

Micro-albuminuria analysis and pregnancy An approach to detect placental insufficiency?

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Abstract

Objective: To assess the value of micro-albuminuria analysis (MA) in predicting clinical complications of placental insufficiency in women with no known risk factor. **Study design:** A blind prospective investigation 20–24 weeks into pregnancy in a nulliparous population with no known risk factor. A reactive strip with a positive threshold value of 10 mg/l is used to detect MA. Judgment criteria concerning the progress of pregnancy are based on blood pressure during the 8th and 9th month of pregnancy and on the 2nd day after delivery, on albuminuria analysis in the 8th and 9th month of pregnancy and by the existence of fetal hypotrophy at birth. **Results:** Some 218 patients participated in the investigation. MA was positive in 62 cases (28.4%). Of the 197 births which occurred 54 (27.4%) cases of positive MA, 34 (17.2%) cases presented positive judgment criteria indicating placental insufficiency. The 21 others pregnancies are in course. MA sensitivity was thus 79.4% and specificity 83.4%. Negative predictive value (NPV) was 95.1% and positive predictive value (PPV) 50%. **Conclusion:** Our test is a reliable, simple and easily reproducible indicator of micro-albuminuria. In comparison with other tests it gives a good detection rate of a risk group for complication of placental insufficiency. NPV is excellent, virtually excluding the occurrence of excessive blood pressure or intra-uterine growth retardation. PPV is less good.

Keywords: Micro-albuminuria analysis; Pregnancy; Nulliparous; Placental insufficiency; Aspirin

1. Introduction

Placental insufficiency is the same anatomical pathology which bring about high blood pressure pregnant women and fetal hypotrophy. It is one of the main causes of maternal and fetal death.

Recent studies have shown that low doses of aspirin are very effective in reducing the incidence of pre-eclampsia (80%) and fetal hypotrophy (50%) in high risk populations [1].

Conversely, aspirin has little or no effect on moderate risk patients and it is necessary to use a method to detect high risk groups [2,3]. The most common method is based on obstetrical antecedents. The main drawback of this method is that it does not apply to first births

(nulliparous) where pre-eclampsia and intra-uterine growth retardation (IUGR) are most frequent.

This paper reviews a simple method we have developed for detecting micro-albuminuria 20–24 weeks after amenorrhoea (WA) in nulliparous patients with no known risk factor and then assesses its predictive value.

2. Instrumentation and methods

2.1. Instrumentation

From 1 July 1995 to 31 December 1995, all nulliparous patients attending obstetrical consultations in our unit in their 20th to 24th week of amenorrhoea (WA) were included in our investigation. Nulliparous patients suffering from cardiovascular or renal disease or high blood pressure were excluded. Only nulliparous

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without any antecedent and without any risk factor were included.

2.2. Method

Urine samples were taken during consultations. Micral Test[®] reactive strips (from Boehringer Mannheim Laboratories SA, France) were dipped in the urine for 5 s and interpreted 5 min later by colorimetric reaction. The semi-quantitative immuno-chemical technique provides a range of indicative values (0, 10, 20, 50 and 100 mg/l). For our assessment we considered that 10 mg/l indicated positive MA. All positive results were then assayed in the laboratory by a quantitative immuno-enzymatic process for confirmation.

Pregnancy was monitored without knowledge of the test result. The following data were collected after delivery:

- maternal blood pressure measured during consultations in the 8th and 9th months of pregnancy. High blood pressure was defined by WHO criteria as higher than 140/90 mmHg;
- urine albumin content analyzed during consultations in the 8th and 9th months of pregnancy and considered as positive if any albumin was detected;
- fetal hypotrophia (i.e. birth weight lower than the 10th percentile of the Lubchenko growth curve);
- high blood pressure on the 2nd day after delivery (> 140/90 mmHg).

Presence of at least one of these criteria was considered to indicate pre-eclampsia or IUGR which are complications of placental insufficiency.

3. Results

During the period concerned, 218 nulliparous patients met study inclusion criteria. Micro-albuminuria (MA) was positive in 62 cases, i.e. 28.4%.

Of the 218 patients 197 subsequently gave birth. The others pregnancies are yet in course.

MA was positive in 54 cases out of 197 (27.4%) with 27 positive (high blood pressure or albuminuria in the 8th and 9th months, IUGR, high blood pressure on the 2nd post-delivery day) and 27 negative indications.

MA was negative in 143 cases (72.6%), with seven positive and 136 negative indications.

