EVALUATION OF THE KONELAB 20XTi CLINICAL CHEMISTRY ANALYZER – CARBAMAZEPINE AND VALPROATE IN SERUM

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XXIX Nordic Congress in Clinical Chemistry, Malmö, Sweden, 24 - 27 April 2004

INTRODUCTION

The aim of this study was to evaluate the performance of the new Konelab 20XTi clinical chemistry analyzer in two TDM tests in serum and to compare the results with those measured by HPLC (carbamazepine) and fluorescence polarization immunoassay (valproate) methods.

The Konelab 20XTi was evaluated according to the guidelines of NCCLS (documents EP5-A and EP9-A) modified by Thermo Electron Corporation (Finland). The daily routines were done according to recommendations of the manufacturer except the calibrations which were performed before every assay.

MATERIALS AND METHODS

Instruments

The Konelab 20XTi (Thermo Electron Corporation, Finland) is a random access, fully automated, selective clinical chemistry analyzer for small and medium size routine and specialty clinical laboratories handling among the basic clinical chemistry tests, Drugs of Abuse testing, Therapeutic Drug Monitoring, as well as other special chemistries. New samples, reagents and cuvettes can be loaded at any time to the analyzer without interrupting the analysis in progress. Routine samples are inserted into segments, which the user may load immediately into the analyzer.

Perkin Elmer Series 200 Liquid Chromatography (quaternary pump, autosampler, diode array detector) controlled by the Perkin Elmer Nelson Turbochrom Navigator program (Perkin Elmer Instruments, Norwalk, CT, USA).

Abbott FLxTDx analyzer (Abbott Laboratories, Abbott Park, IL, USA).

Applications for Konelab 20XTi

Carbamazepine and valproate assays use recombinant DNA technology (US Patent No. 4708929) to produce a unique homogeneous enzyme immunoassay system. These assays are based on the bacterial enzyme ß-galactosidase, which has been genetically engineered into two inactive fragments. These fragments spontaneously reassociate to form fully active enzyme that, in the assay format, cleaves a substrate, generating a color change that can be measured spectrophotometrically at 575 nm. In the assay, analyte in the sample competes with analyte conjugated to one inactive fragment of ß-galactosidase for antibody binding site. If analyte is present in the sample, it binds to antibody, leaving the inactive enzyme fragments free to form active enzyme. The amount of active enzyme formed and resultant absorbance change is directly proportional to the amount of drug present in the sample.

Reagents, Controls and Samples

The reagents, calibrators and controls used in this study are summarized in Table 1.

Reagents used were prepared and stored according to the instructions of the manufacturers.

For the evaluation, Lyphochek®Immuno assay Plus Control samples were dissolved at the same time and stored at –20 C° as well as serum pool.

Controls given in Table 1 were used as material for imprecision.

Table 1. Reagents, calibrators and controls used in evaluation

Analyte	Reagents	Calibrator	Control
Carbamazepine (Konelab 20XTi)	Konelab 981645	Konelab TDM Calibration set B 981648	- Lyphochek®Immuno assay Plus Control, Bio-Rad, Trilevel - Seerum pool
Valproate (Konelab 20XTi)	Konelab 981650	Konelab TDM Calibration set B 981648	- Lyphochek®Immuno assay Plus Control, Bio-Rad, Trilevel - Seerum pool
Carbamazepine (HPLC)	Chromsystem, AED Reagent kit, 23000/HR	Chromsystems, AED Calibration Standard, 22005/HR	Chromsystems, Tri Level AED Control, 0188
Valproate (FLxTDx)	Abbott, Valproic acid Reagent pack, 9514-60	Abbott, Valproic acid Calibrators, 9514-01	Abbott, Valproic acid Controls, 9514-10

Analysis

In order to calculate the within-run, between-day and total imprecision (coefficient of variation, CV%), four control samples were analyzed twice a day with two replicates during 9 to 11 days.

The patient serum samples for the correlation study were first analyzed as a single determination by HPLC (carbamazepine) and FLxTDx (valproate) and then stored at –20 C° until used. The total amount of samples was 73 and 77 for carbamazepine and valproate, respectively. The samples were measured as duplicates in Konelab 20XTi thus having less than 1 hour between first and second run.

The results of the study were calculated by Analyse –it for Microsoft Excel, version 1.65 (Analyse-It® Software Ltd, UK).

