Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 7 (2017) 50–53

Contents lists available at ScienceDirect

Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health

journal homepage: www.elsevier.com/locate/preghy

Visual or automated dipstick testing for proteinuria in pregnancy?

Mauricio E. Correa [a,b], Anne-Marie Côté [a,c], Dane A. De Silva [a], Li Wang [d], Prianthiny Packianathan [e], Peter von Dadelszen [a,f,g], Laura A. Magee [a,f,g,*]

[a] Department of Obstetrics and Gynaecology, University of British Columbia, 4500 Oak Street, Vancouver, BC V6H 3N1, Canada
[b] Department of Obstetrics and Gynaecology, Universidad Austral de Chile, Simpson 850, Valdivia, Chile
[c] Department of Medicine, Université de Sherbrooke, 3001, 12e Avenue Nord, Sherbrooke, QC J1H 5N4, Canada
[d] Department of Pathology and Laboratory Medicine, Children's & Women's Health Centre of British Columbia and the University of British Columbia, 4500 Oak Street, Vancouver, BC V6H 3N1, Canada
[e] Department of Obstetrics and Gynaecology, University Hospitals Leicester, Gwendolen Road, Leicester LE5 4PW, UK
[f] Molecular and Clinical Sciences Research Institute, St. George's, University of London, UK
[g] Child and Family Research Institute, University of British Columbia, 950 West 28th Avenue, Vancouver, BC V5Z 4H4, Canada

ARTICLE INFO

Article history:
Received 20 October 2016
Received in revised form 11 January 2017
Accepted 12 January 2017
Available online 23 January 2017

Keywords:
Pregnancy
Preeclampsia
Proteinuria
Dipstick

ABSTRACT

Objectives: To compare the Multistix 10SG/visual-read with two automated methods (Multistix 10SG/Clinitek 50 and Chemstrip 10A/Urisys 1100) to detect significant proteinuria among high-risk pregnant women.
Study design: Prospective cohort study at British Columbia Women's Hospital & Health Centre, Vancouver, Canada.
Main outcome measures: Diagnostic accuracy determined by sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR−).
Results: 303 (89.6%) of 338 women had a urine sample tested by all three dipstick methods. 196 samples (64.7%) were collected in the morning (subsequent to their first void) and from outpatients. 107 samples (35.3%) were from inpatients at various times throughout the day. A PrCr ⩾30 mg/mmol was present in 46 (15.2%) samples. The sensitivity for proteinuria was higher with Multistix 10SG/Clinitek 50 (65.2%) than with Multistix 10SG/visual-read (41.3%, $p < 0.001$) or Chemstrip 10A/Urisys 1100 (54.3%, $p = 0.06$). Specificity was >90% for all methods studied, although it was highest for Multistix 10SG/visual-read (98.4%) compared with either Multistix 10SG/Clinitek 50 (92.6%, $p < 0.001$) or Chemstrip 10A/Urisys 1100 (95.7%, $p = 0.04$). For all methods, LR+ was good-excellent (>5), but LR− poor-fair (>0.20). 29 samples were discordant for proteinuria between methods. 28/29 women had negative proteinuria by Multistix 10SG/visual-read, but at least 1+ proteinuria by an automated method; 17/28 were false positives and 11/28 true positives.
Conclusions: Automated dipstick methods are more sensitive than visual urinalysis for proteinuria, but test performance is still only poor-fair as a 'rule-out' test for proteinuria. Whether the enhanced sensitivity would be worth the false positives, cost, and personnel training remains to be determined for detection of low-level proteinuria in pregnancy.

1. Introduction

The detection of proteinuria is a key aspect of maternity care. Proteinuria is one of the most common manifestations of pre-eclampsia, and along with hypertension, is the criterion that all guidelines agree defines pre-eclampsia, the hypertensive disorder associated with the greatest maternal and perinatal risks [1].

