

## FIBRIN SEALING - AN ADVANCED THERAPY IN DEALING WITH PREMATURE RUPTURE OF MEMBRANES?

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In 1979 Genz reported two cases of fibrin sealing (FS) therapy in premature rupture of membranes (PRM) (2). In 1980 Diaz-Zagoya et al. reported on in vitro sealing of ruptured fetal membranes with fibrin cryoprecipitate (1). The sealed membranes were able to tolerate hydrostatic pressures on the fetal side up to 60 mmHg without rupture. They concluded that fibrin seals ruptured membranes in vitro.

### PRINCIPLE AND TECHNIQUE OF FS

The principle of FS therapy is to stem the flow of amniotic fluid (AF) and by this means to facilitate the renewal of chorion and amnion. The fibrin in this context has to seal the lower amniotic sac from the cervix. Direct sealing of the ruptured membranes is not possible. The basic principle of clot formation is the polymerisation of the fibrin monomer in the 2nd stage of blood clotting. Fibrinolysis is prevented by the addition of proteinase inhibitors. The fibrin kit contains lyophilized fibrin seal, each ml of which has 75 mg of clottable protein, aprotinin and CaCl<sub>2</sub>. The stabilization of this fibrin solution is achieved by adding 500 IU/ml thrombin. The fibrin seal solution is taken up in a sterile syringe and applied via a canula placed in the cervix. Before and after this procedure the same volume of thrombin-CaCl<sub>2</sub> solution is applied to the endocervix. The position of the cervix has to remain fixed until the FS is complete. The final hardening is achieved after 2 hours.

### PATIENTS AND METHODS

The study was made on 6 patients between the 19th and 30th weeks of gestation. The use of FS was carried out for a total of 13 times; in 5 patients the procedure was employed twice and in one other three times. In one case a cervical suture had already been performed just before; in the other cases the cervix was intact. All patients had been treated with fenoterol and prophylactic antibiotic therapy was employed. The patients were put into lithotomy position, and the vulva, vagina and cervix washed thoroughly with an antiseptic solution. After FS the following daily investigations were carried out for the exclusion of a subsequent developing amnion infection syndrome (AIS): pulse, temperature, ESR, white cell count. The patients were kept under strict bed rest for 10 days after application.

### RESULTS

Apart from one case, where the diagnosis of PRM was questionable, leakage of AF continued over the following 3 days, and furthermore the 2nd and 3rd application of the FS failed to stem the flow.

There existed no relationship between the rupture of membranes and application of the FS, which varied from 1 to 12 days. The fibrin plug would either be reabsorbed or expelled within 3 days. In no case did an AIS develop.

#### DISCUSSION

What can be the reasons for this failure of FS?

- 1.) There is no good evidence for adherence between the fibrin and the endocervix (2).
- 2.) The poor adherence observed may result from too low a fibrin concentration.
- 3.) The cervix consists of a round cylinder rather than two flat surfaces.
- 4.) The endocervix may also be too wet to allow effective hardening of the FS.
- 5.) The continuous formation of AF may exert an increasing pressure upon the region of the fibrin plug.

To attempt to improve the technique we modified the method taking into account point 2 and 4. In vitro experiments were carried out on four fresh human uteruses obtained after hysterectomy from premenopausal women. The endocervix was swabbed as far as possible and the concentration of the FS was increased to 90 mg/ml. The fresh uteruses were placed in a warm chamber at 37 C. Fibrin-aprotinin and thrombin were applied not successively, but simultaneously using a double-syringe. This technique allowed a good initial polymerisation and hardening. But after approximately one and a half hour the fibrin plug showed no adherence when slight traction or pressure at the fundus uteri was performed. The additional introduction of haemostyptic material (Tabotamb) into the cervix did not result in improved adhesive strength.

#### CONCLUSIONS

- 1.) The so-called fibrin plug did not in any case stem the flow of AF.
- 2.) The accessible region of the endocervix was always too wet to allow good contact between FS and the cervical epithelium.
- 3.) The fibrin plug was either reabsorbed or expelled within 3 days of application and this has to be repeatedly renewed.
- 4.) The fibrin plug was not adherent even with careful swabbing of the accessible region of the endocervix and use of 90 mg/ml protein.

#### REFERENCES

- 1.) Diaz-Zagoya, J. and F. Arias: "In vitro" sealing of ruptured membranes with cryoprecipitate. Presented at the 27th Annual Meeting of the Society for Gynecologic Investigation, March 19-22, 1980, Denver, Colorado
  - 2.) Genz, H.-J.: Die Behandlung des vorzeitigen Blasensprungs durch Fibrinklebung. Med. Welt 30, No. 42, 1979, p. 1557
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