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Proteinuria screening using sulfosalicylic acid: Advantages of the method for the monitoring of prenatal consultations in West Africa

Summary

Screening for proteinuria is widely recommended in the monitoring of pregnancy in order to detect preeclampsia. The method often used in primary health care centers (urine heated with acetic acid) has often attained results of over 50% positive cases. This result indicates a considerable lack of specificity outside highly endemic, for urinary schistosomiasis areas. The sulfosalicylic acid test (SSA) represents a simple, reliable and inexpensive alternative. In order to validade this procedure in the conditions of a primary mother and child health (MCH) center, results of the SSA method were compared with standard commercial strip tests a. in a well equipped Swiss laboratory, b. in a school setting in Northern Cameroon. The proportion of agreement between the two methods was 82% (CI 66–98) and 90% (CI 83–96) respectively. The relatively easy implementation of the SSA test in a MCH center in an urban area in Southern Mali lead to results more compatible with what was expected epidemiologically (less than 5% from positive to highly positive results). This experiment confirms that the SSA technique is a simple method, easy to demonstrate and implement, as well as inexpensive. Consequences for monitoring of pregnancies in such conditions are finally discussed.

Screening for proteinuria is a widely recommended method for the prevention of eclampsia in pregnancy[1]. Unfortunately, the implementation of this test in numerous health centers, especially in West-Africa, can present practical problems which challenge its appropriateness. The technique often used consists of heating the urine in a test tube with acetic acid.

In these conditions, monthly rates of proteinuria were often over 50% in the prenatal consultation registry of a mother and child health (MCH) center in Mali. Such results, within the scope of a specific screening, pose problems. Outside the context of a highly endemic proteinuria due to parasitic infections like urinary schistosomiasis, such results indicate a very serious lack of specificity. Thus, in the reported case, the results were simply ignored by the nursing and medical staff. Neither another test to confirm this result nor a medical follow-up were performed in order to check the clinical context of the proteinuria which was discovered.

Looking to improve the performance of this screening for its feasibility and validity, was studied a very simple method, using sulfosalicylic acid (SSA) as reagent. This technique, derived from the one advocated by the WHO for laboratories in primary care centers[2] was selected because of its good specificity, feasibility, reliability, and low cost.

Material and methods

The SSA method were assessed through repeated measures in the laboratory of a Swiss university hospital, and in the field conditions during a schistosomiasis study in school classes in Northern Cameroon and in a MCH primary health center in Mali. The fresh urine was collected in plastic cups. The validity of the method was estimated through comparison with commercial reagent strips.

Determination with reagent strips

The reference test was the ECUR-3 (Boehringer-Mannheim) strips used according to the manufacturers instructions. The results were given using the following semi-quantitative scale:

(–): absence of proteinuria
(+): slight proteinuria (up to 0.3 g/L)
(++): intermediate proteinuria (0.3–1 g/L)
(+++): strong proteinuria (>1 g/L).

Determination by the sulfosalicylic acid (SSA) method

The pH of the urine was verified using a test strip (PB1) and if above 6, one or two drops of 10% acetic acid was added. 2 ml of 3% sulfosalicylic acid was then added. During the trial stages in the health centers, the method was simplified by systematically acidifying with locally available white vinegar.
A semi-quantitative reading scale is presented in Figure 1 where turbidity (after shaking the test tubes) was evaluated according to the visibility of a black line (Figure) or bold printed fonts while looking through them. In this case, the scale was the same, from left to right, as the one above.
Cost calculations were made based on the market price of a kilogram of sulfosalicylic acid in Switzerland and the locally available consumer goods (vinegar, detergents).

Training of unskilled personnel

The simplified SSA method was taught in a few hours (November 1992) to a volunteer matrone with a basic education but without any technical training, in a MCH center in Sikasso, Mali. The training programme consisted of a demonstration of the manipulations of about 15 samples while the matrone repeated the gestures. She then executed, by herself, the same manipulations of 20 urine samples using the technical chart. Egg whites at several concentrations were used in order to produce an artificially positive urine and to check the reliability of results obtained.

Evaluation of the implementation of the new technique

In November of 1993, the implementation of the SSA technique was evaluated together with its integration into the prenatal monitoring activities. The monthly rates of proteinuria were determined using the health center consultation registries in the MCH centers where the sulfosalicylic acid technique had replaced that of the acetic acid.

