Objective

To evaluate the accuracy and intra- and inter-laboratory variability of N8-GP (turoctocog alfa pegol) and Advate® (octocog alfa) activity measurements in clinical laboratories using their routine methods and reagents

Conclusions

Most participating clinical laboratories could accurately measure N8-GP and Advate® using their available one-stage clotting or chromogenic FVIII activity assays, without the need of a product-specific standard

Three silica-based aPTT reagents modestly underestimated N8-GP recovery, ~40–60% of the target concentration

Introduction

N8-GP (Novo Nordisk A/S, Bagsværd, Denmark) is a glycoPEGylated extended half-life (EHL) recombinant FVIII (rFVIII) molecule

Clinical studies have shown that N8-GP is efficacious and safe for the treatment of haemophilia, adolescents and adults1,2,3

Here, we aimed to evaluate the accuracy and variability of FVIII:C measurements among clinical laboratories when using their routine FVIII:C assay procedures

Methods

Invitation letters were sent to laboratories that had participated in a previous field study or are affiliated with the External Quality Assessment Scheme (EQAS) Foundation

Participating laboratories completed a questionnaire about their routine methods, kits and reagents used to measure FVIII:C and were sent a field study kit

Field study sample kits were prepared by EchoSys Inc. (Englewood, CO, USA) and contained samples of pooled congenital haemophilia A plasma (George King Bio-Medical Inc., Overland Park, KS, USA) spiked with 0.03, 0.2, 0.6 or 0.9 IU/ml, N8-GP (rFVIII) molecule (Dublin, Ireland)

Laboratories were instructed to perform triplicate FVIII:C analyses on samples on consecutive days using their routine FVIII:C procedures, reagents, calibrator and instruments

Results

Participating laboratories

In total, 67 laboratories from 25 different countries participated, including laboratories from France (16.4%), USA (11.9%), UK (10.4%), The Netherlands (7.5%), Australia (6.0%), Canada (6.0%) and Japan (6.0%)

Overall, 89.6% of laboratories used the FVIII one-stage clotting assay, 53.7% used the FVIII chromogenic assay and 43.3% used both one-stage and chromogenic assays

One-stage assays and aPTT reagents

Silica-based aPTT reagents were used by 80% of the laboratories, while 30% used ellagic acid-based reagents and 12% used kaolin-based reagents (Figure 1)

One-stage assay measurements

Most aPTT reagents accurately measured N8-GP. However, of the nine one-stage assay aPTT reagents used, three (all containing silica-based contact activators) underestimated N8-GP activity by more than 30% target concentrations

Average measurements ranged 57–59% for APTT-GP 40–83% for TriniCLOT™ and 43–60% for STA®-PTT-Automate of N8-GP target concentration for 0.03–0.9 IU/ml samples. These three reagents were omitted from subsequent statistical analyses of N8-GP

N8-GP mean recovery remained within the acceptable range (±30% of the target concentration) at all concentrations

The overall mean recoveries were 92.5% (95% confidence interval [CI]: 89% ; 96%) of target concentration for N8-GP and 123% of target concentration (95% CI: 120% ; 127%) for Advate®

Variability decreased with increasing concentration, with inter-laboratory variability ranging between 10.9–22.1% for N8-GP and 7.8–22.1% for Advate® (Figure 2)

Chromogenic assay kits results. Mean FVIII:C in percent of target and number of laboratories by target concentration

Figure 3. Overview of chromogenic assay kits

Figure 4. Overview of one-stage clotting assay

References


Conflict of interest disclosure

MH, WHOC, RL and ME are employees of Novo Nordisk A/S. ST, PB and MH received honoraria or consultation fees from Novo Nordisk and Siemens Healthcare, has participated in speaker’s bureau for Novo Nordisk and is a shareholder of the Laboratory Corporation of America.

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