LETTER TO THE EDITOR

Quantifying bovine insulin: conversion of units

Insulin resistance, defined as a condition in which higher than normal peripheral insulin concentrations are needed to achieve ‘normal’ metabolic responses,¹ plays a key role in the pathogenesis of metabolic diseases associated with human metabolic syndrome. This syndrome includes chronic metabolic and inflammatory alterations associated with obesity. Researchers have just begun to elucidate the underlying molecular mechanisms that in cases of obesity may result in tissue-specific inflammasome activation and dysregulation of insulin signaling.² Currently there is also great interest in veterinary medicine in measuring insulin sensitivity of peripheral tissues and insulin secretion by the pancreas. In dairy cows in particular, investigators are trying to apply findings in human metabolic syndrome to further elucidate the pathophysiology of ‘fat cow syndrome.’³

The hyperinsulinemic euglycemic clamp test is generally accepted as the gold standard for assessing peripheral insulin sensitivity, but as it is time-consuming and invasive, it is not suitable for use on a larger scale in epidemiologic investigations. Therefore, in human medicine, surrogate indices, such as HOMA, its log-transformation (log(HOMA)) and reciprocal score (1/HOMA), QUICKI, and RQUICKI,⁴ have been developed to assess insulin sensitivity in large-scale studies. These indices are based on analysis of a single blood sample for determination of peripheral glucose, insulin (µIU/mL), and nonesterified free fatty acids (NEFA) concentrations. Researchers in bovine medicine currently apply these human indices to estimate whole body insulin sensitivity in dairy cow and calf populations.⁵⁻⁷

Most bovine researchers have used ELISA kits designed to quantify human insulin, but now there are specific bovine insulin kits on the market that are preferred
for measuring insulin in bovine plasma or serum. These kits have been specifically
developed, optimized, and verified for determination of bovine insulin concentrations so
that binding to the analyte is favored and nonspecific interference from the bovine
matrix is minimized. In addition, human and bovine insulin differ in amino acids at
positions A8, A10, and B30. Therefore, cross-reaction between human and bovine
insulin in immunologic assays is dependent on the epitope of the anti-insulin antibodies
used and is unlikely to be 100%. For example, Mercodia AB (Uppsala, Sweden)
reported a specificity of 31% for bovine insulin assayed with the Mercodia human
insulin ELISA-kit.

In immunoassays, the amount of antigen present is determined by its binding to
antigen-specific antibodies and is expressed as mass per volume. In bioassays on the
other hand, the biological activity of a substance is determined and expressed in
international units (IU) per volume. The conversion from biological activity (IU) to a
mass unit (mol or gram) requires assignment of a certain biological activity to a certain
amount of substance. For bovine insulin, the World Health Organization (WHO) has
defined one IU of bovine insulin as equivalent to the activity contained in 0.03891 mg
of the international standard for bovine insulin (NIBSC code: 83/511).

To calculate the surrogate indices, it is necessary to express the amount of
insulin in IU (µIU/mL), whereas most of the commercially available ELISA kits that
measure bovine insulin express the results in gravimetric units. Taking into account
species-specific differences between insulin molecules, the conversion factor used to
convert human insulin from mass per volume to IU per volume is not suitable for
conversion of bovine insulin to IU. Thus, manufacturers of quantification kits of
bovine-specific insulin should provide a conversion factor to IU by determining the
agreement between the WHO international standard and their in-house standard for
bovine insulin. For Insulin Bovine ELISA (catalogue #10-1201-01, Mercodia AB), the supplier calculated the conversion factor by preparing 4 independent solutions of 5 different concentrations of the WHO standard. These solutions were analyzed for conformity, pooled, and then analyzed in 3 runs of the ELISA kit. The mean value was used to calculate the conversion factor based on the WHO-defined standard (1 mIU/L = 0.03891 μg/L). The conversion factor for this commercial kit was determined to be: 1 μg/L = 20.56 mIU/L.

In human medicine, lack of standardized insulin assays is currently a barrier to determination of the clinical utility of measures of insulin sensitivity and secretion. In order to make results translatable among laboratories and studies, an Insulin Standardization Workgroup was established. Based on its report, we recommend that bovine insulin concentrations also should be reported in Systeme Internationale (SI) units (pmol/L) and then converted to IU based on biological activity in order calculate the surrogate indices.

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References