There is no reliable strategy available for proteinuria screening among pregnant women. Given its low cost and ease of use; proteinuria screening by dipstick urinalysis is currently the most common method used among women at low or increased risk of pre-eclampsia, and this approach is recommended by international guidelines [2–5]. Different studies have shown poor sensitivity of visual-read dipstick methods for identification of significant proteinuria [6], and this has led dipstick manufacturers to pursue

* Corresponding author at: Department of Obstetrics and Gynaecology, St. George's, University of London, Cranmer Terrace, Room J0.27, London, SW17 ORE, UK.
E-mail address: LMagee@sgul.ac.uk (L.A. Magee).

http://dx.doi.org/10.1016/j.preghy.2017.01.005
2210-7789/

automated readers in an attempt to improve accuracy [2,7]. Although one international guideline recommends that automated readers be used [3], there are limited data to support this approach. We previously reported similar performance of visual- and automated-read urinary dipsticks to identify ⩾0.3 g/d proteinuria in a sub-cohort of high risk pregnant women; however, it is possible that the automated-read dipstick that we used (i.e., the Chemstrip 10A and Urisys 1100 reader) may not be the most sensitive of automated-read strips on the market, and this could have biased our results [7].

This study focused on comparison of dipstick methods in a high-risk population of pregnant women, with significant proteinuria defined as a protein:creatinine ratio of ⩾30 mg/mmol. We compared the ability of the same visual-read dipstick used in our previous study (i.e., Multistix 10SG) to detect significant proteinuria, compared with both the Chemstrip 10A/Urisys 1100 reader and the Multistix 10SG/Clinitek 50 reader.

2. Materials and methods

This prospective cohort study took place at British Columbia Women's Hospital & Health Centre in Vancouver from April 14, 2013 to June 4, 2014. This tertiary centre is the largest maternity care centre in Canada with over 7000 deliveries annually. The study was approved by the University of British Columbia's Clinical Research Ethics Board (H10-02691) as a quality improvement project. Participants were pregnant women who were either outpatients (who were consecutively recruited from the internal medicine, high-risk obstetrics, maternal-fetal-medicine, and diabetes ambulatory clinics) or inpatients (admitted from the assessment room where they were seen for evaluation of hypertension).

As part of normal clinical care, random midstream urine samples were collected from consecutive pregnant women. Each sample was split into three aliquots for analysis. The first two aliquots were used by the clinical staff and the third by the laboratory staff.

At point-of-care, regular obstetric clinic and hospital staff used the first urine aliquot to identify proteinuria by using Multistix 10SG/visual-read test strips (Siemens Healthcare Diagnostics, Inc., Tarrytown, NY). These Multistix 10SG strips categorize proteinuria as negative/trace (<0.3 g/L), 1+ (0.3 g/L), 2+ (1.0 g/L), 3+ (3.0 g/L), or 4+ (20 g/L). Immediately after the visual analysis, the second aliquot was used to assess proteinuria using the automated-read Multistix 10SG with the Clinitek 50 strip reader (Siemens Healthcare Diagnostics, Inc., Tarrytown, NY); as for the visual read, proteinuria was classified as negative/trace (<0.3 g/L), 1+ (0.3 g/L), 2+ (1.0 g/L), 3+ (3.0 g/L), or 4+ (20 g/L). Clinicians involved in the care of the women were masked to the automated-read results.

In the hospital laboratory where the third aliquot of urine was sent, laboratory staff assessed proteinuria using automated-read Chemstrip 10A test strips and the Urisys 1100 analyzer (both Roche Diagnostics, Laval, QC). Chemstrip 10A strips categorize proteinuria as negative (<0.25 g/L), 1+ (0.25 g/L), 2+ (0.75 g/L), 3+ (1.5 g/L), and 4+ (5.0 g/L). All methods consider values of 1+ or more to be 'positive'. Samples with the presence of nitrites by dipstick urinalysis were excluded from the study to minimise any confounding by urinary tract infection.

