

Validation Study: Clarity Multistrip Urocheck

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OBJECTIVE: To test the interchangeability of a previously untested urine reagent strip, Clarity (RAC Medical), with the gold standard, Multistix (Bayer).

DESIGN: Seventy-six urine samples were tested with both the comparator and the gold standard urine reagent strips. Pairs of reagent strips were analyzed in the Clinitek Analyzer, recording the following: leukocytes, nitrite, urobilinogen, protein, pH, blood, specific gravity, ketone, bilirubin, glucose, and color. Data was assessed using statistical comparison of ordinal data (chi-square, Fisher's Exact, kappa, and weighted kappa). This study was approved by the Indiana University-Purdue University at Indianapolis Institutional Review Board.

SETTING: The study took place at Wishard Health Services, Indianapolis IN.

PATIENTS OR OTHER PARTICIPANTS: All urine tested was obtained from patients of the primary care clinic at Wishard Health Services.

INTERVENTIONS: n/a.

PRIMARY OUTCOME MEASURE: The ability for both reagent strips to generate (statistically significant) identical readings across all 11 measurements for each sample.

RESULT: Kappa values were deemed the best indicator to consistently examine the reproducibility of all 11 measurements of the Clarity versus the Multistix. Ten of eleven measurements were concluded to be non-reproducible by the

Clarity strips; nitrite readings achieved a kappa value above 0.85, whereas all other readings achieved kappa values well below the acceptable limits of this investigation (ranging from 0.00 to 0.65).

CONCLUSION: There was a lack of statistically significant agreement between the results of both products and therefore it was concluded that both products cannot be used interchangeably.

INDEX TERMS: Clarity; kappa; Multistix; urine reagent strips.

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Urine reagent strips are routinely used to aid in the diagnosis and monitoring of various disease states. The diagnostic results of two products, Multistix (Bayer) and Clarity (RAC Medical), can be measured in a Clinitek Analyzer. The purpose of this study was to compare measurements generated from the Multistix and Clarity products to assess the potential for interchange among the two products. Ordinal statistical tests were performed to assess the agreement of the products.

Although previous published studies have examined the properties of Bayer Multistix or the ability to have the re-

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sults of the Multistix correctly interpreted by the Clinitek Analyzer,¹⁻⁴ the authors found no studies with compare the reproducibility of Clarity urine reagent strips (or any other competitive urine reagent strips) against Bayer Multistix in a validation study.

MATERIALS AND METHODS

Both the Clarity and Multistix urine reagent strips were tested on 76 urine samples obtained from a patient population who presented themselves for routine care at a county hospital internal medicine clinic. The urine was tested for the following: leukocytes, nitrite, urobilinogen, protein, pH, blood, specific gravity, ketone, bilirubin, glucose, and color. This study was approved by the Indiana University-Purdue University at Indianapolis Institutional Review Board.

The Multistix test strip was initially used to test each urine sample. Once the urine was tested, the strip was then placed

into the Clinitek Analyzer and the results of the analysis were collected; similarly, the Clarity test strip was used to sample the same urine and the results collected. Matching printouts were stapled together to identify matching pairs.

Seventy-six urine samples were tested and 76 pairs of output data were generated. Of the 76 pairs of data, 75 were usable for statistical comparison; one pair was eliminated based on the inability to distinguish between the Multistix reading and the Clarity reading.

The pairs were then statistically analyzed for association. Two tests were used to confirm or deny association between the pairs. Firstly, when applicable, a chi-square test was performed to determine whether or not an association existed. When the chi-square test was not suitable, a Fisher's Exact test was used. In the case when either a row or column sum was zero, neither test could be applied.

Table 1. Reagent comparison

| Test | Bayer Multistix | Clarity Urocheck |
|------------------|---|---|
| pH | methyl red/bromthymol blue | bromcresol green/bromthymol blue |
| Glucose | oxidase, peroxidase, potassium iodide | oxidase, peroxidase, and potassium iodide |
| Protein | tetrabromophenol blue | tetrabromophenol blue |
| Ketone | sodium nitroprusside | sodium nitroprusside |
| Bilirubin | diazonium salt (2,4 dichloroaniline) | 2,4 dichlorobenzene amine diazonium salt |
| Urobilinogen | p-diethylaminobenzaldehyde | p-diethylaminobenzaldehyde |
| Leukocyte | pyrrole amino acid ester, diazonium salt | pyrrole amino acid ester, diazonium salt |
| Nitrite | p-arsanilic with a quinolin reagent | p-arsanilic acid-N-ethylenediamine, tetrahydroquinoline |
| Specific gravity | bromthymol blue, poly (methyl vinyl ether/maleic anhydride), sodium hydroxide | bromthymol blue, poly (methyl vinyl ether/maleic anhydride), sodium hydroxide |
| Blood | diisopropylbenzene dihydroperoxide, tetramethylbenzidine | diisopropylbenzene dihydroperoxide, tetramethylbenzidine |

For all pairs, a kappa and a weighted kappa value were computed to determine the level of association (kappa measures are not affected by zero sum columns or rows). The former is a binary test, determining association based on how many readings are on the diagonal (and hence matching between

pairs) versus how many are off the diagonal (and hence not matching between pairs). The latter assigns weights to values which are non-matching (not on the diagonal), decreasing the measure of association for values which are further from the diagonal. Fleiss-Cohen weights were used in the weighted kappa computation.

