Pregnancy-associated plasma protein A in pregnancy-related gynaecologic emergency

J. Sjöberg
Department I of Obstetrics and Gynaecology, Helsinki University Central Hospital, 00290 Helsinki 29, Finland

Serum concentrations of pregnancy-associated plasma protein A (PAPP-A) were measured in patients with pregnancy-related gynaecologic emergencies including ectopic pregnancy (n = 124) and intrauterine abortion (n = 40). The results were compared with those in normal pregnancy (n = 136) and non-pregnant women (n = 460). In ectopic pregnancy and intrauterine abortion, the PAPP-A levels were lower than in normal pregnancy. In patients with a pregnancy-related gynaecologic emergency PAPP-A was undetectable in 82% of the ectopic pregnancies and in 55% of the intrauterine abortions. Considering the frequency of ectopic pregnancy (35.8%) and intrauterine abortion (52.3%) among all patients with pregnancy-related disorders, the likelihood that a pregnant patient with undetectable PAPP-A has an ectopic pregnancy is 30%, and intrauterine abortion is 29%. These results indicate that although PAPP-A levels in ectopic pregnancy and intrauterine abortion are lower than in normal pregnancy, PAPP-A measurement cannot be used to distinguish between ectopic pregnancy and intrauterine abortion.

Key words: PAPP-A/ectopic pregnancy/intrauterine abortion

Introduction
Conflicting reports have been published on the clinical usefulness of circulating PAPP-A levels in ectopic pregnancy (Sinosich et al., 1983, 1985; Bischof et al., 1983). In previous reports concerning ectopic gestation and PAPP-A, the levels were compared with values in normal pregnancy (Sinosich et al., 1985; Bischof et al., 1983). In women with gynaecologic emergencies it is important first to identify pregnancy-related disorders and, if detected, then to distinguish between ectopic and intrauterine pregnancy. In this study concerning patients with gynaecologic emergencies, pregnancy-related disorders were first identified by a highly sensitive and rapid human chorionic gonadotrophin (HCG) test. In those who had a positive test the circulating levels of PAPP-A were measured in order to assess whether or not the levels could be of any further assistance in distinguishing between ectopic pregnancy and intrauterine abortion.

Materials and methods
Patients and samples
Serum samples were obtained from 52 apparently healthy pregnant women during routine antenatal sessions, and from 84 apparently healthy pregnant women on admission for legal abortion on social grounds in order to estimate the normal range of PAPP-A levels in early pregnancy. A total of 667 serum samples were obtained from 624 women of reproductive age admitted to the Departments of Obstetrics and Gynaecology, Helsinki University Central Hospital, Helsinki, Finland and the Jorvi Hospital, Espoo, Finland because of lower abdominal pain and/or uterine bleeding. Of these, 164 women had detectable HCG (>25 IU/l) in serum and 460 had not. The clinical diagnosis of ectopic pregnancy was obtained for 124 of these patients (158 samples), all of whom were HCG-positive. Forty of the HCG-positive patients (49 samples) had threatened or incomplete abortion. Their final diagnosis was verified by histological examination of curettage specimens. The diagnosis of ectopic pregnancy was verified by histological examination of tissue obtained at surgery. Three ectopic pregnancies were in the ovary.

Fig. 1. Comparison of serum PAPP-A levels in ectopic pregnancy, intrauterine abortion and normal early pregnancy. • = ectopic pregnancy, ○ = intrauterine abortion, LMP = last menstrual period, — = detection limit, 10th and 90th centile from normal pregnancy.
Inhibin A was detected more often in the menstrual fluid samples (28.6%) from 22 patients (55%) with intrauterine abortion, than in ectopic pregnancy (7.6%). In 10 cases (12 samples), Inhibin A was detectable in 134 of 158 samples (84.8%) from 102 women (82%) with ectopic pregnancy.

Results

In ectopic pregnancy the circulating PAPP-A concentrations were within the normal range in 11 out of 124 cases (12 out of 158 samples, 7.6%). In 10 cases (12 samples), PAPP-A was detectable but subnormal, i.e. below the normal 10th centile. PAPP-A was undetectable in 134 of 158 samples (84.8%) from 102 women (82%) with ectopic pregnancy.

In patients with intrauterine abortion, seven out of 49 samples (14.3%) from 40 patients showed a normal PAPP-A value. Subnormal but detectable PAPP-A was observed in 14 out of 49 samples (28.6%) from 11 women. In 28 out of 49 samples (57.1%) from 22 patients (55%) with intrauterine abortion, PAPP-A was below 11 μg/l (Figure 1).

Before eight weeks of gestation PAPP-A was detected more often in the intrauterine abortion group than in ectopic pregnancy (P < 0.01). The same difference was also found in more advanced pregnancies (Table I).

Considering the frequency of ectopic pregnancy (35.8%) and intrauterine abortion (52.3%) among all patients with pregnancy-related disorders, the likelihood of ectopic pregnancy is 30% and in intrauterine abortion 29%, when PAPP-A is undetectable.

Discussion

Previous reports suggest that the PAPP-A measurement in combination with a rapid HCG test would help in the diagnosis of ectopic pregnancy (Simonich et al., 1983, 1985). This study confirms the occurrence of subnormal PAPP-A levels in many cases of ectopic pregnancy. However, in a clinical situation the question is whether or not the circulating PAPP-A level can distinguish between ectopic pregnancy and intrauterine abortion, rather than between ectopic pregnancy and normal pregnancy. Although the number of cases with detectable PAPP-A was greater in the intrauterine abortion group than in the ectopic pregnancy group at 5–8 and 9–15 weeks gestation, the differences are not sufficient to rule out ectopic pregnancy (see Table I).

Because PAPP-A was undetectable more often in ectopic pregnancies (83%), than in intrauterine abortion (55%), the combination of undetectable PAPP-A and a positive pregnancy test requires special attention in the gynecologic emergency. Quantitative assay of HCG may also be useful in connection with PAPP-A measurement, because subnormal HCG levels are reported to predict ectopic pregnancy (Kosasa et al., 1973). However, no conclusion regarding the site of a pregnancy can be drawn on the basis of an undetectable PAPP-A.

Acknowledgements

I wish to thank Professor Markku Seppälä and Ulf-Håkan Stenman for valuable comments on the manuscript, Michael Simonich for the purified PAPP-A and Henrik Althán for the HCG measurements. This study is supported by grants from the Paulo Foundation, the Finnish Cultural Foundation, the Finnish Medical Foundation and the Orion Corporation Research Foundation.

References


Received on May 15, 1987; accepted on July 21, 1987.