INTRODUCTION

The method comparison test protocol used for establishing the performance of the MassTrak Immunosuppressants kit was designed to compare the results obtained for patient samples using the MassTrak method with results obtained for the same samples using similar “home-brew” LC/MS/MS methods.

This decision was based on the CLSI precision protocol, EP5-A2, recommendation requiring that the comparator method should have similar or better precision than the test method (MassTrak). Although immunosuppressants clearly do not meet with the CLSI requirement, we hypothesized that proficiency testing results that included a combination of methods, e.g., chromatographic and immunoassay, could be used as a suitable route to devise such a comparison. For this study, we used results and samples from the Tacrolimus Inter-laboratory Proficiency Testing (IPT) scheme (http://www.bioanalytics.co.uk) since materials were readily available and each laboratory had experience with the survey.

BACKGROUND

Each month, the Tacrolimus IPT scheme distributes three whole blood samples to each of the member laboratories. The samples consist of whole blood from patients receiving tacrolimus (concentration unknown) or drug-free blood that has been spiked with tacrolimus to a specific target concentration. The laboratories analyze the three samples as part of their routine service without knowledge of the tacrolimus concentration. The results are reported back to the IPT scheme for method-specific statistical analysis. Table 1 shows the method groups currently used for the tacrolimus IPT scheme and the approximate number of participating laboratories in each group. The exact number of results returned in each group varies by month.

Table 1: Analytical methods used by the International Tacrolimus Proficiency Testing Scheme.

<table>
<thead>
<tr>
<th>Analytical Method</th>
<th>Approximate Number of Participants</th>
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<tbody>
<tr>
<td>HPLC</td>
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<tr>
<td>Diasorin ProTrac II Tacrolimus</td>
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<tr>
<td>Dade Behring Tacrolimus EMIT 2000</td>
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<tr>
<td>Abbott IMx Tacrolimus</td>
<td>100</td>
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</tbody>
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For each method group, the mean and standard deviation are calculated for each IPT sample. Results that fall within ±3 SDs of the mean are accepted by the scheme and those only outside the window are rejected. The means and standard deviations are recalculated using the accepted data only and a report distributed (see Figure 1). The data are also available for public viewing on the IPT web site (http://www.bioanalytics.co.uk). The data from 71 Tacrolimus IPT samples were compared to Dade Behring Tacrolimus EMIT 2000 results for the Abbott Tacrolimus IMx.

RESULTS

Sample Analysis

A total of 71 Tacrolimus IPT samples were analyzed at two test centres using the MassTrak LC/MS/MS kit during the validation phase1.

Statistical Analysis

The MassTrak results for the IPT samples were compared to the repeated method means for three immunosuppressants: Diasorin ProTrac II (DUSA), Dade Behring EMIT® 2000 Tacrolimus (EMIT) and Abbott IMx Tacrolimus II (MEIA) for that same set of IPT samples. For contraindications, a comparison was also made to the HPLC group of laboratories. Data were processed using the Passing-Bablok Method Comparison algorithm provided in the Microsoft Excel add-in, Analyse-It Clinical Laboratory v1.71.

Figure 1: Example report from the Tacrolimus IPT scheme showing the statistical results returned for each method type. (www.bioanalytics.co.uk).

Figure 2–5 show comparisons of the existing MassTrak IPT results to the method mean results for the Abbott Tacrolimus IMx, Dade Behring EMIT 2000 MEIA, Diasorin ProTrac II EMIT and the HPLC groups of laboratories, respectively. In each case, comparisons for all samples, spiked samples only and patient pools only are presented. The Passing-Bablok Method Comparison parameters for each of the comparisons are summarized in Table 2.

Figure 3: Passing-Bablok method comparison for MassTrak results compared to Abbott Tacrolimus IMx results for all samples. The Passing-Bablok method is a non-parametric method that allows for robust analysis of data from non-normally distributed data. It is based on the Passing-Bablok algorithm provided in the Microsoft Excel add-in, Analyse-It– PRO-Trac™ II (ELISA), Dade Behring EMIT TM 2000 Tacrolimus.

REFERENCES


CONCLUSIONS

We report an indirect comparison of MassTrak using IPT data.

• The MassTrak results did not differ significantly from the other HPLC groups of laboratories for either the spiked samples or the patient pools.

• A significant bias was observed when the results obtained using immunoassay were analyzed for the patient pools reflecting cross-reactivity of the antibodies used in these methods for metabolites.

• We propose that this type of comparison provides a more accurate estimate than a comparison made using immunosuppressant data from a single reference laboratory.

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