The Clarity test strips offered a higher measurement resolution than the Clinitek Analyzer. For example, when measuring the mg/dL of protein, the Clarity strips offered the following incremental readings: negative, trace, 30, 100, 300, and 2000+. The Clinitek Analyzer offered the following condensed reading scale: negative, trace, 30, 100, and ≥ 300 . In this case, the readings from the Clarity test strip which read either 300 or 2000+ were consolidated under the single category of ≥ 300 . Data was consolidated in this manner for all instances when the resolution of the Clinitek Analyzer was less than that of the Clarity test strip; consolidations are not noted in this manuscript.

Although the compounds are related, structural differences exist for the chemical constituents included in the products that are associated with the measurement of pH, bilirubin,

Table 2. Sensitivity of Bayer Multistix and RAC Medical Clarity

| Test Pad | Sensitivity | |
|---------------------------|-----------------|---------------------|
| | Bayer Multistix | RAC Medical Clarity |
| Urobilinogen (mg/dL) | > 0.2 | 0.2-1.0 |
| Bilirubin (mg/dL) | 0.4-0.8 | 0.2-0.5 |
| Ketone (mg/dL) | 5-10 | 5-10 |
| Blood (Ery/ μ L) | 5-20 | 5-15 |
| Protein (mg/dL) | 15-30 | 15-30 |
| Nitrite (mg/dL) | 0.06-0.1 | 0.08-0.1 |
| Leukocytes (Leu/ μ L) | 5-15 | 5-15 |
| Glucose (mg/dL) | 75-125 | 50-100 |
| Specific gravity | --- | --- |
| pH | --- | --- |

Table 3. Summary of kappa values

| Urine test | kappa value | Two-sided <i>p</i> -value |
|------------------|-------------|---------------------------|
| Leukocytes | 0.0269 | 0.5947 |
| Nitrite | 0.8737 | <0.0001 |
| Urobilinogen | 0.0021 | 0.7439 |
| Protein | 0.3349 | <0.0001 |
| pH | 0.4493 | <0.0001 |
| Blood | 0.3000 | <0.0001 |
| Specific gravity | 0.2823 | <0.0001 |
| Ketone | 0.4538 | <0.0001 |
| Bilirubin | 0.0099 | 0.2033 |
| Glucose | 0.6450 | <0.0001 |
| Color | 0.0000 | 0.0000 |

Table 4. Summary of recommendations

| Urine test | Recommendation |
|------------------|--|
| Nitrite | The Multistix and Clarity strips consistently generate the same results and may be used interchangeably for this test. |
| Leukocytes | The Multistix and Clarity test strips are not able to consistently generate the same results and should not be used interchangeably for these tests. |
| Urobilinogen | |
| Protein | |
| pH | |
| Blood | |
| Specific gravity | |
| Ketone | |
| Bilirubin | |
| Glucose | |
| Color | |

and nitrite. It is not known if the structural differences would alter reactivity that could impact the comparability of results in these three categories (see Table 1 for reagent comparisons and Table 2 for the sensitivities of both products).

For the chi-square and Fisher's Exact tests, the null hypothesis of 'no association between testing strips' was tested. Accepting the null hypothesis implies that there is not enough statistical evidence to prove that there is a significant association between the two tests.

The kappa and weighted kappa tests will provide a value between -1 and +1. This provides a level of association between the output of the two testing strips. A value closer to 0 indicates low association and a value closer to one indicates a high association.

RESULTS

With the inability of the chi-square or the Fisher's Exact to accept zero-value rows or columns, these tests were ultimately eliminated as robust measurements of reproducibility for this test. The kappa test was selected over the weighted kappa as a more significant measure of reproducibility, given the binary result expected from the comparison (identical or not identical).

It was determined that there was a lack of statistically significant agreement between the results of both products and therefore concluded that both the Multistix and Clarity cannot be used interchangeably. See Table 3 for a summary of output statistics. See Table 4 for a summary of conclusions.

DISCUSSION

This study suggests that Multistix and Clarity urine strips do not consistently produce the same measurements when used with the Clinitek Analyzer. The products should not be used interchangeably as aids in the diagnosis and monitoring of various disease states.

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