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Perspective

ICMR National Virtual Centre for Clinical Pharmacology with Network of Rational Use of Medicines & Product Development Centres

Background

Clinical Pharmacology involves the development of new drugs; their application as therapeutic agents, and study of adverse effects in individuals and society[1]. The Indian Council of Medical Research (ICMR) has supported the development of clinical pharmacology in India over the last 50 yr through its extramural and intramural programmes by way of training programmes for capacity building and advanced research activities[2-5]. The training programmes also imparted training to the participants from other countries. The Centres of Advanced Research (CAR) were set up in Mumbai, Chandigarh, Puducherry and Hyderabad for research on pharmacokinetics, therapeutic drug monitoring (TDM), pharmacovigilance, clinical trials, pharmacodynamics, pharmacogenetics, traditional medicines, relevant to public health, development of national policies, drug development and education, attracting grants from agencies such as WHO[6].

In 2010, a brain storming session recommended creation of an Institute of Clinical Pharmacology, with public health orientation for safe, effective and economic products and rational use of medicines for Indian population[3]. However, it could not be started due to paucity of funds. The need for an institute was again reiterated in a review of clinical pharmacology research in India[7] for developing products for Indian population and rational use of medicines. Furthermore, it was noted that drug development in academia and Government funded institutions is hampered by inadequate trained manpower, lack of interaction between industry and academia/public research institutions[8,9], and between basic sciences and clinical researchers. In view of above and current scientific developments and to further strengthen clinical pharmacology towards healthcare needs of the country, the National virtual Centre for Clinical Pharmacology (NvCCP) with a network of Product Development Centres (PDCs) to promote drug development in line with the New Drugs and Clinical Trials Rules 2019 notified on 19 March, 2019[10] and Rational Use of Medicines Centres (RUMCs) for cost-effective use, with a Technical Advisory Group (TAG) (deemed virtual centre) of experts from different disciplines for guidance and monitoring progress of these activities was set up in 2019.

Product Development Centres (PDCs)

The envisaged objectives and output of the PDCs were as follows: (*i*) to evaluate (20/yr) completed research projects, for suitability to develop products for human use; (*ii*) recommend suitable products for further validation, studies for investigational new drug (IND) and to develop IND application; (*iii*) carry out Phase I, II, and III clinical trials (two/year); (*iv*) carry out studies for evidence/provide evidence based recommendations for safe and effective use of marketed products using TDM, biomarkers and genetic tests; and (two/year); (*v*) carry out studies for evidence/provide evidence-based recommendation for standard treatment guidelines for public health/Government programmes (two/year). The primary impact will be the development of national asset for conducting clinical trials, publications, training, capacity building, development of guidelines for minimum/optimum requirements for conducting clinical trials, standard operating procedures (SOPs) for clinical trial related activities. Data from clinical trials of marketed drugs will provide evidence base for policies, practice, cost-saving strategies and evaluated recommended projects/products, if successful, will lead to safe and effective products. Eleven institutions and investigators were identified for PDCs, based on their prior work, initiatives taken, publications, departmental infrastructure, faculty that could contribute, availability of collaborating institutes,

previous grants received and were approved in 2019. There were four PDCs in Mumbai, Maharashtra, two in Telangana, and one each in Chandigarh, New Delhi, Lucknow, Kolkata and Patna.

During the first year, these PDCs evaluated completed research projects funded by ICMR and shortlisted five projects for further development. Guidelines for infrastructure and facilities and SOPs required for Phase I studies were prepared. The PDCs also conducted studies for population pharmacokinetics of hydroxychloroquine (HCQ) in healthcare workers and COVID vaccine trials.

Rational use of medicines centres (RUMCs)

Widespread overuse, inappropriate selection of antimicrobials and high level of polypharmacy[11] leading to adverse drug reactions (ADR), antimicrobial resistance, lack of effect, increasing cost to patient and society have been noted[12-16]. Globally, half of the medicines use has been found to be inappropriate[17]. In UK, 7-10 per cent of prescriptions of newly graduated doctors were found to contain errors[18,19]. Inadequate education, ineffective, insufficient regulation around appropriate medication use were found to be the important reasons[11]. Hence, prescribing competency for medical graduates was included in the curriculum[20]. In view of this, in 2019, the ICMR set up a network of RUMCs (rational use of medicine centres) in the departments of Pharmacology of various teaching medical institutions located in different parts of the country with the following envisaged objectives and output: (*i*) Prescription audit/research, evaluate, analyze, interpret, for WHO indicators, inappropriateness, use of irrational fixed-dose drug combinations (FDCs), non-national list of essential medicines (NLEMs), identify gaps and errors, (for 1000 prescriptions per year), contribute to national database, recommend corrective steps; (*ii*) develop online training course for prescribing skills (PSC) (for interns, Government medical officers, private general practitioners); (*iii*) based on the Medical Council of India (MCI) curriculum, university curriculum, with prioritization based on published literature, experience, develop curriculum (for 2 modules, review two modules developed by other centre); (*iv*) develop training modules for the course based on standard treatment guidelines, standard treatment workflows and other resources, (for 2 modules, review 2 modules developed by other centre); (*v*) develop assessment questions, validate for two modules, review two modules developed by the other centre. The envisaged impact of these centres was as follows: the online PSC made available to all interns, practitioners in the country. Pre-test and post-test assignments will add to the training experience and assess change in knowledge. Prescription research will evaluate approximately 10,000 prescriptions. Data of all centres will be aggregated and published and will also be used in revising the content of the online course and provide inputs for NLEM revisions.

Fifteen non-ICMR institutions and investigators were identified based on their prior work, initiatives taken, publications, departmental infrastructure, faculty that could contribute, link with collaborating institutes, and previous grant received. Five RUMCs were also set up at the ICMR institutes. These centres were approved in 2019 and set up in the same. There were two centres each in Kolkata, Ludhiana and New Delhi, and one each in Mumbai, Puducherry, Ahmedabad, Chandigarh, Patna, Bhopal, Vadodra, Vellore and Bangaluru. The six centres in ICMR Institutes were at National Institute for Research in Reproductive and Child Health (NIRRCH) and National Institute of Immunohematology (NIIH), Mumbai, National Institute of Cholera and Enteric Diseases (NICED), Kolkata, National Institute for Research in Tuberculosis (NIRT), Chennai and The Rajendra Memorial Research Institute of Medical Sciences (RMRIMS), Patna, National institute of Epidemiology (NIE), Chennai.

During the first year, RUMCs constituted RUMC committees of clinicians from clinical departments and community medicine, and developed curriculum, training modules and assessment questions for prescribing skill course (PSC). The online course for PSC was launched in September 2020 by the Director General, ICMR, with the ICMR-National Institute of Epidemiology through Government of India SWAYAM portal. Approximately 5000 prescriptions were captured by the RUMCs and analyzed. Safety and efficacy of hydroxychloroquine for prophylaxis against COVID-19 in healthcare workers was also studied.

Way forward

This initiative of the ICMR has a vision to create a national platform to promote new therapeutic products as an outcome of research from Indian institutions, to create competency for rational use of medicines and has a goal of providing cost-effective

healthcare. The research activities are undertaken under a virtual center with network of various centres, funded for five years. Subsequently, there will be a need to establish a permanent centre with physical infrastructure that will enable a robust mechanism for catering to the research on different aspect of product development and other areas of clinical pharmacology with translational potential for the benefit of the Indian population.

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