These data are shown in Table 1. These results enable statistical parameters to be calculated. Thus, for 17.2% placental insufficiency in our population, sensitivity was 79.4%, specificity 83.4%, the negative predictive value (NPV) 95.1% and the positive predictive value (PPV) 50%.

4. Discussion

The histological substratum of placental insufficiency is endothelial in origin, associating disseminated intra-vascular coagulation (DIVC), vasospasms and microangiopathy [4]. Lesions occur early in pregnancy. The symptoms observed are caused by effects on different maternal organs (placenta, blood, heart, brain, liver and kidney). In the kidneys, the effect on glomerular filtration leads to micro-albuminuria. Micro-albuminuria is defined as the presence of albumin in urine at concentrations lower than 200 mg/l [5]. This value is currently accepted for the assessment of the gravity of gestational diabetes [6,7].

We used a blind prospective study. The results of the tests carried out between the 20th and 24th WA were unknown to the practitioners and no change was made in the way pregnancy was subsequently monitored. No specific treatment was given. The relatively small sample of patients (218 over a period of 6 months) is due to the fact that early months of pregnancy are handled by non-hospital practitioners and are only referred to our unit in the 6th month.

Our results are satisfactory and comparable with those of Hasslacher [5]. False negatives (7 cases) concerned two cases with moderate high blood pressure (145/90 and 145/100 mmHg), three very slight cases of albuminuria and two cases with intra-uterine growth retardation (IUGR) (2250 g at 40 WA and 1950 g at 36 WA). In no cases high blood pressure on the 2nd day following delivery patient was considered to have been caused by placental insufficiency.

The 27 false positives always corresponded to MA figures less than 20 mg/l.

Approximately 0.5% of the cases could be explained by cross-reactions with other proteins (hemoglobin, transferrin, ...). Nevertheless the Micral-Test[®] we used seems a good semi-quantitative method for the assessment of urinary albumin concentration [5]. Other tests [8] also based on a colorimetric reaction seem to be satisfactorily sensitive for screening proteinuria.

As to the value of screening placental insufficiency, a literature search seems to show that opinions diverge widely [9–12].

Table 1
Micro-albuminuria in detecting placental insufficiency

Micro-albuminuria placental insufficiency	+	–	Total
+	27	7	34
–	27	136	163
Total	54	143	197

Sensitivity, 79.4%; specificity, 83.4%; positive predictive value, 50%; negative predictive value, 95.1%.

Among all studies reviewed, only one, [11], does not believe that the analysis of micro-albuminuria in urine has any predictive value whatsoever. However, the assays made by this author were at different gestational ages and, additionally, the sample of patients developing pre-eclampsia was small [14] vs. the control population (193 cases). Conversely, the other studies [5,10,12] show that micro-albuminuria assay is a good predictor of the occurrence of placental insufficiency value (particularly negative).

One problem remains, the definition of the normal lower limit for micro-albuminuria.

Some authors [5,13], state that micro-albumin is present physiologically in urine at concentrations less than 20 mg/l. Others [10], state that micro-albumin is not. We personally prefer this latter hypothesis and think that the micro-albumin detected by the Micral Test[®] at its first positive threshold (10 mg/l) is abnormal.

Many screening tests are used for placental insufficiency. Some clinical or biological tests are not satisfactory either because of their low predictive value or due to mediocre feasibility or reproducibility which makes them unsuitable for screening [15,16].

Uterine Doppler between 20 and 24 WA is currently being assessed. Although its predictive value appears to be good in risk populations [17,18], it is not as effective in general and low risk populations [19–21].

Using an approach similar to that adopted for these three latter investigations (blind prospective study, calculations of sensitivity and specificity, NPV and PPV), our results for micro-albuminuria score better for PPV, the most useful parameter for screening. A subsequent phase will consist in assessing the efficacy of prescribing aspirin when MA is positive, as has already been completed for positive uterine Doppler results [22,23].

5. Conclusions

The Micral-Test[®] is a simple, precise, easily reproducible, semi-quantitative test with little multicollinearity for the assessment of micro albuminuria with an apparently good screening value to assess a risk group women for clinical complications of placental insufficiency.

Its excellent NPV virtually excludes the occurrence of placental insufficiency when MA is negative.

Positive values can suggest the use of aspirin-based anti-platelet aggregating treatments.

However, PPV is only around 50% and our sample population was not sufficiently large.

Other studies into micro-albuminuria are necessary to assess its screening value for placental insufficiency fully.

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