Expansion and Evolution of TDM and CT

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Scope of the lecture:

Personalized patient care becomes a global trend in medicine particularly for pharmacotherapy. This talk firstly intends to review the past progress of TDM and CT with respect to science and clinical implementation. Technical and scientific evolution was a key to drive TDM and CT. Clinical implementation often depends on education and system of medical service. Science has no boarder whereas clinical practice is challenging for further expansion of TDM and CT globally.

Learning objectives:

The audience can learn:
1. Technical evolution which produced TDM and CT,
2. Scientific evolution which accelerated TDM and CT,
3. A gap between science and clinical implementation,
4. Future perspective for global expansion.

Extended abstract:

Medicine has two sides; bright side is treatment efficacy and dark side is toxicity. The former is described as pharmacology and the latter belongs to toxicology. There is an important common mechanism between them; the magnitude of action of drugs or chemicals depends on the exposure to human body, in other words drug/chemicals concentration in the body. Thus, measurement of the concentration of drug/chemicals is essential to understand a quantitative relationship between drug exposure and efficacy/toxicity, and how to improve efficacy or avoid toxicity. This describes a fundamental doctrine of our Association, IATDMCT and this is why the IATDMCT covers both sides of pharmacology (TDM) and toxicology (CT) in human body.

Clinical application of the TDM concept into general practice started around 1980s. The research and studies were made much earlier, but an important turning point was the development of simple and rapid assay system using immunoassay. With general spread of new immunoassay, TDM was implemented into practice in many hospitals. This movement emerged in 1980s in mainly North America, West Europe and Japan, which in turn the first ICTDM Congress was held in 1988 in Japan and the IATDMCT was born in 1990 in Europe.

Scientific evolution was another key for driving forward TDM and CT. Traditional pharmacology and toxicology discussed based on dose or amount of chemicals, and their interpretation was made by empirical basis. With the progress of analytical methods, we were able to get more insight into quantitative causal relations for inter-individual variability in efficacy and toxicity. A huge number of clinical studies have been published to demonstrate drug/chemicals exposure is much more important than the exposed amount to interpret and predict the individual variability. A standard dose is useful for majority of patients but not for all patients, while pharmacokinetics-based individual dosing can provide an optimal treatment for every patient. Another important technical evolution was invention
of personal computers which enable bed-side pharmacokinetic optimization using TDM data. Development of the dose optimization algorithms and software also contributed to implement TDM into clinical practice. Pharmacokinetic and pharmacodynamic modeling and simulations are one of important backbones for sophisticated application of TDM and CT.

The concept of TDM was firstly applied to digoxin, aminoglycosides and anti-epileptic drugs. Then TDM was expanded to transplantation for precise control of immunosuppression using cyclosporine, tacrolimus and mycophenolate. Now a days, TDM is essential when people use immunosuppressant for transplantation. Recently, the application of TDM is further expanding to oncology. Our association consists of a variety of experts with multidisciplinary backgrounds such as medicine, pharmacy, laboratory chemistry and pathology, therefore we can take a leading role to enlighten and implement the TDM in new therapeutic fields such as oncology.

Human genomics can revolutionize medical science. A big movement of ‘Precision Medicine’ has a potential to change the concept of medical service from traditional population-based therapy to individualized therapy. However, there is a limitation in pharmacogenomics. Genomics can be a useful tool for choosing targeted drugs for particular sub-population who express the drug target, such as companion diagnostics in oncology. But, genomics does not answer drug dose which should be optimized based on patient’s pathophysiological conditions, for example renal dysfunction. My solution is the integration of genomics and drug concentration measurement to develop a comprehensive dosing algorithm. TDM can play an important part of Precision Medicine.

As mentioned above, TDM emerged in Western countries and Japan. The Japanese Society of TDM (JSTDM) was born in 1984, which has longer history than the IATDMCT. Several years ago, Chinese Society of TDM was officially established and shows rapid growth in their activity. The regional meetings of the IATDMCT were recently held in South America and India. TDM is definitely expanding to the rest of world. The membership of IATDMCT is remarkably increasing in Asia during last 4 years. The IATDMCT is an Association for leading science, clinical practice and education of TDM and CT. Science has no boarder whereas clinical practice is challenging depending upon the medical service system of each country, which we need to collaborate for further expansion of TDM and CT globally.