Title - Violating the basic tenets of care – looking back on years of Evidence Based Medicine

Abstract - Evidence-Based Medicine (EBM) came into fashion nearly three decades ago. However, over this short period, this system of medical philosophy has come to dominate the medical practice worldwide. Never in the history of medicine could a single way of medical practice could dominate the healthcare systems of diverse countries like EBM did, that too within such short time span. But, it is high time we should ponder over the pros and cons of EBM and if this way of medical practice is to be allowed to continue, we should consider integration of additional inputs from the traditional ways of medicine.

Main Article - Nearly three decades have elapsed since the Evidence-Based Medicine Working Group came up with the basic concepts and premises of Evidence-Based Medicine (EBM) (1).

To provide some kind of philosophical background for the move towards EBM from the traditional authoritative medical practice, the Working Group had used Thomas Kuhn’s (2) concepts of the scientific revolution and his phrase ‘paradigm shift’.

While numerous scholars have argued that Kuhn’s concepts of scientific revolution and paradigm shift are for the physical sciences only and should not be used to interpret the progress of medical sciences, I, personally, find the Working Group’s use of those terms justified. However, though the Working Group tried to explain that the revolution, and the accompanying shift in paradigm, had occurred in the medical science itself through the popularity of randomized controlled trials (RCT), I think that the true paradigm shift had occurred in the economics of medical research and healthcare that demanded a shift of medical thought process from traditional way of caring for patients to EBM.

At a risk of oversimplification, Thomas Kuhn’s concepts can be summarized as follows : the progress of science is not a slow gradual one, but occurs in sudden jumps i.e. scientific revolutions. At any given period, under the prevailing paradigm of ‘normal science’, all

scientific activities are used to solve puzzles arising out of the existing scientific paradigm - until some scientific revolution comes to replace the existing paradigm. However, today’s revolution becomes tomorrow’s orthodoxy – normal science – and the regular scientific activities under the new paradigm try to solve new puzzles within this new paradigm.

Over the past few decades, a kind of revolution occurred in the methodology of medical research – particularly in the aspects of how it is done, why it is done, where it is done and most importantly, how such research activities are funded. In this new paradigm of corporate profit-driven enterprise of medical research, EBM has come up as the most effective and efficient puzzle-solver.

Another one of Kuhn’s key concepts – the concept of ‘incommensurability’ (2) between the pre- and post-revolutionary scientific paradigms, a concept first propounded by Paul Feyerabend (3) – is also applicable here. Kuhn noted, proponents of the competing paradigms fail to make contact with others views as there is seldom any continuity between the two very different paradigms - the pre- and post-revolutionary scientific ideas are incommensurable to each other. To put this theory in the context of medicine, medical research – and the way evidence are generated from such activities – at its present avatar, is barely explainable from the traditional medical value system, since two systems belong to very different paradigms.

In this era of financial profit-driven medical research, instead of finding effective cure for existing life-threatening diseases, a major part of research activities is spent on finding out illnesses to develop and promote the newer expensive drugs – a concept barely understandable from traditional medicine’s point of view - so much so that we must appreciate the foresight of Ivan Illich (4) : “The medical establishment has become a major threat to health”. Even when the life-threatening diseases are addressed, focus is on the chronic treatment – instead of finding a cure – because, that is where the money is. When those new drugs comes into market, they get their approval without any "evidence" of proper benefit - at least not the way benefit was defined by the previous generation of medicine. For example, analysis of new cancer medicines approved by the European Medicines Agency between the year 2009 and 2013 revealed that most anti-cancer drugs approved within that time span got their approval without evidence of benefit on survival or improvement in quality of life. And when the results of those medicines were followed up over some three or four years after coming into market, their benefits were still doubtful. (5) Without the dogma of EBM, such research activities could hardly succeed. And drug companies, particularly in oncology, are trying hard to find newer and novel endpoints for their clinical trials - endpoints which might earn them a quick approval, but hardly relevant in clinical settings.

Coming back to EBM, exactly what kind of evidence are we talking about? As we all know, there is a hierarchy of evidence, as per EBM guidelines. Mechanistic reasoning e.g. pathophysiologic rationale is not encouraged by EBM. But, when the newer technologies are readily incorporated in routine practice and RCT protocols – without sufficient evidence in favour of it – should not that count as mechanistic reasoning? Afterwards, use of newer technology becomes commonplace and such use gets almost post facto validity. Every new drug is compared to placebo only. Particularly in the arena of oncology medicines, the scenario has deteriorated to such low levels that the USFDA had to come forward with a detailed guideline for the drug industry to systematize and restrict the use of placebos in the cancer drug development trials. (6)