Analyses

In all studies, all proteinurias from slight (+) to strong (+++), were considered as a positive result. Two types of analyses were conducted. In the first, the validity of the SSA method was estimated in comparison with the strip test method which was considered as the reference. As the test strip method is also a screening method, it cannot be considered as "a gold standard", but a widely accepted reference.
In the second analysis, it was considered that these two semi-quantitative techniques should be compared between two observers testing the same samples. To test statistically the agreement between these two methods, we used the Kappa method, calculated according to the formula discussed by Grant[3].

Evaluation of the SSA method

The validity of the SSA method was evaluated in two different contexts: firstly, the optimal surroundings of a university hospital in Switzerland; and secondly, during a field study of schistosomiasis in Northern Cameroon. Tables 1 and 2 show the comparative results. Table 3 present the validity indexes

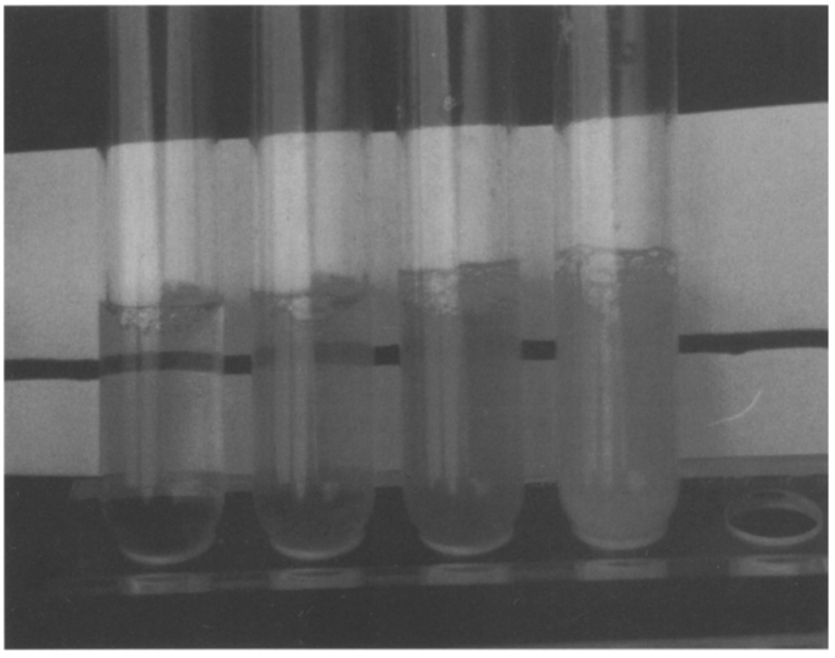

Figure 1. *Visual scale with the SSA methode. The black line is perfectely visible behind the first tube (left; negative result; protein concentration around 0); the line is less visible behind the second tube (weak positive result; protein concentration below (0.3 g/L); the line is quite not visible behind the third tube (positive result; protein concentration between 0.3 and 1g/L); the line is not visible behind the last tube (right; strong positive result; protein concentration of more than 1g/L).*

		Strips reference +	–	
Screening SSA	+	17	3	20
	–	1	87	88
		18	90	108

Table 1. *Comparison of SSA and test strips methods: Swiss hospital.*

		Strips reference +	–	
Screening SSA	+	78	0	78
	–	9	258	267
		87	258	345

Table 2. *Comparison of SSA and test strips methods: schools in Cameroon*

of the SSA method, and the concordance between the two methods, for each of the studies.
The high concordance rate for the two methods can be seen in Table 3. For both studies, the estimate made using Grant's method, which is more suitable here than the Kappa coefficient, shows proportions greater than 80% (the minimum lower limit of the estimation being 66% for the laboratory study). In the school study in Cameroon, the high prevalence of proteinuria was associated with urinary schistosomiasis. Given the laboratory conditions in Geneva, the SSA screening identified a larger number of positive results than the test strip method, which corresponds to a lack of specificity of the method in these conditions. For this reason, and because of the absence of pathological consequencies of the low proteinuria levels, we adopted, for field application in prenatal consultations in Mali, a higher level of detection based on the degree of turbidity (see Fig. 1).

