Analytical Comparison Between Point-of-Care Uric Acid Testing Meters

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ABSTRACT

Background: Gout is a chronic, painful, debilitating form of arthritis resulting from elevated levels of serum uric acid (sUA), termed hyperuricemia. Hyperuricemia is caused by either overproduction or, more commonly, inadequate excretion of uric acid. Resultant monosodium urate crystal deposition in joints/soft tissue can cause attacks of severe pain, swelling, and inflammation (ie, flares), as well as the development of tophi. A key goal in gout treatment is achievement of sustained lowering of sUA. A point-of-care (POC) test meter that gives accurate and reliable sUA measurements may have the ability to improve patient care through more frequent testing and improving individualized gout management. Such a device can provide a convenient and rapid measure of a patient's sUA levels to monitor and immediately adjust therapy to achieve sUA targets recommended in international guidelines. In addition, a device for home use could enhance patient disease understanding and may promote treatment compliance.

Methods: 5 commercially available uric acid meters were acquired (UA*Sure*®, BeneCheck™ Plus, Kernel MultiCheck, EasyTouch® GU, and HumaSens^{plus}). All devices were CE marked and approved for European market use only. Analytical performance in all experiments was determined using a single batch of manufacturer test strips. Precision characteristics of each meter were identified by using each device to measure the same finger prick blood samples using 6 replicates taken from 3 healthy volunteers repeated over 3 consecutive days. Meters identified with a precision coefficient of variation (CV) <17% then had accuracy determined by comparing sUA measurements with a laboratory uricase reference method, as well as the linearity of measurement determined by blood spiking with known UA concentrations. Ease of use observations were also made on each instrument.

Results: Performance of the UA*Sure* device was found to be suboptimal from precision and ease-of-use perspectives, due to difficulty experienced in obtaining sUA readings. Ease of operation of a POC meter is essential to ensure successful adoption by patients, and so, this meter was not evaluated further. The Kernel and EasyTouch meters, which in appearance seem to be similar devices, demonstrated CVs of 25.9% and 27.2%, respectively. Due to the high CVs these 2 meters were discontinued from further evaluation. Both BeneCheck and HumanSens^{plus} had acceptable precision values across the 54 samples measured (CVs: 9.5% and 11.5%, respectively). In 3 healthy volunteers the BeneCheck and HumanSens^{plus} meters gave sUA values that were concordant with the uricase test (mean accuracy of 103% and 107%, respectively) and had averaged spiked blood recoveries across 4 sUA concentrations of 114% and 129%, respectively.

Conclusion: The HumaSens^{plus} and BeneCheck meters were easy to use and have appropriate analytical characteristics to allow reliable sUA monitoring. These POC uric acid testing meters may help with detection of hyperuricemia, and thereby assist in the assessment of urate-lowering therapy effectiveness, achievement of target sUA levels, and potentially preventing complications of hyperuricemia and gout.

BACKGROUND

- Gout, the most common form of inflammatory arthritis, is a urate crystal deposition disease caused by the metabolic disorder hyperuricemia (defined typically as serum uric acid [sUA] >6.8 mg/dL)[1]
- Hyperuricemia leads to deposition of monosodium urate crystals in musculoskeletal structures (eg, joints), kidneys, and other connective tissues, leading to acute gout flares, painful and disfiguring tophi, as well as kidney stones and uric acid nephropathy[2]
- Gout is a chronic, progressively degenerative disease that can manifest and worsen even when a patient is asymptomatic and not experiencing flares; if not appropriately treated, joint destruction, bone erosion, and kidney damage may result[3]
- A key goal in the treatment of gout is to lower sUA levels to <6.0 mg/dL (<5.0 mg/dL in certain populations, eg, tophaceous gout)[4,5]
- A point-of-care (POC) test meter can provide a convenient and rapid measure of a patient's sUA levels to monitor and adjust therapy to achieve sUA targets recommended in international guidelines[4,5]

OBJECTIVE

- The objective of this study was to compare the precision and accuracy of 5 commercially available POC uric acid testing meters available in Europe

METHODS

- 5 commercially available uric acid meters were acquired: UA*Sure*® (Apex Biotechnology); BeneCheck™ Plus (General Life Biotechnology Company Ltd); Kernel Multi Check (U R Diagnostics); EasyTouch® GU (Bioptik Technology); and HumaSens^{plus} (Human).
- All devices were Conformité Européenne (CE) marked and approved for European market use only
- Key technical characteristics of each POC meter are shown in **Table 1**

Table 1. Technical Characteristics of POC UA Testing Meters

	 EasyTouch GU	 BeneCheck Plus	 HumaSens^{plus}	 UA*Sure*[a]	 Kernel Multi Check
Testable analytes	G, UA	C, G, UA	C, G, UA	UA	C, G, UA
Blood required, µL	4	1.0–1.5	1.0	4–6	≤4
UA test time, sec	20	15	15	30	20
UA range, mg/dL	3–20	3–20	3–20	3–20	3–20
Memory capacity	100 tests	50 tests	50 tests	50 tests	50 tests

G, glucose; UA, uric acid; C, cholesterol.
[a]UA*Sure* not evaluated further.

