Rational use of drugs in dermatology: A paradigm lost?

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What is Rational Therapy?
The World Health Organization (WHO) has defined rational use of drugs as: “Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.” This is also referred to, in brief, as the five ‘right’s, i.e., the right drug at the right dose by the right route at the right time for the right patient.

A major step towards rational use of medicines was taken in 1977 when the WHO established the 1st Model List of Essential Medicines to assist countries in formulating their own national lists. The present definition of rational use was agreed at an international conference in Kenya in 1985. In 1989, the International Network for the Rational Use of Drugs was formed to conduct multidisciplinary intervention research projects for promoting more rational use of medicines. A review of all published intervention studies with adequate study design was presented at the 1st International Conference for Improving the Use of Medicines in Thailand in 1997.

The opening remarks by the WHO on its “Rational Medicine Use” webpage summarizes the existing situation: “Irrational use of medicines is a major problem worldwide. WHO 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 (emphasis ours). The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards.” Such misuse of medicine and the resultant wastage has a skewed distribution in low-income countries, as evidenced by a much larger share of medicine spending in the total health expenditure in these countries compared to that in the high- and middle-income countries.

Irrational use of medicines is endemic in all countries. It occurs in every health care setting, hospitals, private clinics and homes. Medicines are prescribed when none are required; patients are treated with wrong medicines, or useless or unsafe medicines; medicines are used in incorrect dosage and duration; more medicines are prescribed than are necessary, often without regard to potentially serious drug interactions; and medicines are used incorrectly by patients. The quality of drug treatment is adversely impacted by these factors. In such a scenario, health care expenditure escalates, and the chances of adverse drug reactions and development of antimicrobial resistance increase.

At present, numerous critical problems faced by dermatologists in India and elsewhere, be it unresponsive dermatophytosis or disfiguring dermatoses and skin infections resulting from the misuse of modified Kligman’s triple combination creams in the eternal quest to turn fairer, can be directly ascribed to irrational drug use by dermatologists, other physicians and nonphysicians including patients. Thus, we found it highly appropriate to revisit the basic tenets of rational drug use, a paradigm that has, unfortunately, relegated very much to the background among physicians and health policy planners alike.

Sources of Irrationality in Prescriptions
The major forces leading to irrational prescribing habits can be categorized as those deriving from patients; prescribers; workplace; supply system, including industry influences, regulation, drug information and misinformation; and a combination of these factors.

Poor training and education: Ignorance of the prescriber
In this day and age, when the medicolegal costs of medical practice are mounting, such ignorance may prove catastrophic for individual practitioners. This is a disturbing and pervasive factor and is a matter of great concern. Prescribers must regularly update themselves by reading scientific publications. This would make the prescriber practice evidence-based dermatology rather than generalize the limited personal experience.

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Dermatologists prescribing potent steroid–antibacterial–antifungal topical combinations to treat superficial fungal infections or advising mometasone-containing modified Kligman’s regimen for application on women’s face for an extended duration are not rare examples. It is reported with reference to topical corticosteroids that peer pressure, rapid ‘feel good’ effect and ignorance about harmful effects lead to continuation of treatment beyond the prescribed duration. It is much easier to prescribe a systemic immunosuppressive than prescribe, educate and motivate a patient to use topical steroids in such a condition as localized or mild bullous pemphigoid, though there is good quality evidence to use the latter as first-line therapy in this scenario.10

In India, this problem is compounded by the fact that, literally, everyone can and do prescribe dermatological medications, particularly the topical applications. According to industry data, dermatologists’ prescriptions account for a minor proportion of sales of topical medications – other specialists (pediatricians, internists etc), general practitioners, over-the-counter sales, pharmacists and self-prescription account for the major percentage of procurement of these products. This adds another dimension to this problem.

