SHORT COMMUNICATION/KURZMITTEILUNG

Estimation of Decision Criteria for the Uric Acid Concentration for the Early Diagnosis of Gestosis

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Dedicated to Prof. Dr. M. Knedel on the occasion of his 60th birthday

Summary: An increase of the serum uric acid concentration in pregnant women can indicate an EPH gestosis with a high risk. Above a uric acid level of 270 μmol/l (and of 315 μmol/l after the 32nd. week of pregnancy) the gestosis has become moderate. An increased risk for mother and fetus must then be assumed. This decision point is estimated by comparing three techniques: The ROC-curve-method and the determination of the maximal efficiency and of the maximal information content.

Methods

The uric acid concentration was determined according to Haeckel (8) in 140 sera from 29 pregnant women without gestosis, in 241 sera from 63 women with moderate and in 48 sera from 21 women with severe gestosis. The clinical classification of the gestosis occurred as recommended by Goecke & Schwabe (1). Further details are reported elsewhere (3, 9).

It has been postulated that the uric acid concentration in serum or plasma could play such a role in the diagnosis of gestosis (2, 3). The urate clearance is affected in pregnant women with gestosis leading to an increase of the uric acid concentration in the blood. This rise correlates with the severity of the clinical symptoms (3).

The usual reference value for women of the uric acid concentration in serum cannot be used to differentiate between pregnant women without and with gestosis, since the urate clearance is elevated up to 1.5 times the postpartum value (4). Consequently the serum uric acid concentration is lower than normal in pregnancy. In the second half of pregnancy the urate level slightly rises towards more normal values (3).

The present study was undertaken to determine the decision level of the serum uric acid concentration in pregnant women as a useful aid in the early diagnosis of gestosis. The theory of the diagnostic value of clinical chemical tests (5–7) offers several methods to determine such decision criteria. Since only few comparative studies have been performed with these techniques we have applied three different methods.

Methods

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All groups were divided into 2 parts, one up to the 32nd. week of pregnancy (fig. 1a) and one from the 33rd. week until the birth date (fig. 1b). The prevalence of gestosis was 22.64% (20.85% mild gestosis, 0.85% moderate gestosis, and 0.94% severe gestosis, total number of pregnancies observed 12751 between 1969 and 1977).

The receiver-operating-characteristic (ROC) curve is constructed from

\[ P(\text{T} / \text{D}) = \frac{\text{TP}}{\text{TP} + \text{FN}} \]

and from

\[ P(\text{T} / \text{D}) = \frac{\text{FP}}{\text{TN} + \text{FN}} \]

according to l.c. (5), (7) and (10).

P (T/D) is the sensitivity and P (T/D) equals (1-specificity). TP means true positives, FN false negatives, FP false positives and TN true negatives. The slope of the tangent is calculated by the following formula

\[ P(\text{D}) = \frac{\text{TN} + \text{FP}}{\text{FN} + \text{TP}} \]

Introduction

EPH-gestosis (edema-proteinuria-hypertension gestosis) is a clinical syndrome which can lead to eclampsia, placental insufficiency and finally to intrauterine fetal death. EPH-gestosis can be classified in several stages as recommended by Goecke & Schwabe from the Organisation Gestosis (1): mild, moderate and severe gestosis. Edema, proteinuria and hypertension together are not obligatory for the diagnosis of gestosis. In some cases the differential diagnosis may become difficult especially in mild and monosymptomatic forms. Therefore, other diagnostic parameters are sought to increase the chance for the early detection of a high risk group of pregnant women.

During the first 32 weeks the uric acid concentration remains fairly constant and then starts to rise continuously up to the end of pregnancy.

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number of pregnant women without gestosis divided by the
number of patients with gestosis = a posteriori prevalence).
The efficiency (11) is the sum of true positives (TP) and true
negatives (TN) divided by the sum of all true and false test
results (TP + TN + FN + FP).
The information content I (bit) is calculated from prevalence,
diagnostic specificity and sensitivity using the formula published
by Metz et al. (12).
The a priori prevalence was used to calculate the information
content:
\[
\begin{align*}
\text{Mild gestosis } P (K) & = \frac{2659}{12751} = 0.2085 \\
\text{Moderate gestosis } P (K) & = \frac{108}{12751} = 0.0085 \\
\text{Severe gestosis } P (K) & = \frac{120}{12751} = 0.0094 \\
\end{align*}
\]
Results
ROC-curve
In figure 1 receiver-operating-characteristic (ROC) curves are
shown. The optimal decision criteria is defined as the point
where a tangent with the slope \( P (D)/P (D) \) hits the ROC-curve.
This tangent was graphed for the mild gestosis group. The data
obtained with this technique are summarized in table 1. This
technique could not be applied for the data presented in
figure 1b, because of the uneven characteristics of the ROC-
curve.

