to be used as a medicine. It means that those medicines have not gone through the rigorous process of pre clinical & clinical trials and the registration procedures.

**Off label use:** The licensed medicines used outside the conditions of the license (e.g. if the license permits use of a medicine only by intravenous injection, giving the same medicine as an intramuscular injection). Similarly if a medicine is licensed to be used only in one indication, using the medicine for other indications also described as off label use.

A recent study of children in hospital in five European countries reported that over two thirds (67%) were receiving an unlicensed or 'off label' medicine preparation. Doctors are permitted to use unlicensed and off label medicines; however such uses should be justified. Monitoring for safety of medicines is very important in these instances. A study in paediatric wards showed that the ADRs occurred in association with 3.9 % of the licensed medicine prescriptions and 6 % of the unlicensed or off-label medicine prescriptions. Doctors caring for children should take adequate measures to prevent or minimize use of off label or unlicensed medicines.

## Appendix 4

### Format of a prescription

1. Prescription sheet with adequate space and columns.
2. Specific cages to fulfill all the requirements that were specified in this document.
3. Should be able recognize the prescriber Telephone umbers to contact
4. Tick box to indicate that specific instructions were given
5. Promote avoiding poly pharmacy
6. Feasible to audit

## Appendix 5

### Indicators for audit of rational prescription in children

AT INSTITUTION LEVEL compare with other institutions

- Overall use of drugs/ cost of drugs per 1000 OPD patients – antibiotics, vitamins, ...
- Overall use of drugs/ cost of drugs per 1000 in-ward hospital patient days
- Number of drugs per prescription– polypharmacy
- Percentage of prescription with antibiotics – over use of antibiotics
- Percentage of prescriptions with unnecessary use of drugs
- Number of prescriptions with drugs outside the ‘national list’
- Percentage of patients with IV drugs
- Percentage of prescriptions NOT in accordance with the national protocols – eg – antibiotics for watery diarrhoea, antibiotics for asthma, antiepileptics for febrile fits, meningitis treated by drugs outside the protocol
- Prescriptions NOT using the most economical option
- Percentage of prescriptions with trade names

### REPORTING INCIDENCE

- **Incidence of wrong prescriptions**
  1. Avoided at pharmacy/nurse
  2. Given, but no consequences
  3. Given, causing adverse effects
  4. Given, causing death
- **Incidence of wrong dispensing**
  1. Confusion due to wrong prescription
  2. No confusion at prescribing
  3. Led to litigations
  1. No consequences
  2. Caused adverse effects
  3. Caused death

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