Studies and implementation of the technique in Mali

In the MCH center in Mali, 80 urine samples were tested from pregnant women during a prenatal check-up. The urine readings were done separately for each method, at two different times. Five urine samples were found positive (6.2%) with both methods, no discordance at all was observed between the two methods. Due to the strong proportion of alkaline urine (47/80:59%), it was decided to acidify systematically the urine

	I. Swiss hospital Estimation	CI 95%	II. Schools, Cameroon Estimation	CI 95%
Sensitivity	94.4%	70.6–99.7	89.7%	80.8–94.9
Specificity	96.7%	89.9–99.1	100.0%	98.2–100.0
Prevalence	16.7%	10.51–24.60	25.2%	20.79–30.2
Predictive positive value	85.0%	61.1–96.0	100.0%	94.2–100.0
Predictive negative value	98.9%	92.9–99.9	96.6%	93.5–98.3
Observed agreement	0.963		0.974	
Agreement due to chance	0.710		0.636	
Kappa coefficient	0.872		0.928	
Kappa standard error	0.096		0.054	
Z	9.08		17.29	
P value	0.0000		0.0000	
Proportion of agreement (Grant)	0.82	0.66–0.98	0.90	0.83–0.96
Positives, strips alone	1 (1%)		9 (3)	
Positives, SSA alone	3 (3%)		0 (0)	

Table 3. *Comparative indices of the SSA and test strips methods.*

with local white vinegar, thus simplifying the teaching of the technique.
The matrone working in the MCH center was then in charge of teaching the method to two of her colleagues (one nurse, one auxiliary). During 1993, the technique was progressively implanted in two other health centers in the city. Figure 2 shows the evolution of the monthly proteinuria rates in the three MCH centers concerned, before and after the introduction of the technique.
In the first center, 1421 prenatal check-ups were registered before the introduction of the new method, between August and November 1992. Of the 1019 (72%) patients having had a urine test, 666 (65%) were considered positive. The percentage decreased sharply after the introduction of the new method. From the point of view of the quality of care, the SSA test allowed the staff to rely on these results of the screening and thus follow more closely the positive patients. One can notice a peak in the detection of the proteinuria (January 1993) which corresponds to a change of the personnel in charge of these analyses; the new technician was in fact not trained in the SSA method.

Costs

The price of a kilo of sulfosalicylic acid is 90.– Swiss Francs which seems to be a maximum on the world market. In the conditions described above, 200 grams are sufficient to supply 3 MCH centers for a full year. This represents 5000 tests for a total of 18.– Swiss Francs (=72 FF, US $13). The price for the equivalent quantity of test strips would have been at least 20 times higher.

Discussion

Like all preventive measures, and particularly within the context of limited professional and material resources, any intervention in the prenatal monitoring program should be analyzed carefully. It would also be advisable to study extensively the place of proteinuria detection during pregnancy as a screening element for the detection of preeclampsia[4].
In fact, any screening program must be critically evaluated, notably: the procedures, costs, the results of its application in a specific epidemiological context, and finally, the impact on the health problem which the screening is presumed to answer. Proteinuria screening of pregnant women ought to be submitted to such evaluations in various contexts. The evaluation criteria should include two levels: results, based on the proportion of women correctly identified and adequately treated or followed-up by health services, and impact; defined here as the proportion of complications avoided, including eclampsia and retarded intrauterine development. From this point ov view, the effectiveness of prenatal proteinuria screening, within the context of West African health services, still needs to be proved conclusively.
Our analysis showed an example of an unsuitable, and potentially harmful, screening technique. The study shows how a basic laboratory in a district health clinic, too often considered an indispensable instrument to all medical activities, can become a weak link in a health care system, as well as be responsible for inappropriate treatment and demotivating the personnel. External quality control, based on surveillance of monthly operating statistics, and internal, centered on the consistency of techniques between lab assistants, would have revealed this problem. In the described case, the adaptation of known techniques using local means allowed the correction of this anomaly. Where this correction is not achievable, one must consider the abolition of an ineffective test. Our experiment shows that simple screening techniques,