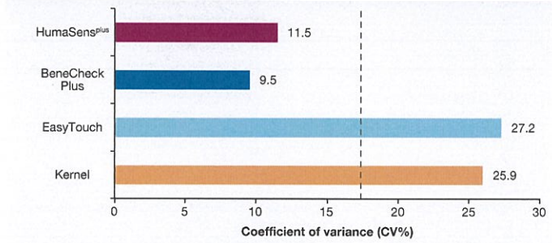
- Analytical performance in all experiments was determined using a single batch of manufacturer test strips for each device
- Precision measurement was determined by using each device to measure sUA from the same finger prick blood samples using 6 replicates taken from 3 healthy volunteers repeated over 3 consecutive days for a total of 54 replicates/device
- Per the recommendation of the College of American Pathologists (CAP), meters identified with a precision coefficient of variation (CV) <17% then had their accuracy determined; those with CV ≥17% were not tested further
- Accuracy of each device was determined by measuring sUA in 3 replicates of finger prick blood samples taken from 3 healthy volunteers repeated over 3 consecutive days, for a total of 27 replicates/device
  - sUA measurements compared with those using a laboratory uricase reference method, performed as per manufacturer's instructions (Sigma Aldrich, UK)
- Linearity of measurement was determined with each device from 6 replicate sUA measurements after spiking blood with 2, 4, 6, or 8 mg/dL UA concentrations
- Subjective ease of use observations were also made on each instrument, based on:
  - How well the supplied information describes the procedure and the use of the test result
  - How well the packaging and inserts help patients to actually start using the kit
  - How confident the end user can be that all required kit pieces and instructions are in place

RESULTS

Precision Measurements

- The UA*Sure* meter had a lengthy start-up time, and reliable results were difficult, even after multiple attempts over several days (perhaps due to the larger blood volume required compared with the other devices)
  - As a result, the meter was not evaluated further
- The Kernel Multi Check and EasyTouch GU meters demonstrated CVs of 25.9% and 27.2%, respectively, did not meet the standard 17% CV threshold, and were not tested further (**Figure 1**)
- Both the BeneCheck Plus and HumaSens^{plus} meters had acceptable precision values across the 54 samples measured (CVs: 9.5 and 11.5%, respectively)

Figure 1. Precision of POC UA testing meters

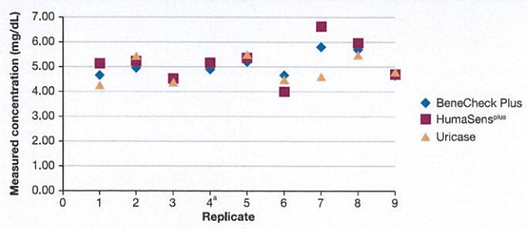


Dashed line represents precision cutoff of CV 17%, as recommended by College of American Pathologists; values greater than 17% represent non-acceptable precision.

Accuracy of BeneCheck Plus and HumaSens^{plus} POC meters

- Accuracy of the BeneCheck Plus and HumaSens^{plus} meters was tested using 9 replicates from 3 volunteers over 3 days and comparing the results with those using a laboratory uricase method (**Figure 2**)

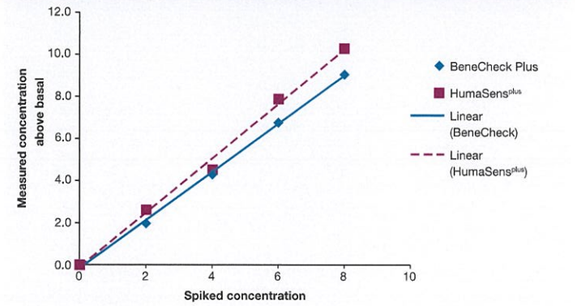
Figure 2. Accuracy of POC UA testing meters vs reference standard (uricase)



Each data point represents mean of 3 replicates for each individual.
[a]No uricase result for replicate 4 due to unacceptable precision.

- Mean accuracy was 103% and 107%, respectively, compared with the uricase method
- Linearity of both POC meters was also determined, with averaged spiked blood recoveries across 4 sUA concentrations of 114% and 129% for BeneCheck Plus and HumaSens^{plus}, respectively (**Figure 3**)
- Both meters gave linear responses from ~6 mg/dL UA (unspiked blood) to ~16 mg/dL

Figure 3. Linear response of BeneCheck Plus and HumaSens^{plus} POC meters to added UA



CONCLUSIONS

- BeneCheck Plus and HumaSen^{plus} meters were easy to use, with appropriate precision and accuracy characteristics to allow reliable sUA monitoring
- UA*Sure*, Kernel Multi Check, and EasyTouch GU POC meters did not meet precision or accuracy standards and/or their ease of use was not acceptable
- Reliable POC uric acid testing meters may assist people with hyperuricemia or gout in the assessment of urate-lowering therapy effectiveness, achievement of target sUA levels, and potentially prevent complications of hyperuricemia and gout
- A POC test meter that gives accurate and reliable sUA measurements may improve patient care by enabling more frequent testing and improving individualized gout management
- A device for home use could enhance patients' understanding of the disease and may promote treatment compliance

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Disclosures

Jonathan Paraskos, Zsofia Berke, Jason Cook, Martin Braddock, Adam Platt, and Glen Hughes are employees of AstraZeneca. Jeffrey N. Miner is an employee of Ardea Biosciences, a wholly owned subsidiary of AstraZeneca.

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