Irrational beliefs: Costlier drugs are better/the more the number of drugs the better (polypharmacy)

“The more the merrier” is another common symptom of irrational prescribing habit. Polypharmacy is defined as the concomitant intake of five or more medications by the patient.11 WHO has recommended that the average number of drugs per prescription should not be more than two.12 Using multiple drugs may lead to adverse drug reactions, increase the risk of drug interactions, dispensing errors, decrease adherence to drug regimens and unnecessary drug expenses.

Too much reliance on pharma industry claim about efficacy of drugs

Many corporate entities resort to advertisements with misleading claims and other unethical promotional activities. This adversely affects the prescribing behavior of the physicians and misleads patients. Added to this is the aggressive and largely unregulated pharmaceutical marketing whereby the practitioners’ major resource for updating pharmacological knowledge is the industry rather than authoritative scientific literature.13

Commerically driven motive: Inducements

This is, perhaps, the most well-known among all the factors behind irrational prescribing habits, so much so that all other factors behind this phenomenon are frequently allotted significantly less space and time in any discussion on the subject. Industry largesse in the forms of expensive gifts and hospitality influences prescribing behavior and compromises our position as ethical and rational caregivers. Regulatory control on manufacturing practices, promotional activities by the industry and dispensing by pharmacists may play a major role in ensuring rational prescriptions. To have a meaningful effect, these three sectors have to be controlled simultaneously and equally well.

Succumbing to pressure from patients

Patients often come armed with the belief that there is “a pill for every ill.” Their demands and expectations often compel physicians to choose the easy path of medicine on demand rather than the tedious alternative of patient education, e.g., methotrexate in limited extent of psoriasis vulgaris; or oral antifungals for a long duration in elderly patients with onychomycosis instead of offering no treatment; or maintaining a vitiligo patient with several metabolic disorders on oral immunosuppressives rather than just topical medication. Misinformation about the drugs may sometimes lead to drug abuse such as chronic use of steroids as self-medication in many chronic illnesses.

Adverse workplace situation: Excessive pressure/nonavailability of medicines/investigation facility

Understaffed and overpopulated outpatient departments, drug shortage, inadequate laboratory backup and a limited inventory of drugs with unreliable supplies from which a choice must be made are some of the issues which most doctors from resource-poor settings, such as ours, grapple with on a daily basis.

Doctored clinical practice guidelines

The all-pervasive influence of the industry applies not just to the individual practitioner but may extend to the authors of clinical practice guidelines as well. Influencing the authors of these guidelines can have a substantial impact on drug use, as the information disseminated by way of these is transmitted many times over to the readers and can thereby influence the practice of a large number of physicians. A study on the extent to which the authors of guidelines interact with the pharmaceutical industry estimated that 87% of authors had some form of interaction with the pharmaceutical industry, 58% had received financial support to perform research, and 38% had served as employees or consultants for a pharmaceutical company.14

However, not only the industry, global guidelines can be doctored even by venerable institutions like the WHO for diverse considerations ranging from the political to scarcity of resource for allocation. A case in point is the current 1-year multidrug therapy regimen for leprosy that was given a global push by the WHO in the absence of any good and reliable evidence in its favor.15 No randomized controlled trial (RCT) has supported the reduction of treatment duration from 24 months to 12 months in multibacillary leprosy.16

Not only guidelines, the generation of primary evidence itself in the form of RCTs is under a cloud; the pharmaceutical industry’s influence on medical research having increased enormously in the last few decades. As indicated by the European Dermatoepidemiology Network (EDEN) psoriasis project, only a quarter of all RCTs published on psoriasis from 1977 to 2000 were conducted without direct sponsorship from pharmaceutical companies.17 This proportion has got only more dramatically skewed in favor of the industry from then on.18 Such statistics clearly points to risk of bias for a large chunk of evidence being generated nowadays and evokes scepticism about the very foundations of evidence-based medicine (EBM) and rational therapy.

