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Perspective

Rational use of medicines: Cost consideration & way forward

Rational use of medicines involves their correct/ proper/appropriate use so that their selection, dose, duration are according to the guidelines, suitable for clinical needs, at the lowest cost to the provider, community and the patient, and are dispensed correctly and taken properly[1]. The right drug of right quality, safety and effectiveness should be available, affordable and marketed correctly and the infrastructure should be appropriate for the individual and the community. Complementary terms such as responsible use of medicines, prescribing efficiently have also been used by some instead of 'rational use'. If the use of medicine is not as per these conditions, it is considered as irrational or incorrect, improper and inappropriate use[2]. It is estimated that the use of half of the medicines is improper in prescription, dispensing, selling or administration and not as per guidelines in 30-40 per cent patients from private or public sector[2].

The common types of irrational use include failure to prescribe, dispense, and use medicines as per guidelines, use too many medicines, inappropriate use of antibacterials, overuse where not required, underuse where required, inadequate use for chronic diseases, overuse of injections, self-medication and use of expensive low-efficacy, low safety drugs. Irrational use results in morbidity, mortality, adverse drugs reactions (ADRs), poor outcome of cure, control, prevention of disease, antimicrobial resistance and financial loss. Irrational use has resulted in chloroquine-resistant falciparum malaria in 90 per cent countries, 2-40 per cent primary drug-resistant tuberculosis, 10-90 per cent ampicillin sulphamethoxazole / trimethoprim-resistant shigellosis[3]. This has led to the use of expensive second-line drugs. Antimicrobial resistance is estimated to cost US$ 4000-5000 million annually in the USA[2]. Adverse medicines events are estimated to cost £466 million annually in the UK and up to US$ 5.6 million per hospital per year in the USA[2]. Half of the ADRs are preventable with rational use[2].

Non-communicable diseases (NCDs) are on the rise, 80 per cent of its burden can be reduced by appropriate use of medicines[4]. In a study from India, 69.2 per cent of money spent on medicines in private sector and 55.2 per cent in public sector was found to be wasteful[5].

Irrational prescribing of drugs is a malady of excess and lack of access specially in rural India. Prescribers are undertrained, uninformed and overworked. Clinical guidelines and unbiased information on drugs are not available easily. Medicines and appropriate formulations are not available, not affordable, and quality and storage may not be as per standards[6]. Pharma industry also influences directly and indirectly prescribing practices[7]. In the US per physician US$ 61000 are spent on promotion[7]. Medicine shortages are faced, specially of low-cost generics, due to non-availability of raw material, law enforcement halting production, voluntary recall, poor inventory ordering and supply chain, fewer companies making old and less profitable drugs. There is a lack of advanced warning/ information about shortage, there is trouble in finding alternatives and hence risk of adverse patient outcome[8].

It has been shown that policies and interventions such as a multidisciplinary national body, local drug and therapeutics committees developing clinical guidelines and essential medicines list, independent medicines information, problem-based training to students, continuing education as part of professional licensure requirement, sufficient budget for medicines and staff, streamlined procurement, storage, dispensing, public education, appropriate enforced regulations and avoidance of perverse incentives, marketing and profiteering by industry, improve rational use indicators[9]. The rising costs of medicines, increase in NCD, ageing population with a need for preventive and chronic care have resulted in increasing urgency to improve prescribing efficiency. More specifically,

supply-side reforms such as compulsory price cuts, measures to lower generics prices, reference pricing in a class and delisting cost-ineffective drugs and demand side reforms such as academic detailing, prescribing guidance with electronic prescribing support system, prescribing targets, financial incentives to enhance substitution and to generic drugs can improve prescribing efficiency[10].

The government has taken initiatives such as centralized procurement (as in Delhi, Rajasthan and Tamil Nadu States in India), strengthening drug and food regulatory system with new drug testing laboratories in States to assure quality of medicines, drug price control of essential medicines and use of generics (costs half to one tenth of branded drugs) to ensure access to quality medicine. In the US, the use of generics saved US$ 217 billion in 2012[10], cost of generic drugs decreased during 2003-2009 period, while of branded drugs, it increased by 6-7.9 per cent[11].

