Editorial

Fixed dose combinations in diabetes: Indian innovation, Indian pride

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Introduction

Today, when we read diabetes guidelines recommending early use of combination therapy, we tend to forget that Indian diabetologists have been using this form of treatment for over 40 years. Today, when the pharmaceutical industry celebrates the approval, by the Food and Drug Administration (FDA), of a fixed dose combination (FDC) for diabetes, we do not realize that these combinations were the norm in India nearly half a century ago.

Fixed Dose Combinations of Indian Origin

One specific endocrine field in which Indian contribution has not been highlighted is that of FDCs. The first FDC approved in the USA was Glucovance (glibenclamide + metformin) in 1999.[1] Readers of IJEM may not realize, however, that most Ayurvedic preparations are, by definition, FDCs. The FDC preparation Chlorformin (phenformin 25 mg + chlorpropamide 50 mg) was launched by Cadila (now Zydus group) in the early 1970s, and was a popular drug. Experienced physicians swear by its efficacy and sustainability of action over decades, with a minimal rate of secondary failure. Although this economical drug (price 15 paise per tablet) was discontinued, in spite of protests from the Indian medical intelligentsia, because of safety concerns, other FDCs were developed by the Indian pharmaceutical industry. Glucored (glibenclamide + metformin) and Glynase MF (glipizide + metformin) from Sun and USV were the trail blazers, and had helped hundreds of thousands of patients by the time FDCs were accepted in the west.

It is understandable that our younger readers go through recent papers extolling the rationale and virtues of FDCs and get the feel that these are a Western innovation. What factors have led to this school of thought? And, should IJEM set the record straight?

History of Medical Innovation

The development of medicine has taken multiple paths. Early physicians probably learnt their science by observation, trial and error. Tribal medicine men, for example, would have noted a specific beneficial or deleterious effect caused by eating certain plants, animals or their parts, either in animals or in humans. This observation then translated into use of these products, in a processed or semi-processed form, as medication. Acute observational skills and acumen would mean a larger, more versatile knowledge pool of potential medicines, which would lead to greater success as a physician.

As civilization progressed and languages began to be written, this knowledge was transferred to paper. The early physicians, whether Indian, Chinese, Greek or Egyptian, were able to record their observations related to pathology, clinical features, diagnosis and therapy for future generations.[2]

It is during this age that many medical innovations arose in India. The volumes written by Charaka and Sushruta are full of original observations, discoveries, inventions and innovation. For example, Charaka clearly describes the different types of diabetes, suggests nutritional and pharmacological therapy, identifies goitre and expands

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upon the sciences of aphrodasiacs and anti-ageing.[3] It is another matter that we often tend to ignore or brush aside these precious pearls of knowledge.

The eighteenth century brought about a Renaissance in Europe, which was limited not only to the arts but also spread to science, specifically to medicine. Interest began to grow in medical research and publications began appearing on topics ranging from anatomy and physiology to epidemiology and therapeutics. Animal dissection (or vivisection) and human cadaveric dissection were allowed, and by using these tools, physicians began to expand the frontiers of medical knowledge.

India, however, took the opposite path. While the west awakened from a prolonged slumber, Indian science went into hibernation (or rather, aestivation). Whatever foundation of objective observation, reasoning, judgment and action had been laid down by our physician forefathers was forgotten. Dogma and rigidity replaced science and innovation, and virtually no contribution was made by Indians to the growth of modern medicine. It took an Englishman, Sir Ronald Ross, to discover the cause of malaria[4] that was rampant in Asia and Africa, not in his home country. It was another European who discovered the etiology of leprosy, and yet another who learnt the secrets of kala-azar.

Gradually, however, as modern medical colleges were established in India, we began to improvise, innovate and invent new techniques and therapeutic modalities. Many of these, however, were limited to the place of origin, as Indian doctors struggled to find a footing in the west-dominated medical publishing industry. During this time, the concept of evidence-based medicine began to replace experience-based medicine, which we were familiar with. Randomized controlled trials began to be considered the gold standard of medical research,[5] replacing observational trials and case series, with which we had more experience.

Even when Indian research was published, it was usually in print media whose circulation was limited to domestic consumption. Even this was a challenging task for the pioneering editors, who often faced economic challenges beyond the comprehension of today's generation.[6] The Worldwide Web was not available, and circulating our journals globally was an impossible dream. Because of all these and other socio–politico–economic factors, Indian medical experience was not able to have the global impact that it deserved.

Perhaps because of the lack of digital imprint or internet at that time, or because of socio–politico–economic constraints, Indian innovations in the field of diabetes did not have the global impact that they deserved. Perhaps methodological limitations prevented these innovators from highlighting their pathbreaking work. Most probably, however, it was a combination of humility ("have I really done something that great?") and overwork ("I can either sit down to write a paper or see the hundred patients lined outside my chamber") that prevented them from publishing their data.

These factors have contributed to the lack of awareness of this fact: anti-diabetic FDCs are, to the best of our knowledge, an Indian innovation, of which we can be justifiably proud.

There are many such practices and experiences that we should share with the rest of the world. IJEM invites contributions from its readers to be published as Letters to Editor or as Brief Communications, which put on record such innovations, inventions and improvisations. In this way, IJEM will serve as a medium for best-practice sharing and help strengthen its global readership in its fight against disease. With such "affirmative action," IJEM hopes to provide means of information sharing for readers who may not have the time to write full reviews or articles. It also hopes to be able to record, in both digital and print format, the vast wealth of clinical experience and knowledge that our senior colleagues from across the world have to share with us. The editors also hope to stimulate a debate on these and other, often controversial, issues related to endocrinology, providing a two-way communication channel for readers. Its open-access model, promising both free publication and free download, will continue to make latest advances in endocrinology and metabolism accessible to all.

The IJEM is confident that this will be an enriching experience for global, not just Indian, endocrinology.

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