The Impact of Irrational Drug Use

The impact of irrational drug use is not difficult to decipher. Reduction in the quality of drug therapy leads to inferior health outcomes in terms of morbidity and mortality, wastage of resources leading to reduced availability of necessary drugs, increased costs, increased risk of side effects and drug interactions, increased risk of transmission of diseases through unsafe injections when multiple injectables are used and the proliferation of antimicrobial drug resistance.19 There is also an adverse psychosocial impact of irrational prescribing by way of perpetuation of the notion that every symptom requires a medication.7 In one study of a single district in
India, a staggering 69.2% of the money spent on drugs in the private sector and 55.4% in the public sector was wasteful. Rs. 14.76 crore was wasted on irrational prescriptions in this district in a single year, i.e., 67.6% of the district’s total drug consumption.20

Criteria for Rational Choice of Medicines

1. Efficacy: This should be the principal selection criterion. Every practitioner should give priority to drugs of proven efficacy. Only those drugs for which adequate scientific data are available from controlled clinical trials and/or epidemiological studies and for which evidence of effectiveness in a variety of settings has been obtained should be prescribed. Newly released products should only be used if they have distinct advantages over the products currently in use. The chosen drug then should be used for the optimum duration by an appropriate route of administration.

2. Safety: From a list of drugs with similar efficacy, one must choose the safest drug. The needs of special populations, such as the infants and children or the elderly etc., must be kept in mind.

3. Suitability: Is the drug suitable for the individual patient we are treating? Is the patient pregnant or planning pregnancy? What if the patient is currently breast-feeding her baby? Is there any comorbidity, such as liver or kidney disease that may cause the drug to be unsafe at the usual dosage? Routinely ask the patient about the drugs (s) he is currently taking. Patients often do not volunteer this information unless specifically asked about. One major issue here is drug interaction that may reduce/dangerously increase the drug level.

4. Where two or more drugs appear to be similar, preferences should be given to drugs which have been most thoroughly investigated and those with the most favorable pharmacokinetic properties.

5. The cost of treatment, and especially the cost–benefit ratio of a drug or a dosage form, should be the major criterion for selection of a particular drug. It should be remembered that the cost of treatment includes the following parameters:
   i. Direct cost of the purchase of drug;
   ii. cost involved in the administration of drug;
   iii. cost involved in the monitoring of adverse effects (liver function test, renal function test, electrolyte level, ocular examination, etc.);
   iv. cost involved in the treatment of adverse drug reactions;
   v. cost of treatment failure; and,
   vi. expenses involved in visiting the hospital for administration of drug (with travel expenses loss of working hours should also be considered)21

6. Thousands of fixed ratio combinations are available in the market. Fixed-ratio combination products are only acceptable when the combination has a proven advantage over single compounds administered separately as per their therapeutic effect, safety, compliance or cost.

Evidence-based Medicine and Rational Drug Therapy

The principles of EBM are intricately related to the rational use of medicines. Choice of medicines for a particular disease condition should always be based on the available evidence about the efficacy and harm of a medicine or procedure. Though the two paradigms seem to converge at some points and diverge at others, in reality, it should be a continuum, rational therapy taking off where EBM ends. EBM promises to increase the reliability of interventions and improve patient outcomes. However, it is often at odds with unquantifiable patient experiences, values and preferences,22 and this is the crux of the epistemic problem of EBM as it attempts to apply a model of rationality that privileges quantifiable evidence in medical practice. This is where rational therapy may come to its rescue by protecting, on one hand, medical decision making from the dogmatic, the subjective and the arbitrary and, on the other, permitting qualitative patient experiences, values and preferences to play a legitimate role in rational diagnostic and therapeutic decision making. The paradigm of rational therapy, thus, bridges the two worlds of EBM and patient-centred medicine,23 a gap that seems unbridgeable to many.

Irrational Practice in Dermatology

In a study of its kind, therapeutic audit of dermatological prescriptions was carried out in the outpatient clinic of the Government Medical College Hospital, Nagpur. Among the 190 prescriptions audited, polypharmacy was found to be widely prevalent. Drug dosages were not mentioned in a majority of prescriptions. In four cases, patients were prescribed drugs without a diagnosis.24

Some examples of commonly encountered irrational dermatological practice

Prescribing retinoids without proper counselling

We have seen many examples of even reputed dermatologists prescribing retinoids without any mention in their prescriptions of the cautions and precautions regarding these drugs’ serious adverse effects, particularly their dreaded teratogenic effects.

