Overcoming challenges in research and development of rare eye diseases

Rare diseases are rare, as the name suggests, but their overall burden is high. There are as many as 7000 rare diseases and 300 million people with rare diseases worldwide. Seventy-two percent of these diseases are genetic and 70% of them start in childhood. Rare eye diseases (REDs) are the leading cause of visual impairment and blindness in children and young adults in Europe. This heterogeneous group of conditions includes over 900 eye disorders ranging from relatively prevalent disorders, such as retinitis pigmentosa, to very rare entities, such as developmental eye anomalies.[1]

The disorders are complex because their landscape is constantly changing, as new conditions are being identified and reported regularly in medical literature.[2] Apart from a few diseases, where significant progress has been made, the field of research and development of RED is still at a nascent stage, and steps need to be taken to overcome the challenges. A fundamental challenge is that relatively little is known about the pathophysiology or the natural history of these diseases as the pool is very small, and it often results in inadequate clinical experience. Therefore, the clinical explanation may be skewed or partial. The challenge becomes even greater when these diseases are chronic in nature, where long-term follow-up is particularly important. As a result, published data on long-term treatment outcomes are often incompletely characterized.

This makes it necessary to collaborate with international and regional organizations for research, with the physicians who work on any rare eye disease and with patient groups and families dealing with the consequences of these disorders. This will help us gain a better understanding of the pathophysiology of these diseases, and the therapeutic effects that would have a meaningful impact on the lives of patients. The registries of rare diseases represent an important approach for gathering epidemiological information and relevant samples for clinical research while being essential for feasibility studies, especially for enrolment in clinical trials and the establishment of treatment protocols.[3] A hospital-based national registry for rare eye diseases is needed. This registry can be a guide to future research. There is also a need to review and, where possible, modify clinical trial norms, keeping in mind the challenges, without compromising on the safety and quality of the drugs or diagnostic tools.

Availability and access to medicines are important to reduce morbidity associated with rare eye diseases. Despite progress in recent years, effective or safe treatment is not available for most of these diseases. Hence, even when a correct diagnosis is made, there may not be an available therapy to treat them. Of all of the rare diseases, less than 5% have therapies available to treat them. About 95% of rare diseases have no approved treatment, and less than 1 in 10 patients receive disease-specific treatment. Where drugs are available, they are prohibitively expensive.

As the number of persons suffering from individual rare diseases is small, they do not constitute a significant market for drug manufacturers to develop and bring drugs for them to the market. For this reason, rare diseases are also called "orphan diseases" and medicines that are used to treat them are generally referred to as "orphan drugs".[4] Where drugs are available, the prices are extremely high, apparently to recover the cost of research and development. The process from the discovery of a new molecule to its marketing is long (ten years on average), expensive (several tens of millions of euros, pounds, etc.) and very uncertain (out of ten molecules tested, only one may have a therapeutic effect). Developing a drug intended to treat a rare disease does not allow the recovery of the capital invested for its research. At present, very few pharmaceutical companies are manufacturing such drugs globally.

Countries have dealt with this unique problem of high cost through various means that were suited to their local needs. Instruments like the Orphan Drug Act (ODA) in the United States of America (USA) and Canada, provide incentives to drug manufacturers to encourage them to manufacture drugs for rare diseases. The ODA was first signed into law in 1983 in USA. The incentives include tax breaks and seven years of market exclusivity to recover the cost incurred in research and development. These acts are needed in other countries too. The economic incentives and safeguards offered under the Act ensure benefits to local patients. However, the exorbitant prices of drugs for REDs have led to concerns even in developed countries about maintaining sustainability of funding or reimbursement programs.

The process of repurposing drugs for new indications, compared with the development of novel orphan drugs, is another time-saving and cost-efficient method resulting in higher success rates, which can therefore drastically reduce the risk of drug development for rare diseases. Although drug repurposing is not novel, new strategies have been developed in recent years to do it in a systematic and rational way.[5] In such a case, the drug is not new but this new indication for the orphan disease may be "Orphan". Discovery of biosimilars also is an effective way of decreasing the prohibitive costs of treatment.

The creation of an integrated research pipeline is needed to start the development of new drugs, for which pharmaceutical companies would be encouraged and research organizations as well as funding agencies would be involved in this important endeavor.

Promotion of local development and manufacture of drugs for rare eye diseases by public and private sector pharmaceutical companies at affordable prices, and taking legal or legislative measures for creating conducive environment for indigenous manufacturing of drugs at affordable prices are recommended.

Prevention is always better than the cure, and hence, we need to take steps to create awareness amongst all levels of health care personnel as well as the public. This will encourage people to seek pre-marital genetic counselling, identification of high-risk couples and families, and also result in prevention of births as well as early detection of rare eye diseases. Simple standard protocols/algorithms would be developed for screening and diagnosis to avoid missing cases and provide the best possible management.

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About the author

Dr. Mohita Sharma, MS

Dr. Mohita Sharma is the founder and Chairperson of Tirupati Eye Centre, an iconic eye institute in Noida for the past 22 years. She is working there as a senior eye consultant specializing in phacorefractive surgery. She has done extensive work on premium intraocular lenses and presbylasik surgery. She is also the Founder Secretary of Women Ophthalmologists Worldwide network (WOW) and Women Ophthalmologists Society (WOS) in India which is a conglomeration of more than 2500 women ophthalmologists. WOS has a Women in Research (WINR) arm which promotes research in ophthalmology and involves several women as well as men ophthalmologists from across the country. This research arm also has a Rare Eye Diseases (RED) group which is carrying out work across the country on selected rare eye diseases to create ophthalmic registries. Dr. Sharma is involved in global clinical trials and research and has been an invited speaker for more than 400 national and international conferences. This RED special issue of IJO is dedicated to the selfless, sincere and collective efforts, and synergy of energies by the members of WOS and WINR, so ably led from the front and inspired by Dr. Sharma.