Clinical Laboratory Innovation by LC-MS/MS

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Scope of the lecture:
General information of LC-MS/MS in clinical laboratory.
Introduction of analyzer based sample preparation technology.

Learning objectives:
1. Pros and cons of LC-MS/MS in clinical laboratory.
2. Benefit of automation and integration of sample preparation and LC-MS/MS.
3. The impact of new technology toward the laboratory innovation.

Extended abstract:
Based on experience as a scientist of mass spectrometry, overview of the technology on tandem mass spectrometry coupled to liquid chromatography (LC-MS/MS) for clinical laboratory is introduced in this session.
In a decade, mass spectrometry has widely adapted in practice of clinical laboratories. Mass spectrometry has respect characteristics of specificity, high sensitivity and capability of multi-compounds detection. Compering to immunoassay technic, mass spectrometry reduces cost for new methods development. Therefore, many clinical laboratories developed clinical tests themselves with mass spectrometry. For example, monitoring of immunosuppressant, 25-hydroxyvitamin D and screening and quantitation of opioids [1]. Measurement of these drugs and metabolites by mass spectrometry contributes to clinical therapy in the field of Therapeutic Drug Monitoring (TDM), pain management and endocrinology.
LC-MS/MS also contributes to the standardization of widely spread clinical test. To improve the quality of clinical therapy, conformity of test result, which does not rely on instruments, laboratories and methods, is very important. In the United States, Center of Disease Control (CDC) provides Vitamin D Standardization-Certification Program (VDSCP). Reference values of test samples are measured by LC-MS/MS method in National Institute of Standards and Technology (NIST) for VDSCP. On the other hand, LC-MS/MS is mainly used in large private laboratories and laboratories in research hospitals. Because operation of LC-MS/MS requires many human interventions on sample preparation and data processing. Trained personnel who has knowledge and experience of LC-MS/MS analysis are required even in the daily operation. Improvement of automation on sample preparation is desired to accelerate the utilization of LC-MS/MS in clinical laboratories [2]. To adapt the routine work of clinical laboratories, it is critical for LC-MS/MS to improve the automation and to reduce manual processes.
To challenge the innovation of LC-MS/MS in clinical field, a new concept of sample preparation (CLAM-2000, Shimadzu) was engineered. The instrument realizes automated sample preparation of protein precipitation and filtration with features of traditional clinical analyzer. After sample preparation, the vials are automatically send to autosampler without human intervention. CLAM-2000 communicates with LC-MS/MS and send trigger signal to start analysis with small interval between LC-MS/MS analyses. While LC-MS/MS is analyzing a sample, next sample is prepared in CLAM-2000. Therefore, sample preparation does not slow down the through put of LC-MS/MS analysis. Plate type sample containers are used for the many traditional automated sample preparations for LC-MS/MS, which require batch analysis. CLAM-2000 processes samples one by one and allows to analyze from a sample to sixty samples in a batch. This feature also provides the flexibility in operation of

emergency sample. After pausing the instrument, emergency sample can be loaded into the sample storage of instrument in the middle of a batch with prioritized order. As the result, turnaround time (TAT) of emergency sample are improved. This new technology shows that automation and integration of sample preparation and LC-MS/MS eliminate many human interventions. It also expects to reduce human error as well. In addition, CLAM-2000 shows potential of flexible operation of LC-MS/MS as same as traditional clinical analyzers. It makes LC-MS/MS more accessible to clinical laboratories.

Fig.1 Automated and Integrated system
CLAM-2000 coupled to LCMS-8060

[1] R. Verplaetes, J. Henion, Quantitative determination of opioids in whole blood using fully automated dried blood spot desorption coupled to on-line SPE-LC-MS/MS, Drug Testing and Analysis, 8 (2016) 30-38.
[2] Y. V. Zhang, A. Rockwood, Impact of automation on mass spectrometry, Clinica Chimica Acta 450 (2015) 298 – 303.