A SOFTWARE TOOL FOR PERSONALIZED OPTIMAL DOSAGE FOR IN-VITRO FERTILIZATION

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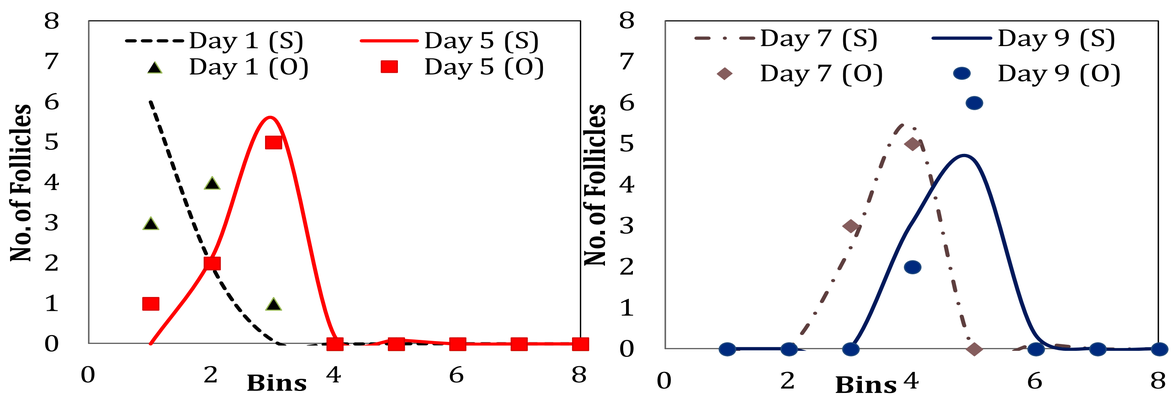
INTRODUCTION

- **The success of IVF depends upon successful superovulation, defined by the number and uniformly high quality of eggs retrieved in a cycle**
- **The daily dosage of hormones required for this stage, is customized for each patient based on almost daily ultrasound and blood test. Although there are the general guidelines for dosage, the dose is not optimized for each patient, and complications, such as overstimulation, can occur**
- **Cost of testing and drugs make superovulation stage very expensive**
- **To overcome these shortcomings, a mathematical procedure and software is developed which can provide a customized model of this stage regarding the size distribution of follicles (FSD) obtained per cycle as a function of the drug dosage used. We had data for 100 patients, and we validated customized model for each patient by comparing follicle size distribution on day 11.**
- **Customized optimal drug dosage procedures are developed for each patient using optimal control methods with the targeted FSD.**

RESULTS AND DISCUSSIONS

Model Validation Results



Comparison of Follicle Size Distribution (FSD) from clinical data & model predictions for two patients
(O) - Observed data (S) - Model predicted distribution

- **The customized models for each patient predicted the outcome (mature follicle count on day 11) accurately for more than 90 % of the patients.**
- **The error in prediction was less than 10%.**

The OPTIVF Software

- **The model and optimal control methods are implemented in integrated software for clinical trials called OPTIVF.**
- **Software uses two-day data from the patient of follicular distribution and hormone dosage as an input to the model**
- **Optimization based parameter estimation (iterative) of the moment model is carried out to customize the model for each patient**
- **The parameters then are used along with the iterative optimal control capability to find optimal drug profile for the remaining days of the cycle**

Results from Optimal Control for All Patients

- **Model predicted dosages start at lower dosages from 225 – 300 IU and result in lower cumulative dosages**
- **Reduced overall dosages for by 20 to 40 % for more than 80 % of the patients.**
- **48 of the 49 patients show higher mature follicles for the optimal control profile than the patients with physician specified dosage.**
- **No correlation found between the age of patients and higher doses of 300-450IU**
- **Example: Cumulative dose for a patient is found to be 2662.5 IU compared to clinician prescribed dose of 3600 IU**
- **75% reduction in testing and monitoring requirements**

Clinical Trial Results

- **A small double-blind clinical trial with 20 patients was also conducted in India. The results from the trial show that the dosage predicted by using the model is 40 % less than the suggestion made by the IVF doctors**
- **Additionally, the number of mature follicles obtained at the end of the cycle using the model-predicted dosage was significantly higher than the physician suggested dosage**
- **The testing and monitoring requirements for patients using optimized drug dosage is reduced by 72%**

Clinical Trial Information	FSH *Doctor's Recommendation*	FSH *Optimal value using model*	No. of Follicles (9 ≤ Mean size ≥ 11)		% reduction in FSH
Patient 3 Follicle # 11	1950	1162.5	5 (Dr. Rec.)	11 (opt)	40.4

120%

CONCLUSIONS

This poster presents a software decision support tool called OPTIVF for doctors to determine optimal hormonal dosage for each day of can IVF cycle personalized for each patient. OPTIVF provides a custom model for each patient based on drug chemistry and individual responses for any protocol used for follicle stimulation. The model predicts the follicle size distribution (FSD) obtained each cycle as a function of the drug dosage used. The model also predicts the estrogen levels for each patient on various days of a cycle. Customized optimal drug dosage procedures are calculated for each patient using optimal control methods with the targeted FSD. Thus, OPTIVF provides a daily optimal drug dosage customized for each patient with the data from each patient's first two days of a cycle. We have used data from100 patients to validate the approach.

A small double-blind clinical trial was also conducted. The results from the trial show that the dosage predicted by using the model is 20 to 60 % lower than the dosage chosen by the IVF doctors. Additionally, the number of mature follicles obtained at the end of the cycle using the model-predicted dosage was significantly higher than with the physician suggested dosage. The testing and monitoring requirements for patients using optimized drug dosage is reduced by 72%.

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