Prescribing medicines without proper monitoring of their adverse effects

There exist standard monitoring guidelines for prescription of drugs such as methotrexate, azathioprine or retinoids. Yet, careless prescriptions without any monitoring are frighteningly common.

Ignoring the likelihood of potentially serious drug interactions

Prescriptions of isotretinoin together with tetracyclines (doxycycline or minocycline) for the treatment of acne is not uncommonly encountered. As both drugs can cause pseudotumor cerebri, concurrent administration increases the chance of this potentially serious adverse drug reaction. Potentially fatal drug interaction can occur if azathioprine is prescribed in its usual dosage in a patient who is on allopurinol therapy for hyperuricemia.

Biotin for hair loss

In recent times, pharma companies have marketed a plethora of preparations containing mega dose biotin, an essential B vitamin whose deficiency is extremely rare, claiming curative effect in hair loss. In publication databases, we have failed to locate a single publication documenting the efficacy of biotin in any kind of alopecia. Yet, it has become one of the most frequently prescribed medicines by Indian dermatologists for all types of hair loss.
Antioxidants/Supplements
Antioxidants are promoted for the treatment or prevention of a host of chronic diseases. Despite innumerable clinical trials involving millions of participants, no therapeutic efficacy for any disease has been found in their favor. To the contrary, there exists evidence of definite harm from their regular use. There is not a single dermatological condition for which there is any reliable evidence of efficacy of antioxidants, yet many dermatologists almost routinely prescribe these products for a wide variety of conditions.

Use of herbal medicines
The production of herbal medicines is highly commercialized in India. The consumers are bombarded on a daily basis in print media, television and the internet by advertisements claiming miracle cure of all sorts of ailments, and routine use of such products for self-care is extremely common. No mechanism exists in India for testing the safety and efficacy of these products. Unfortunately, many qualified dermatologists in India often include herbal medicines in their prescriptions. This cross-practice, apart from being plain illegal according to the law of the land, frequently entails unnecessary cost and often do harm to the patients. This practice should be condemned by professional associations.

Role of Consumers in Rational Therapy
The consumers are as essential a component in the dispensation of rational therapy as the prescribers. The patients take the all-important decisions of when to seek health care, from whom and whether to follow the prescriptions, influenced by the popular knowledge, attitude and perception regarding drug use. Thus, compliance or adherence to the treatment does not depend solely on the narrow confines of the physician-patient interaction, but several psychosocial factors beyond that. This is important to address as adherence, or the lack of it, is not only a major factor behind the development of antimicrobial resistance but also impinges upon the quality of life of the patients, affects their productivity and serves to increase health care expenditure.

Self-Medication
A major problem in many countries, such as ours, is that people can freely buy medicines over-the-counter that should be prescriptions-only. Self-medication with prescription drugs is a peculiar problem, particularly endemic in the developing countries like India, where pharmacies freely supply all kinds of medicines over-the-counter, as do informal drug shops and small groceries.

Dermatology practice in India is plagued by another additional impediment – here almost none of the topical medications, including superpotent topical steroids, are prescriptions-only products, inexplicably so. No wonder that topical steroid misuse, noticeably by patients themselves, has now attained the scale of almost a public health crisis of sorts. Such regulatory deficiencies add to the challenges of even a committed physician to practice EBM and rational therapy in a meaningful manner.