In the rare occurrences when they are compared to an existing effective therapy, the design of the clinical trial is invariably a ‘non-inferiority’ one. Results from RCTs with positive findings are published with much advertising, whereas the trials with negative results are rarely published. Even, the results of ‘non-inferiority’-designed RCTs are misrepresented to make the new drug look superior. So, in the basic process of generating the evidence, the balance is tilted towards any new drug whatsoever. Two decades ago, Bodenheimer noted that the major financial burden of new drug development was borne by the pharmaceutical industry and he also observed some hindrances when authors went on to publish negative or unsatisfactory results. (7) The situation has worsened. Delgado et al in their meta-analysis of clinical trials, results of which were published in three major journals between 2013 and 2015, found that the randomized controlled trials which were funded by companies with commercial interests were more likely to show favourable outcome and this difference is mainly due to unusual surrogate endpoints adopted by the for-profit funded clinical trials. (8)

While there is distinct bias towards generating evidence in favour of newer therapies, further problem arises in adopting that evidence to treat individual patients. As an inevitable corollary to the basic tenets of EBM, ethnic diversities are ignored to treat all human beings, throughout the world, as a monolithic community – otherwise, one could hardly be able to incorporate the so called level I evidence generated from one RCT to treat an individual patient residing at the other end of globe. Furthermore, statistical data obtained from a group of patients can be extrapolated to another similar group of patients, but application of this same knowledge to an individual patient is problematic. (9) Data obtained from experimenting upon a group is of course a good evidence to act upon to another equally matched group, but what happens when the groups are not matched. But, who cares?

Therefore, in this new paradigm of corporate profit-driven medical research, EBM has become an excellent puzzle-solver by helping such research activities gather evidence in favour of all kinds of newer technologies and therapies and by promoting them effectively. EBM has become so successful in this endeavour that the state-funded healthcare system of the developing countries have reached the level of near bankruptcy – and the developed nations are not falling behind either – by chasing the newer, expensive – but, not necessarily superior – technologies and therapies.

Therefore, while EBM has been spectacularly successful in inflating the profits of corporate health industry, there are plenty of data to display that this constant drive to chase the latest expensive technologies and therapies – an inevitable adverse outcome of EBM, particularly in its present form – has proven to be disastrous for the state-supported healthcare systems throughout the world. Still, it might be too early to refute EBM, particularly its basic principles, though its socio-economic consequences are all too clear. Therefore, in addition to a thorough knowledge in medical statistics, as touted by the proponents of EBM, individual physicians should better travel back in time, take some valuable inputs from the great Hippocrates and Galen, gather some training in rationality, logic, ethics and be socially responsible. That should be the only way forward.

Alfred Worcester said almost a century ago : "The younger members of the profession, although having enormously greater knowledge of the science of medicine, have less acquaintance than many of their elders with the art of medical practice….. Primarily, it (i.e. the art of medical practice) depends upon devotion to the patient rather than to his disease." (10) In its present avatar, EBM encourages more to focus upon the ailment an individual is suffering from than the individual human being. A generation of physicians taught on these principles might be more beneficial for the healthcare industry than the individual patients. If EBM is allowed to reign, more attention needs to be paid on the source of funding behind the evidence, why and how should that evidence be interpreted before applying such for the care of an individual patient and when should the physician look beyond the evidence to care for an individual human being.

References :

1) Evidence-Based Medicine Working Group. Evidence-based medicine. A new

approach to teaching the practice of medicine. JAMA. 1992 Nov 4;268(17):2420-5.

PubMed PMID: 1404801.

2) Kuhn TS : The Structure of Scientific Revolutions, Chicago, Ill; University of

Chicago Press, 1970

3) Feyerabend P : “Explanation, Reduction and Empiricism”, in H. Feigl and G.

Maxwell (ed.), Scientific Explanation, Space, and Time, (Minnesota Studies in the Philosophy of Science, Volume III), Minneapolis: University of Minneapolis Press, 1962

4) Illich, Ivan. Medical Nemesis;the Expropriation of Health; New York; Pantheon Books, 1976

5) Davis C, Naci H, Gurpinar E, Poplavska E, Pinto A, Aggarwal A. Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13. BMJ. 2017;359:j4530. Published 2017 Oct 4. doi:10.1136/bmj.j4530

6) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/placebos-and-blinding-randomized-controlled-cancer-clinical-trials-drug-and-biological-products

accessed on 12/07/2020

7) Bodenheimer T. Uneasy alliance--clinical investigators and the pharmaceutical industry. N Engl J Med. 2000;342(20):1539-1544. doi:10.1056/NEJM200005183422024

8) Falk Delgado A, Falk Delgado A. The association of funding source on effect size in randomized controlled trials: 2013-2015 - a cross-sectional survey and meta-analysis. Trials. 2017;18(1):125. Published 2017 Mar 14. doi:10.1186/s13063-017-1872-0

9) Tonelli MR. The philosophical limits of evidence-based medicine. Acad Med. 1998;73(12):1234-1240. doi:10.1097/00001888-199812000-00011

10) Worcester, A.The care of the aged, the dying and the dead (1935), Baltimore & Co, London