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# A Decision Support Tool for Optimized Personalized Drug Dosage Profiles for Superovulation in In-Vitro Fertilization with Early Clinical Trial Results

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## Abstract

**OBJECTIVE:** Superovulation is a drug-induced method that enables multiple ovulation per menstrual cycle and is a vital component of a successful IVF cycle. Although there are general guidelines for dosage, the dose is not optimized for each patient, and complications, such as overstimulation, can occur.

To overcome the shortcomings of the current IVF practice of dosage profile determination by trial and error, a mathematical procedure and a decision support tool was developed which can provide a customized model of this stage regarding the size distribution of follicles obtained per cycle as a function of the chemical interactions of the drugs used and the conditions imposed on the patient during the cycle. Uncertainty and risk are modeled and included in optimal drug dosage decisions. This talk describes the theory, model, the optimal control procedure, and the decision support tool for improving outcomes of IVF treatment for both antagonist and agonist protocols used in real practice. We present preliminary results of the results of early clinical trials carried out in India in last three months.

**MATERIALS & METHODS:** In our earlier work, we developed models for agonist and antagonist protocols based on analogy between superovulation and the particulate process of batch crystallization. It was shown that the model could be customized for each patient using the two two days of follicular data (day 1 and day5 or 6) from that patient. It was found that the model predictions are reasonably accurate for most of the patients. The optimal control method is then applied to optimize the dosage profile for each patient. The primary outcome measures studied include the proportion of women with an appropriate number of retrieved oocytes), total hormonal dosage employed during the cycle, and serum oestradiol concentrations on rHCG day, % follicles retrieved, % MIIs in follicles, Number of MIIs.

**RESULTS:** The validation of the procedure was performed using retrospective as well as data from clinical trials from more than 100 patients. Customized patient-specific model parameters are obtained by using initial day1 and day5 data for each

patient and validated. The model is then used for predicting the customized optimal drug dosage for each patient on days 5 through the trigger day.

Preliminary results from the trials show that the dosage predicted by using the model is 40% less than the suggestion made by the IVF clinicians using their standard orotocols. The testing and monitoring requirements for patients using optimized drug dosage is reduced by 72%. For most of the patients, this approach resulted in optimal number of MII follicles.

**CONCLUSIONS:** A mathematical-based approach to dosage profile determination results in optimal mature follicles with reduced dosage and need for testing.

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