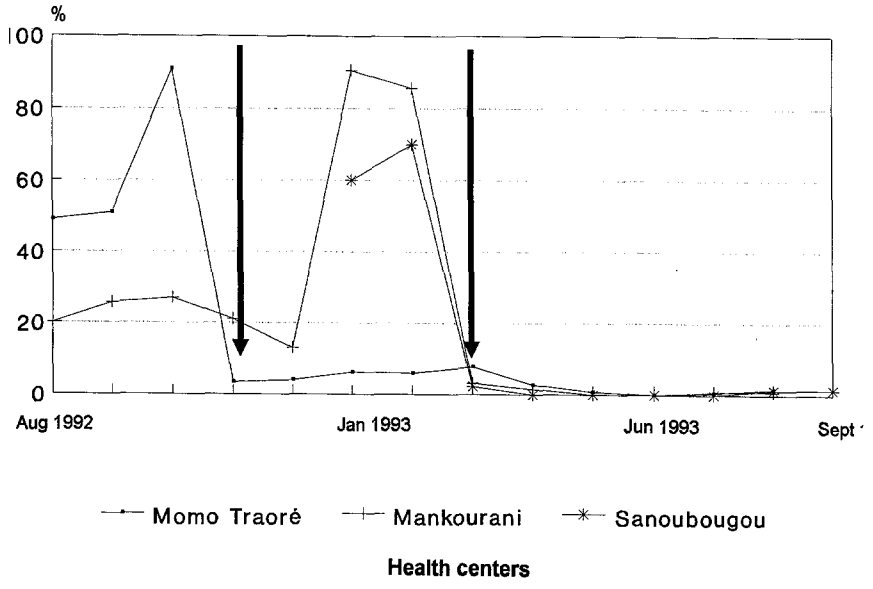

Figure 2. *Prevalence (%) of proteinuria among out-patients (prenatal screening) of three health centers in Sikasso (Mali), between August 1992 and September 1993, before and after the introduction of the SSA technique (⬇).*

though classical, well accepted (even requested), yet non valid, unreliable and certainly ineffective, must be imperatively abandoned, or at least be replaced by a satisfactory alternative. Such screenings generate useless costs, inappropriately mobilize personnel resources, and bring about no improvement in the quality of care to the patient. On the contrary, as the results cannot be taken seriously, they place the patient into the situation of having her condition neglected when she may need effective intervention.

Compared to test strips, the sulfosalicylic acid method demonstrated its validity, ease of execution in laboratory conditions or in the field, and lower cost. Optimal sensitivity of the test can be defined by modifying the detection level using a reading scale based on the turbidity of the solution. The reliability of a large number of field tests does not differ from the conditions of a well-equipped laboratory. Due to its simplicity, the demonstration of the technique to unskilled personnel presents no particular problems. In Mali, the person trained initially was able to transmit the method successfully to her colleagues. The introduction of this new technique in three MCH centers resulted in an important decrease in the number of falsely detected proteinurias during prenatal consultations.

This report showed that it is possible, even in a context with very limited resources, to replace an ineffective method by a better one, equally simple to use, and where the results compare favorably to those of widely accepted standards (test strips).

Zusammenfassung

Proteinurie aus Screeningtest bei Sulfosalicylsäuretherapie: Vorteile bei der Schwangerschaftskontrolle in Westafrika

Während der Schwangerschaft wird ein Screening bezüglich Proteinurie allgemein empfohlen. Die Sulfosalyzilsäurenmethodik (SSA) ist diesbezüglich eine einfache und zuverlässige Methode. In afrikanischen Verhältnissen wird vor allem die Essigsäurenmethodik angewandt. Sie ist jedoch nicht zuverlässig; so waren in einem Gesundheitszentrum in Mali 66% der Resultate positiv. Um die mit SSA erhobenen Resultate zu validieren, wurden sie nicht nur in einer Schule in Kamerun, sondern auch in einem Labor in der Schweiz bestimmt. Die Übereinstimmung der Analyse war hoch. Die Einführung des Harneiweiss-Screenings mittels SSA in einem Gesundheitszentrum in einer Stadt in Mali hat sich seither ebenfalls bewährt.

Résumé

Dépistage de la protéinurie: Intérêt de la méthode de l'acide sulphosalicylique dans une consultation prénatale en Afrique de l'Ouest

Le dépistage de la protéinurie est une mesures de surveillance de la grossesse largement recommandée. La méthode de dépistage à l'acide acétique n'est pas fiable: dans un centre de santé au Mali, 66% des examens étaient positifs. La méthode à l'acide sulfo-salicylique (ASS) représente une alternative simpe et fiable. Nous avons comparé les résultats de la méthode ASS avec des bandelettes réactives: 1. dans un laboratoire en Suisse; 2. en milieu scolaire au Cameroun. La proportion d'accord entre les deus examens était, respectivement: 1. de 82% (66–98); 2. de 90% (83–96). Son introduction dans les Centres de SMI d'une ville du Mali a permis une amélioration durable de la qualité de la surveillance des grossesses. Cette expérience confirme qu'il s'agit d'une méthode simple, facile à démontrer et à réaliser et très bon marché.

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