Analytical Considerations When Selecting Laboratory Reference Reagents for Routine Use and for Evaluating POC Blood Ketone Monitoring Systems

Yasunobu Tsuchiya*, Yasunobu Ozawa*, and Masaru Yamamoto**

*Medical Instrument Center, Technical Service Team, Nipro Corporation, Kusatsu, Shiga, Japan,

** Medical and Scientific Affairs, Nova Biomedical, Mita, Tokyo, Japan

Background: In 2014 Sodium Glucose Co-transporter-2(SGLT2) inhibitors were introduced in Japan for the treatment of type II diabetic patients. One of the side effects of this class of products is the increase of ketone bodies caused by the lack of sufficient glucose supply to the cell which activates lipid metabolism. Thus the monitoring of ketone bodies, specifically β-hydroxybutyrate (BHB), is important in type II as well as type I diabetic patients. In Japan this has led to a number of clinical laboratories adding BHB to their test menu. In addition there is increased interest in validating and using POC blood ketone monitoring systems. Standardization of BHB methods is not well established and in Japan five different sources of BHB reagents for clinical chemistry analyzers are commercially available. The aim of this study was to assess the linearity and calibration alignment of the five different BHB reagents in conjunction with a POC blood ketone monitoring system (BKMS).

Materials and Methods: Commercially available BHB reagents, Kainos 3HB (Kainos) Auto Wako 3HB (Wako), Ketone-H (Serotec) 3HB (Serotec), Ketone TestB (Sanwa) were run on a JEOL BM6050 laboratory analyzer. POC ketone testing was performed with StatStrip Ketone BKMS (Nova Biomedical). For the linearity and calibration alignment assessment a series of ten whole blood samples were prepared by mixing different amounts of a high level BHB whole blood sample (7 mmol/L) with a low level BHB blood sample (<1mmol/L). The samples were tested using the POC BKMS, centrifuged and the plasma measured using the five laboratory BHB reagents sets. The default settings on the chemistry analyzer dilutes the plasma sample 5 fold in addition each plasma sample was diluted a further 4 and 8 fold with saline representing a final dilution of 20, and 40 fold .

Results The POC BKMS showed good linearity across the whole measurement range (0.1-7.0 mmol/L). Three of the laboratory reagents also showed good linearity across the measurement range. The 3HB-L reagent Kainos and Serotec 3-HB laboratory reagents were only linear to 1.0 mmol/L using the 5 fold plasma sample dilution factor. When using a plasma sample dilution factor of 20 fold, these two reagents along with the other three reagents showed good linearity comparable to POC BKMS across the full concentration range. Further dilution of the plasma samples of up to 40 fold resulted in an overestimation of BHB values with the laboratory BHB reagents.

Conclusion: The dynamic range of the most reagents for chemistry analyzer is up to 1 mmol/L, thus caution should be taken measuring DKA patients' specimens with elevated levels of BHB. Some chemistry analyzers, such as BM6050, are programed to dilute the test sample by default and the dilution effect multiply if the sample dilution process is programed to the chemistry analyzer. This could lead to erroneous results, whereas the POC BKMS gave reliable BHB values across the clinical BHB range. It is important to validate the linearity of laboratory BHB methods before implementing routinely and before using for evaluating POC BKMS.