Also in the hospital laboratory, the third aliquot was prepared for determination of the protein:creatinine ratio (PrCr), our standard for determination of proteinuria; this practice is consistent with international guidelines [1–5] that have presented PrCr as an alternative to the traditional 24 h urine collection given its time consuming nature to collect and its substantial inaccuracy [8]. The urine aliquot was then centrifuged at a speed of 1500 rpm per 5 min, and later tested for protein and creatinine concentrations (and then the PrCr calculated) in batches on an automated analyzer (VITROS 5600, ortho-Clinical Diagnostics, Rochester, NY). Urine protein was measured using a user-defined assay with pyrogallol red reagent (Randox Laboratories, Crumlin, UK); the assay's limit of detection is 0.01 g/L with a CV of 2.99% at a concentration of 0.238 g/L. Protein results below the level of detection were approximated to 0.01 g/L rather than biasing the results by excluding these samples. For urinary creatinine analysis, an amidohydrolase enzymatic method was used (Ortho CREA (IDMS) slides); the limit of detection of this assay is 0.106 mmol/L, with CV of 2.0% at a concentration of 5.3 mmol/L.

2.1. Data analysis

Diagnostic accuracy was determined by calculating sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR−); LR+ and LR− were interpreted as excellent (>10 or <0.10, respectively), good (5.1–10 or 0.10–0.19) or fair-poor (2.0–5.0 or ⩾0.2, respectively) according to accepted standards [9]. The diagnostic accuracy values were calculated with 95% confidence intervals. Analyses were performed using SPSS 21 (SPSS Inc.). Between-methods results for sensitivity and specificity were compared using the McNemar Test [10,11]. The sample size was calculated with Nquery using the McNemar test for paired proportions. To compare the sensitivity of two tests (visual vs automated-read dipsticks), we needed 29 discordant pairs to demonstrate a statistically significant difference between methods at an alpha level of 0.05 and with power of 80%.

3. Results

Of 517 samples collected from 338 women, we included 303 (89.6%) samples that were both: the last sample taken from each woman and tested by all three dipstick methods. Most samples (196, 64.7%) were obtained from women attending outpatient clinic appointments, and all of these samples were collected in the morning (although they were not first-voided samples). The remaining 107 samples (35.3%) were obtained from inpatients and the samples were collected at various time points throughout the day.

The prevalence of a PrCr ⩾30 mg/mmol in this cohort was 15.2% (46/303 samples). The median (IQR) PrCr was 12.7 mg/mmol (9.0, 21.6).

Table 1 shows that the sensitivity for detection of proteinuria varied between dipstick/dipstick reader combinations. The sensitivity for proteinuria was higher with the Multistix 10SG/Clinitek 50 (65.2%) than with the Multistix 10SG/visual-read (41.3%, $p < 0.001$) or the Chemstrip 10A/Urisys 1100 (54.3%, $p = 0.06$). However, all sensitivities were <70%. Specificity was >90% for all methods studied, although it was highest for the Multistix 10SG/visual-read (98.4%) compared with the Multistix 10SG/Clinitek 50 (92.6%, $p < 0.001$) or the Chemstrip 10A/Urisys 1100 (95.7%, $p = 0.04$). The LR+ (point estimate and lower limit of the 95% CI) was good-excellent (i.e., >5.0) for all methods, with the highest value for the Multistix 10SG/visual-read (26.5, 95% CI 9.5, 74.5) compared with the Multistix 10SG/Clinitek 50 (8.8, 95% CI 5.5, 14.3) or the Chemstrip 10A/Urisys 1100 (12.7, 95% CI 6.7, 24.0). The LR− (point estimate and lower limit of the 95% CI) was poor-fair for all methods (i.e., >0.2).

There were 29 women with urine samples that were discordant for dipstick proteinuria between methods. One woman had a positive result by Multistix 10SG/visual-read and Multistix 10SG/Clinitek 50, but a negative result by Chemstrip 10A/Urisys 1100. The other 28/29 women had negative results by Multistix 10SG/visual-read, but at least 1+ proteinuria by either the Multistix