Efficiency test
Another procedure to determine decision criteria is to calculate
the efficiency for several uric acid concentrations (7). It indicates
the percent of patients correctly classified (diseased and non-
diseased) (11).
The concentration with the highest efficiency is chosen as the
decision point. The decision criterion with the highest efficiency
is justified (10) because both false positive and false negative
results can have serious consequences for pregnant women (7).

Tab. 1. Diagnostic specificity, sensitivity and efficiency of the uric acid concentration and decision criteria for the early detection of
gestosis.

<table>
<thead>
<tr>
<th>Before the 32nd. week of pregnancy</th>
<th>After the 32nd. week of pregnancy</th>
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</thead>
<tbody>
<tr>
<td>Decision criteria</td>
<td>Diagnostic criteria at the recommended decision</td>
</tr>
<tr>
<td>Determined by</td>
<td>ROC</td>
</tr>
<tr>
<td>ROC curve</td>
<td>212</td>
</tr>
<tr>
<td>ROC curve</td>
<td>268</td>
</tr>
<tr>
<td>ROC curve</td>
<td>310</td>
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</tbody>
</table>

Fig. 1. Receiver-operating characteristic curve. The sensitivity
\( P (T/\bar{D}) \) of the uric acid concentration in sera from preg-
nant women (1a: up to 32nd. week of pregnancy; 1b: from 33rd. week until birth date) is plotted against
\( P (T/\bar{D}) \). Mild gestosis \(-\)-, moderate gestosis \(-\)-, and severe gestosis \(-\)-.
Fig. 2. The efficiency of the serum uric acid concentration dependent on various decision criteria (abscissa) to detect mild (●—●) and moderate (X—X) gestosis up to the 32nd. week of pregnancy. Arrows mark the point, where the efficiency has just reached its highest value.

Fig. 3. The information content of the serum uric acid concentration for the detection of mild gestosis up to the 32nd. week of pregnancy. The moving average was calculated from n = 9.

Fig. 4. The information content (a priori prevalence X—X, a posteriori prevalence ●—●) and the efficiency ○—○ of the serum uric acid concentration for the detection of mild gestosis from the 36th. week of pregnancy until birth date. For the information content a moving average was calculated from n = 9.
Information content

A third method for determining decision points is the information content according to Büttnner (5):

$$I_{xy} = f(P(K), P(T/K), P(T/K'))$$

This information gain by the diagnostic test is derived from the variables of the ROC curve and the prevalence $P(K)$ of the disease to be detected.

The information content related to the uric acid concentration is presented in figure 3–6. Distinct peaks where the information content is maximal can easily be recognized. The decision criteria corresponding to these peaks are also summarized in table 1.

The peak position was independent of whether the a priori or a posteriori prevalence was used (fig. 4). In figure 4 and 6 the information content was compared with the efficiency. In figure 4 both techniques led to different peak values. An explanation for this discrepancy cannot be offered.

Discussion

The ROC-curve technique could only be applied for the first half of pregnancy. Although the decision points for moderate and severe gestosis could hardly be derived from the graph presented in figure 1a, the data corresponded well with those obtained by the other procedures. The efficiency maximum could be recognized for all experimental conditions, but was less precise than with the third method. The calculation of information content appeared to be best suited to estimate the decision criteria for the present purpose, although it may be advisable to apply both techniques.

It could be that a parallelism exists between the uric acid concentration and the risk, in pregnant women, of the development of eclampsia and of fetal distress. However, this hypothesis was not investigated in the present study. We only tried to determine the cut-off point and decision level for the uric acid concentration for the differentiation between pregnant women with and without gestosis.

A uric acid concentration of 220 $\mu$mol/l up to the 32nd week of pregnancy, and of 260 $\mu$mol/l after this period is recommended (tab.1) as the decision point in the differential diagnosis of mild gestosis. The chance of developing a more severe form of gestosis increases with the uric acid concentration.

Above a uric acid level of 270 $\mu$mol/l, or 315 $\mu$mol/l the gestosis has already become moderate. Since the risk for mother and fetus has then also increased, all cases with a uric acid concentration above this level should be observed carefully.

**Fig. 5.** The information content of the serum uric acid concentration for the detection of moderate gestosis up to the 32nd week (· · · · ·) and from the 32nd week (X X X X X) of pregnancy.

**Fig. 6.** Information content (*—^··^··) and efficiency (X—X) of the uric acid concentration for the detection of severe gestosis up to the 32nd week of pregnancy.

References


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