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Alpha-foetoprotein in threatened abortion

by

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The prognosis of threatened abortion is still an unsolved problem, nor is it often easy to determine its cause, at least before the abortion occurs. The methods hitherto used have been confined to determining the hormonal production of the trophoblast (HCG, HPL, E_3) by direct or indirect methods such as the study of the vaginal receptor. One new prospect could be that of a non-trophoblastic index, such as alpha-foetoprotein, which is produced by the embryonic foetal liver and by the yolk sac.

The purpose of this study is to evaluate the validity of the determination of alpha-foetoprotein as a prognostic index in threatened abortion and to make a comparison with the data already present in the literature.

MATERIAL AND METHODS

Plasma alpha-foetoprotein was determined in 108 pregnant women between the 7^{th} and 21^{th} week, clinical signs of threatened abortion being present.

At the same time, a control group of 123 pregnant women were examined in which gestation proceeded entirely normally to term.

The plasma determinations were done by the radio-immunological method (double antibody) using the kit made available by the Sorin company.

RESULTS

Concentration of alpha-foetoprotein in normal pregnancies

Because of the skewed distribution of results, was not calculated the mean and standard deviation but was used a non-parametric method based on centiles, the arithmetic mean being unduty increased by few wildly high results. The centiles were approximated in the least square by a polynomial of 3^{rd} degree.

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Concentration of alpha-foetoprotein in threatened abortion

During the first five months of pregnancy (below 21 weeks) in the pregnant women who overcome the threatened abortion the concentration of alpha-foetoprotein was almost always between the 10th and the 90th centile (Tab. I).

In those cases which ended in spontaneous abortion the levels of alpha-foetoprotein were more frequently found to be below the 10th centile or above the 90th centile. This trend is more evident only after the 12th week of pregnancy, when the abnormal level of alpha-foetoprotein is associated with death of embryo in about 73% of cases (Tab. 2).

Tab. 1. *Pregnant women who overcome the threatened abortion.*

AFP	below 12 weeks	13-15 weeks	16-18 weeks	19-21 weeks
N. of values below 10th centile	7	4	0	0
N. of values between 10th and 90th centile	12	17	8	4
N. of values above 90th centile	1	1	0	0

Tab. 2. *Pregnant women who had spontaneous abortion.*

AFP	below 12 weeks	13-15 weeks	16-18 weeks	19-21 weeks
N. of values below 10th centile	21	13	12	9
N. of values between 10th and 90th centile	23	5	2	6
N. of values above 90th centile	6	6	1	9

DISCUSSION

Seppälä & Ruoslahti found that after the 13th week of pregnancy, abortion occurred much more frequently in pregnant women with abnormal serum levels of alpha-foetoproteins, that low levels indicated a condiction affecting the embryo and that high concentration were associated with intra-uterine death.

In pregnancies that developed normally, the level of alpha-foetoprotein before the 13th week exceeded that of non-pregnant subjects only in 50% of cases, and in 30% of cases in threatened abortion ([1]).

In a subsequent investigation the same authors reported that the increase in serum alpha-foetoproteins was associated with death of the product of conception in 70% of cases; that in high risk pregnancies danger to the foetus could be expected in 60% of cases with this dosage and that in 92% of cases a normal level of alpha-foetoprotein corresponded to normal foeto-placental function. When the alpha-foetoprotein exceeds 800 ng/ml there is danger for the foetus or intra-uterine death in 85% of cases; when it exceeds 1000 ng/ml death always occours. This increase preceded the death of the foetus ([2]).

Cohen, Graham & Lau concluded, with the « counter-immunoelectrophoresis » method, that death or foetal illness occurs in all cases in which the alpha-foetoprotein exceeded 250 ng/ml ([3]).

Seller, Creasey & Alberman studied the levels of alpha-foetoprotein in the amniotic fluid in 54 cases of unavoidable spontaneous abortion. If serious abnormalities of the chromosomes or of the neural tube were not present, the concentration of alpha-foetoproteins was always less than 50 ng/ml. In the opposite case the latter was greatly increased ([4]). Grella, Ros, Manganelli & Cer-

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ruti found that in case of threatened abortion with an unfavourable result the alpha-foetoprotein presented values of less than normal when the plasma and urinary level of HCG was still normal. On the other hand, in the case of treatened abortion with a favourable result, alpha-foetoprotein always remained normal.

In case of foetal death, as described by Seppälä & Ruoslahti, there was a sudden and marked increase of alpha-foetoprotein followed by a fall ([5]). Garoff & Seppälä in 112 women with threatened abortion observed that maternal alpha-foetoprotein level was raised in 5,4% of cases, all of them ending in abortion or foetal death ([6]).

Higher maternal alpha-foetoprotein levels were subsequently observed by Seppälä when foetal death occurred during the second trimester: in 12 out of 23 cases the alpha-foetoprotein concentration was above the upper normal level ([7]).

Rodeck, Campbell & Biswas found that in pathological pregnacies the alpha-foetoprotein values fell below the 5th percentile much more often than in phisiological pregnancies, but that ¾ of the values obtained in the pathological pregnancies fell within the 90th percetile. No correlation was found between plasma alpha-foetoprotein and foetal risk, decelerated intra-uterine growth and perinatal mortality. They concluded that alpha-foetoprotein is not valid test for predicting a healthy foetus ([8]).

Kunz & Keller compared the predictive value of alpha-foetoprotein in 65 cases of threatened abortion, between the 6th and the 20th week of pregnancy, with estimation of HCG, HPL, progesterone and oestradiol. Values of alpha-foetoprotein below the normal range predicted abortion in 38% of patients while normal values confirmed the continuation of pregnancy with an accuracy of 30%. They affirme that alpha-foetoprotein is an unsuitable method for this purpose ([9]).

Morin determinated the maternal plasma alpha-foetoprotein level in 18 cases of threatened abortion: in the 4 cases ended in spontaneous abortion the alpha-foetoprotein was within the normal range ([10]).

CONCLUSIONS

The present investigation, carried out on a larger number of cases than that referred to in previous publications ([5,11]), confirms the value of a finding of alpha-foetoprotein in making a prognosis in threatened abortion, but only if the gestational age has exceeded 12 weeks. Abnormally low or abnormally high values should also be considered pathological; corresponding clinical signs are more often found at the 2nd trimester of pregnancy.

SUMMARY

The maternal plasma alpha-foetoprotein and the outcome of 108 cases of threatened abortion were compared. The level of this protein was more frequently below the 10th centile or above the 90th centile in the cases ended in spontaneous abortion. The prediction of the outcome of pregnancy has clinical value only after the 12th week.

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