

Cross-Reactivity of New Insulin Analogs in Insulin Assays

carta ao editor

TO THE EDITOR

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INSULIN MEASUREMENT HAS important applications in clinical practice. Besides providing information about insulin dynamics in patients with diabetes mellitus and insulin resistance, it has a special place in the differential diagnosis of hypoglycemic conditions. Insulin measurement is based in immunoassay techniques, initially radioimmunoassay (RIA) and nowadays immunometric assays. One of the advantages of the transition of RIA to immunometric assay was the superior specificity of the latter, resulting in lower values (1). Specificity of the new immunometric assays is, in fact, quite strict, with almost no cross-reaction with proinsulin or C peptide. In the last years, several insulin analogues, with different profiles of action based on point modifications of the insulin molecule, have been described (2). To define their cross-reaction in the new immunometric assays is of evident clinical importance. We studied four preparations of insulin analogs: (a) insulin aspart (NovoRapid, Novo Nordisk), with aspartic acid substitution for proline in B28; (b) lispro insulin (Humalog, Eli Lilly), with an exchange between B28 (proline) and B29 (lysine); (c) glargine insulin (Lantus, Aventis), with glycine instead of asparagine in position A21, and two additional arginine residues at the end of B chain; and (d) detemir insulin (Levemir, Novo Nordisk), with a fatty acid chain linked to the lysine residue B29. All insulin preparations were obtained commercially as 100 U/mL preparations. The assay studied was an immunofluorometric assay provided by PerkinElmer, based on two highly specific monoclonal antibodies that show some cross-reaction only with Des 64-65 split proinsulin (10%). The results obtained are depicted in figure 1. The only

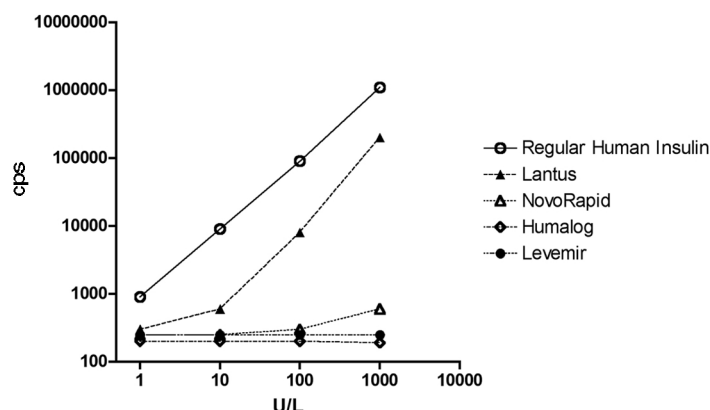


Figure 1. Study of the cross-reactivity of four insulin analogs in the PerkinElmer immunofluorometric assay. The reference preparation (Regular human insulin) showed a response curve that was superimposable with the standard provided with the assay kit. Cps= counts per second.

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insulin analog that showed cross-reactivity was glargine insulin (13.5%), others were all below 1%. This definition is very important because recent publications have shown that the different assays available are not uniform in terms of cross-reactivity with the new insulin analogs (3,4). Some assays show high cross-reactivity with all analogs studied, and some almost none. To our knowledge, this is also the first study describing cross-reactivity with the new analog preparation detemir insulin. To know what you are, or can be measuring, is one of the basic principles in order to provide an assay result of the higher diagnostic sensitivity and specificity.

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