RESULTS

Imprecision

Within-run, between-day and total coefficient of variation (CV%) of carbamazepine and valproate analyzed in Konelab 20XTi are presented in Tables 2, 3 and 4.

Table 2. Within-run imprecision

Analyte (unit)	Mean (SD)	CV%	n
Carbamazepine (µmol/l)	12.6 (0.47) 34.9 (0.80) 56.0 (0.51) 29.0 (0.49)	3.5 2.3 0.9 1.6	40 44 44 40
Valproate (µmol/l)	216 (5.35) 495 (9.20) 729 (13.18) 506 (7.61)	2.5 1.8 1.7 1.5	44 44 44 36

Table 3. Between-day imprecision

Analyte (unit)	Mean (SD)	CV%	Days
Carbamazepine (µmol/l)	12.6 (1.01) 34.9 (2.34) 56.0 (3.10) 29.0 (1.20)	7.7 6.6 5.5 4.0	10 11 11 10
Valproate (µmol/l)	216 (9.43) 495 (17.66) 729 (24.80) 506 (15.03)	4.3 3.5 3.3 3.0	11 11 11 9

Table 4. Total imprecision

Analyte (unit)	Mean (SD)	CV%	Days
Carbamazepine (µmol/l)	12.6 (1.20) 34.9 (2.47) 56.0 (3.23) 29.0 (1.39)	9.1 7.0 5.7 4.6	10 11 11 10
Valproate (µmol/l)	216 (11.48) 495 (20.54) 729 (28.09) 506 (21.25)	5.3 4.1 3.7 4.2	11 11 11 9

Correlation

The regression analysis of the results are presented in Figures 1 and 2.

Figure 1. Method comparison (n = 73) of serum carbamazepine between Konelab 20XTi and HPLC

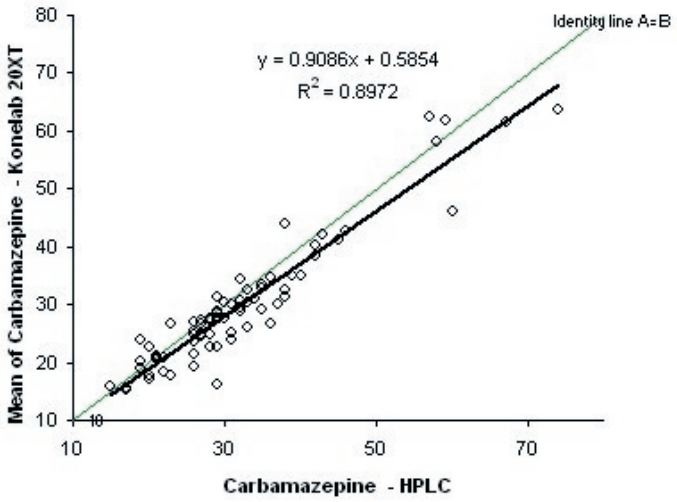
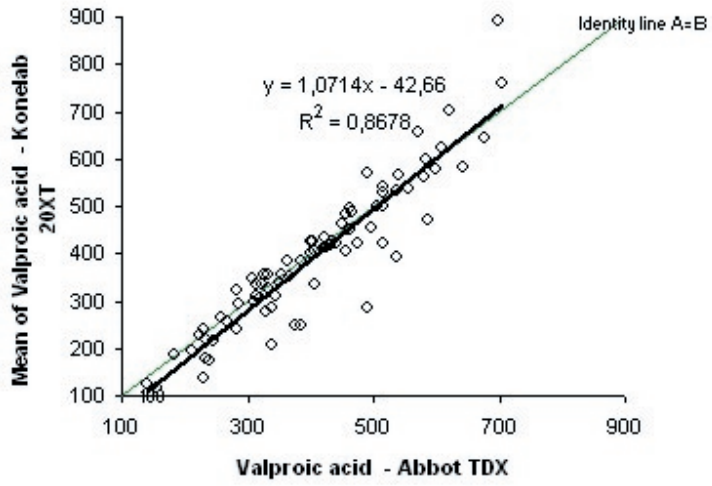


Figure 2. Method comparison (n = 77) of serum valproate between Konelab 20XTi and FLxTDx



CONCLUSION

The analytical performance of evaluated Konelab 20XTi was good. The proposed requirements for imprecision fullfilled in both analytes. Both TDM methods were precise and correlation to the existing methods was reasonable. We concluded that Konelab 20XTi is a reliable analyzer for quantative determination of serum carbamazepine and valproate levels in small to medium size laboratories.