Translational research aims to “translate” findings from basic and fundamental research into medical practice in order to improve health outcomes for patients and populations. Different definitions of translational research have been proposed but the term is broadly applied to research that brings laboratory findings to the point of care in clinical settings. This is often described as “bench-to-bedside”. Translational research involves translation of knowledge and skills in two areas; 1) the process of applying findings generated through laboratory research in basic science and preclinical studies, to the development of trials and clinical research in humans; 2) research aimed at enhancing the adoption of best practice in the community. Cost-effectiveness of prevention and treatment studies is also an important part of translational science. Essentially, translational research is about closing the gap between scientific knowledge gained in basic science and daily clinical practice.

A simplified model of translational research consists of a two stage approach (T1 and T2). In this model, T1 refers to the “bench-to-bedside” approach which translates knowledge from basic science into development of new treatments, and T2 refers to translating findings from clinical trials into everyday practice. A more elaborate model of translational research describes five stages (T1-T5). In this five-stage scheme, T1 involves basic research, while T2 involves pre-clinical research, T3 involves clinical research, T4 explores clinical implementation, and T5 involves implementation at the public health level. The details of these different stages are given here only to illustrate the process of translational research and stress the fact that this type of research represents a continuum from laboratory to patients and populations.

Translational research is a relatively new research discipline but it has become increasingly important. The National Institutes of Health (NIH) in the USA has made translational research a major priority. It has established centres of translational research at its institutes and launched the Clinical and Translational Science Award (CTSA) program in 2006. It is estimated that the NIH invests over $500 million per year for translational research, while the United Kingdom has invested £450 million over 5 years to establish translational research centres. Journals devoted to the discipline include Translational Medicine, Journal of Translational Medicine and Translational Psychiatry. Translational Psychiatry is a relatively new journal with the first issue being published in 2011. This journal however already has an impact factor of 5.538 which demonstrates the scientific importance of this field.

This brief introduction to translational research may give a rather erroneous impression that translational research is mainly for developed countries, where high technology laboratories carry out research in drug and vaccine discovery, which is then translated to patients. This is not the case. A cursory look at the different stages of translational research will clarify this. As mentioned above in the five stage model of translational research, T4 explores clinical implementation, and T5 involves implementation at the public health level. This can be carried out in resource poor settings, with minimal laboratory support. The following examples of research from developing countries will help to illustrate how translational research is essential and indeed feasible in developing countries.
The International Diabetes Federation launched an initiative, termed D-START (diabetes – supporting translational research twinning). D-START focuses on the implementation of translational research projects in prevention of type 2 diabetes in low and middle income countries. This initiative aims to bring together highly committed experts and investigators in diabetes research from developing countries to collaborate with researchers in developed countries. D-START proposes a workable model of collaborative research to promote high quality translational research in developing countries. The programme proposes a designated ‘coordinating site’ and ‘implementation site’. The coordinating site is the organization responsible for the design of the study framework and provides expertise and consultancy to the implementation site. The implementation site is proposed to be an institution, based in a developing country, responsible for carrying out the study with the commitment of their healthcare organization.

Examples from our own research also illustrate the potential for translational research in developing countries. The first involves the use of Lithium to treat bipolar affective disorder during Ramadan. Lithium is one of the most effective treatments commonly used in psychiatry for bipolar affective disorder, however Lithium has a narrow therapeutic index range of 0.8–1.2 mmol/L. Blood serum levels above 1 mmol/L can be toxic with levels above 1.4 mmol/L proving fatal. Serum levels can potentially rise to toxic levels during fasting in the month of Ramadan with prolonged periods of food and fluid restriction. There has been little guidance or evidence for clinicians on controlling for this, as studies have been limited to case reports or studies of very small sample size.

We first conducted a clinical study using a before and after design, comparing the serum lithium in patients who were stable on Lithium, before, during and after Ramadan. However, the study has limitations as it does not have a control group, as it is almost impossible to recruit a non-fasting sample in the province of Khyber Pakhtunkhwa. To combat this problem and in collaboration with the Department of Pharmacy at Peshawar University in Pakistan we developed an animal model. In the first study of its kind, we were able to demonstrate that it is possible to study the effects of Lithium in rats in conditions mimicking those encountered during Ramadan. Rats were administered lithium and kept fasting in environmental conditions that typically mimic Ramadan. A control group of non-fasting rats were administered lithium under the same environmental conditions. This study provides valuable insight for clinicians and enables findings from laboratory research to be translated into clinical practice.

A second example looks at treatment adherence in schizophrenia. Treatment adherence in psychiatry is a major problem and in the case of severe mental illness such as schizophrenia, less than half of patients comply with treatment. Evidence suggests that in general medicine, fixed dose combination (FDC) medications, which are formulations with more than one active ingredient in a single capsule or tablet, offer significant advantages in improving patient adherence. This has been successfully used in chronic conditions such as cardiovascular disorders. In psychiatry, however, fixed dose combination medications are generally not available, despite the fact that different combinations of medications are often used. In the treatment of bipolar affective disorder, for example, a combination of antipsychotics and mood stabilizers such as Sodium Valproate or Lithium are routinely prescribed and recommended in guidelines. We have developed a program of research that translates knowledge of the use of fixed dose combination medications into clinical practice. In collaboration with pharmacy departments in two universities in Khyber Pakhtunkhwa, we recently published a paper which describes the development of a fixed dose combination medication containing Aripiprazole and Sodium Valproate. The former is an antipsychotic indicated in treatment of bipolar affective disorder, while the latter is a mood stabilizer recommended in many treatment guidelines for use in bipolar affective disorder. This is a novel fixed dose combination medication. Our group has now completed the animal studies that describe the pharmacodynamics of this product, and the resulting manuscript has been submitted for publication. Subsequently we plan to conduct clinical trials to complete the translational research cycle.

These examples illustrate the multidisciplinary nature of translational research and the possibility of developing and conducting translational research in a developing country like Pakistan. A collaborative research approach is essential for this to be successful. The need for such a collaborated effort was highlighted almost a decade ago, but unfortunately there has been little progress since then. It appears that clinical research is still dominated by studies in patient populations, which rarely inform clinical practice and basic scientists are often conducting laboratory research which has no immediate effect on patient treatment. Translational research has the potential to bridge this gap. It is time to change the mind-set and come out of our silos to design, plan and disseminate research that informs clinical practice.

PREFERENCES