A study in the Philippines found that people keep copies of prescriptions for re-use. In India, reusing prescriptions ad nauseam belonging to a neighbour for a different clinical condition and who is of a different gender and age-group is a commonplace affair. Physician consultations are perceived to be expensive and repeated use of prescriptions is seen as a legitimate way to economize. Sometimes people even self-medicate with prescription drugs on the advice of traditional healers or quacks or the friendly neighbourhood shopkeeper. People keep stocks of leftover medicines in their homes, and re-use them or give them to neighbours or relatives who request them. This is considered to be a particularly desirable benevolent activity. These practices also occur in countries where dispensing of medicines is regulated more strictly, but, naturally, less often. Internet has expanded the horizon in self-medication practices by opening the option of buying medicines, available only on prescription in one country, which can now be obtained by post from a country where regulation is less strict. Immigration and increased mobility mean that more people buy medicines where it is easy to obtain them or obtain them through family and friends.

What is to be Done?

- Always keep yourself thoroughly updated about the efficacy and safety of drugs from credible sources such as journals, reference books, treatment guidelines, drug formularies, drug bulletins, web references, drug information bulletins, and scientific sessions
- The “P” drug concept: WHO has introduced the P or personal drug concept which is very useful in easily selecting and prescribing the appropriate lines of therapy of most clinical conditions. P-drugs are drugs you have chosen to prescribe regularly, and with which you have become familiar. They are your priority choice for given indications. For example, in pemphigus vulgaris, azathioprine and mycophenolate mofetil have similar clinical response rates. Yet, one dermatologist may prefer azathioprine and the other may prefer mycophenolate mofetil. Both are equally rational in making their choice. They only have different P-drugs in the form of azathioprine and mycophenolate mofetil, respectively
- The concept of P-drugs is rooted in the observation that most physicians use only 40 to 60 drugs routinely. One must develop a personal inventory of drugs (such as antibiotics) which practitioners should be thoroughly acquainted with. P-drugs will differ from country to country, and between doctors, because of varying availability and cost of drugs, different national formularies and essential drugs lists, medical culture and individual interpretation of information. However, the principle is universally valid. There is the allied concept of P-treatment. It has to be remembered that both are not the same. The key point is that not all diseases need to be treated with a drug. Not every P-treatment includes a P-drug.
- Always be sceptical about pharma industry claims regarding their products, particularly the newly introduced drugs. Evaluate the claims from creditable sources. Pharma company brochures often cite references to support their claims, but more often than not these sources are irrelevant, unscientific and from in-house publications or dubious journals. Base your own judgement on high-quality studies published in reputed peer-reviewed journals. In the internet era, it is not very difficult to look for and find evidence, or the lack of it, from online resources
- Role of regulatory authorities: Thousands of irrational and inefficacious single drugs or drug combinations are marketed and widely available in the Indian drug stores. Unfortunately, the drug control authorities in India are too lenient in permitting entry of formulations without evaluating the necessity or rationality of the formulations.
Moreover, there is no centralized agency for maintenance of uniform standards of drugs. Every state has its own controlling authority, and it has been seen in the past that drugs banned in a state easily get permission to market from the drug control authority of another state. The requirement is of a more stringent, unified and centralized control authority that allows marketing of only those drugs/combination that have documented efficacy.

**Conclusion**

We consider adhering to policies of rational therapy practices on the part of every dermatologist to be the need of the hour. This is even more relevant today in view of the misuse of topical steroids and the phenomenon of antimicrobial resistance that includes in its ambit unresponsive dermatophyte infections, issues that have taken the shape of public health disasters in this country. Confronting the regulatory authorities, approaching the judiciary, the executive and the administration for all the loopholes in the health and pharmaceutical sectors that make self-medication, availability of irrational drug combinations and misuse of medications in general so easy, is a must, but not enough. As we know so well, the outcome in these forums is not under our control. Inculcating rational drug practices in our therapeutic interactions is one way we can become the change we want to see in the prevailing environment. It is easier said than done, however. We can hope for no systemic support in our endeavour. Rational therapy, that was the WHO’s baby in its Alma Ata years, has all but abandoned by WHO itself. But it remains a powerful paradigm, waiting for us to reclaim and put to good use for mitigating many of the inconsistencies that have crept in our way of managing patients and diseases.

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