Title PROPOFOL IN GENERAL ANESTHESIA FOR I.V.F.(BY VAGINAL AND TRANSURETHRAL ROUTE)-FOLLICULAR FLUID CONCENTRARION AND CLEAVAGE RATE.

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Introduction.Effects of general anesthesia on oocytes during in vitro fertilization had been studied recently(2,3).For ambulatory retrieval of oocytes under an ultrasonically guided technic,we studied propofol(diisopropylphenol)a new short acting agent very effective for ambulatory surgery.It has no mutagenic effects on the 5 usual tests,so it could be used as an induction agent for ambulatory retrieval of oocytes.The aims of this study were:1/to investigate the follicular fluid concentration(FFC) of propofol,2/to study the cleavage rate under this technic of anesthesia.

Methods.After approval by the Hospital Ethics Committee,20 unpremedicated healthy women gave their informed consent to enter the study;no choice was made considering the indication of in vitro fertilization.Intravenous catheters were inserted in both arms,one for administration of fluids and drugs, the other for sampling of venous blood.Alfentanyl 0.5mg was injected while patients were breathing 100% 02, 2 minutes later a single bolus IV dose of 2.5mg/kg propofol was injected.Anesthesia was maintened with N20/02 50%/50%,supplemented by halothane 2% for few minutes,then 1%.Blood and oocytes were taped at the same time.We obtained 109 samples of each(2 to 8 for a patient).Blood samples were collected in tubes containing EDTA,mixed and stored at 4°C to await analysis.Follicular fluid(FF)was mixed with 1/4 of its volume with nutritive fluid B2,to obtain a constant dilutant ratio for each sample.After removal of the oocytes,FF was collected and stored at 4°C.For each FF sample hematocrit and proteins were measured and we eliminated samples polluted by blood(hematocrit more than 8%)or saline(proteins under 20g/1).So we analysed 85 FF samples.Propofol levels were measured in plasma and in FF,after methanol extraction, by an HPLC method indicated by ICI Pharmaceutical Division.The limit of the assay is 0.05mcg/ml.Oocytes were graded as mature or immature.For analysis each value less than 0.05mcg was noted 0.For statiscal analysis results were pooled by interval times of 3 minutes.Correlations between variables were investigated by Student t test and ANOVA.A probability value less than 0.05 was considered as statistically significant.

Results. Duration of surgical procedure ranged between 17 to 35 minutes.Times of sampling ranged between 8 to 35 minutes after propofol injection,and most of the samples were taped during the first 20 minutes.Propofol blood concentration(BC)is rather lower than in previous study(1):0.65mcg/ml±0.21 (0.36-1.17)between the 8th and the 11th minute.Propofol FFC shows wide individual variations among the patients:with flat curves,increasing curves and decreasing curves.The ratio of propofol FFC/BC is 0.2 ±0.11(0.05-0.48)during the first interval 8 to 11th minute.We observes a non statistically significant elevation of propofol FFC between the 8th and the 20th minute,and a statistically significant drop during the interval 20-23 minutes;then propofol increases but not significantly.The cleavage rate for mature oocytes is the same(0.7)for the first 20 minutes than for the interval between 20 and 35 minutes.Cleaved mature oocytes were in FF with FFC 0.13±0.08mcg/ml(0-0.33) and uncleaved oocytes were in FFC 0.08± 0.05mcg/ml(0-0.19),the difference is statistically significant.

Discussion. Considering the great volume of distribution of propofol(1),finding it in FF seems normal. Statistically significant drop of FFC between the 20 th and the 23th minute can be related to the excretion of the drug from the FF or to a bias because of the few number of samples in this interval:10 samples We have a short surgical procedure and,within 35 minutes,cleavage rate is constant:70%.Propofol seems to have no effects on cleavage rate in our study,considering the moment of taping and FFC.In fact mature oocytes which don't cleave were surrounded by FF containing significantly less propofol than those which cleave.So ,the first results allow us to think that between less than 0.05 and 0.33mcg/ml,propofol is not deleterious for oocytes.These warrant further investigations.

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PROPOFOL LEVELS

IN PLASMA AND FOLLICULAR FLUID