There has been an increase in the availability of information on the internet and mobile phones, electronic medical records, social media and predictive analyses are being used to understand patient behaviour. There is an increase in insurance by the government and private companies. To avoid misuse, overuse, self-medication, prescription-only drugs are to be dispensed only on prescription by the qualified medical doctors. However, in remote areas, public health programmes are implemented by caregivers, paramedics, health workers and practitioners of alternative systems of medicines, who are not authorized to prescribe modern medicines. Drugs are expected to be used for approved indications. However, in reality drugs, for example, for children are used off label. Ranibizumab registered for neovascular age-related macular degeneration and diabetic macular oedema, costs US$ 2033 per dose. Bevacizumab by the same company costs 1/20th of the ranibizumab, is not registered, but used for the same indication off label[12].

Standard treatment guidelines should be unbiased and evidence-based. However, getting evidence is expensive and may not be unbiased. In one study, 58 per cent of authors of standard treatment guidelines were found to have received funding from pharmaceutical industry[13]. Generic drugs cost less; however, companies with patents, after expiry of patent, try to buy out generic companies to block competition. Insurance companies switch up to 70 per cent of drugs to cut costs. However, switched drug may not be identical and can cause adverse reactions, poor recovery rates and relapses[14].

Longer patent period is allowed by the government to encourage the development of antimicrobials. However, this causes increase in cost.

Thus, there is a conflict between private gain and freedom, and societal need and social costs.

Way forward

Clinical guidelines for rational use of medicines should be developed for each level of care, for paramedical staff in primary healthcare clinics, doctors and specialist in the referral hospitals, based on prevalent clinical conditions, training and skills of available prescribers[15]. Information on effectiveness, social acceptability, user satisfaction, safety and costs should be taken into consideration as has been done for standard treatment guidelines (STG) for bronchial asthma[16]. Pharmacoepidemiology, drug utilization, economic analysis research and Pharmacovigilance Programme of India should be encouraged. This will provide evidence-based reliable relevant inputs for therapeutic guidelines, preventing ADRs, developing educational programmes, media campaigns for healthcare providers and society, and for assessment of safety, efficacy and need for new drugs by the Central Drug Standard Control Organization.

Pharmaceutical companies should be required to submit pharmacoeconomic data to rationalize cost of new drugs. Low cost, effective, evidence-based treatment schedules such as metronomic scheduling using low oral doses of methotrexate + celecoxib for head and neck cancer[17], and single dose regimen of liposomal amphotericin with better patient compliance for treating leishmaniasis are required[18].

Standards for quality of medicines specially for biosimilars need to be decided, and development of generics should be seen from public health perspective. Bioavailability studies are done to verify if generic drugs are bioequivalent to innovators with similar drug level profile. However, for liposomal and other targeted drug delivery system where drugs are similar but not same, specific preclinical, clinical studies may be required besides physiochemical standards[19].

Conclusion

In conclusion, short- and long-term strategies need to be formulated. Despite government policies to reduce cost and develop national guidelines, conflicts, contradictions and dilemmas remain. There is non-availability of doctors in remote areas causing

irrational use of drugs by unauthorized health practitioners; drugs are used off-label due to lack of data and formulation. Commercial interests hamper the use of generic drugs. Insurance companies' policy to substitute alternative to reduce cost affects quality of care and conflict between private gain and freedom and societal need affects reduction in cost. Learning from past experience in different countries, the way forward is to develop evidence-based simple STGs and algorithms for different healthcare levels (primary, secondary and tertiary) and healthcare professionals (health workers, general practitioners and specialists) for common conditions and emergencies. The STG and algorithms should be publicized, promoted and easily available through the internet, mobile applications and printed version. It would be useful to develop patient information pamphlets for educating patients and society about rational use of medicines.

Drug utilization, pharmacovigilance, pharmacoepidemiology and pharmacoeconomic studies should be carried out to provide reliable relevant information and feedback to revise the guidelines and package inserts and policies. At present, product package insert is for the physicians. There is a need to make patient-oriented package insert. Collaborative research on low-cost treatment, standards for generics, biosimilars and drug delivery systems, appropriate price control, innovative interventions and strategies to reduce irrational use would be additional long-term activities that will promote rational use of drugs and reduce their cost.

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