

Preliminary Comparison of Algorithm-Interpreted Fertility Monitor Readings with Established Natural Family Planning Methods

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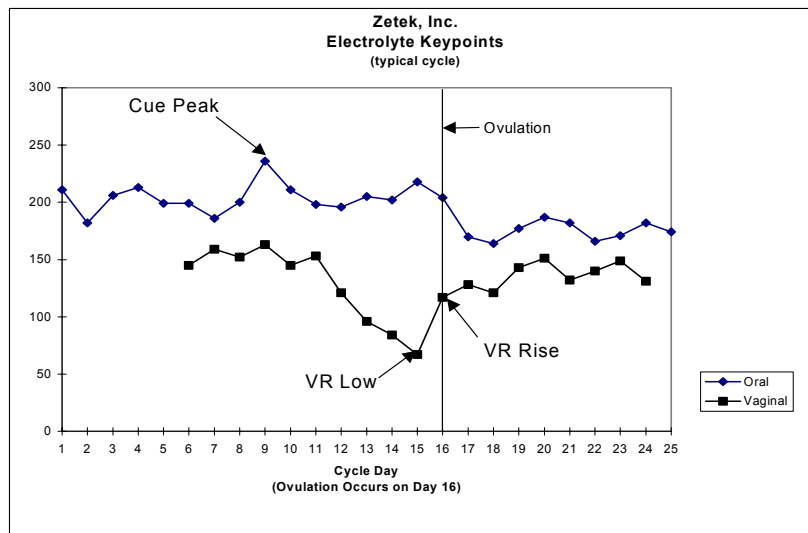
Women experienced in established NFP methods provided records of 53 cycles. Twenty-four cycles were contributed by women in the 2001 study; an additional 29 cycles from an earlier study were evaluated retrospectively using the OvaCue® algorithm. In addition to maintaining their ongoing fertility observations, all subjects took oral electrolyte readings daily, vaginal electrolyte readings during the fertile window as specified by the algorithm, and urinary luteinizing hormone (uLH) tests on days identified by the algorithm as days of maximum fertility. The fertile window (FW) was defined as the five days preceding ovulation and the day of ovulation (Wilcox, *et al*). Each method was examined to determine how closely it defined the FW both as a means to achieve and to avoid conception.

The OvaCue and the sympto-thermal methods were closely correlated, especially in defining the end of the FW. The OvaCue was found to be more effective than other methods in determining the beginning of the FW. Overall, the OvaCue algorithm analysis correctly identified all FW days in over 99% of cycles. Sympto-thermal method identified 87.38% of FW days.

Results of this preliminary study will be used to structure a larger-scale comparison of the NFP and electrolyte methods to be conducted in cooperation with established NFP teaching centers.

Measurements of salivary and vaginal electrochemical characteristics taken with the Cue® Ovulation Predictor have been shown to be useful for prediction and confirmation of ovulation in spontaneously ovulating women (Albrecht 1987¹, Fernando 1985², 1988³). This apparatus has been approved by the FDA and used by couples seeking to conceive since 1985. Measurements are taken using two transducers—

one for daily oral readings and another for vaginal readings to be taken during the period from the Cue Peak™ until confirmation of ovulation. These electrolyte readings previously have been charted manually and interpreted by identifying three keypoints in the charts: the Cue Peak, the nadir of the vaginal readings (VR Low) and the rise from that nadir (VR Rise). The reproductive cycle keypoints are identified in the chart below:



The U.S. FDA mandates that the labels for the Cue and OvaCue include the phrase “Not for Contraception.” The Company and physicians recommending the instrument to infertility patients have interpreted this labeling requirement as a restriction of the Cue’s use for timing of abstinence by couples seeking to avoid conception during any given cycle. However, the practice of natural family planning (NFP) is in no sense limited to contraception or “avoidance” of conception. NFP principles more broadly involve control of the timing of conception and include planning to achieve conception. It is in the context of that principle that the study of the effectiveness of the Cue method for NFP use is appropriate.

The OvaCue® Fertility Monitor, a new embodiment of the Electrolyte Method™, eliminates the need for manual charting. The monitor records up to four months of oral and vaginal readings and will interpret those readings automatically. The OvaCue will reply to the

inquiry “Calculate Fertility” with a fertility status indicator for that cycle day (progress bar from 1 to 7) and indicate the expected maximum fertility days for the cycle, assuming readings have been taken and the Cue Peak was found. Once the VR Low is identified, the OvaCue will also confirm that ovulation has occurred and post-ovulatory infertility has begun for the duration of that cycle. The instrument will also allow those readings to be downloaded to a computer for permanent storage and use with the OvaGraph™ software.

Four studies have been carried out in which NFP signs were compared to the manually charted Cue readings (Barrett 1985⁴, Fazleabas 1990⁵, Fehring 1994⁶, Moreno 1988⁷). Similarly, the current study was undertaken to compare the algorithm-interpreted readings (OvaCue/OvaGraph) to several established methods of NFP. A secondary aim of the study was to develop a clearly defined protocol for use of the OvaCue system by couples wishing to avoid or postpone conception.

MATERIALS AND METHODS

SUBJECTS

Data were obtained in 24 cycles from 11 women. Subjects were recruited through referral by recognized instructors of several NFP methods and through a special interest user list on the internet.⁸ All subjects were spontaneously ovulatory and had menstrual cycles ranging in length from 24 to 36 days. After reviewing a detailed outline of the study and receiving answers to any questions, each woman submitted a signed letter of informed consent.

In order to augment testing of the automated algorithm, 29 cycles of data from an earlier study⁹ were included in this study and processed by the OvaGraph fertility software. The OvaGraph computer program contains the same data-interpretation algorithm incorporated into the OvaCue monitor. Subjects in this group had also received full information and given their informed consent.

EXPERIMENTAL MEASUREMENTS

Subjects used the OvaCue instrument according to standard instructions, taking oral readings daily and vaginal readings on days when prompted by the device or when the algorithm indicated any level of fertility. Observations of fertility signs were recorded according to each subject’s present standard NFP practice. Cervical mucus quality and quantity (“mucus”), cervical position and openness (“cervix”), and basal body temperature (BBT), where part of the subject’s standard method, were recorded. The designation “sympto-thermal” was applied to those cycles in which a combination of mucus and/or cervical evaluation with use of the BBT post-ovulatory shift was used. A broad range of NFP methods was represented, with variations among centers as well as among users in format and nomenclature. However, insufficient numbers of subjects using any single method prevented inter-method comparisons.

Urine luteinizing hormone (uLH) was measured using the Lady Ovulation Tester¹⁰ on days identified by the OvaCue algorithm as days of maximum fertility. In the cycles from the previous study, daily 24-hour urine was collected on expected days of maximum fertility as determined by the researchers (Barrett 1985) based on the peak in Cue oral readings. These samples were analyzed for LH using standard laboratory methods. The day of peak concentration of urinary LH was taken as the day of ovulation (Wilcox 1995¹¹).

DATA ANALYSIS

In conformity with previously reported procedures (Albrecht 1985), oral readings were standardized relative to the preovulatory peak in the oral readings (Cue Peak) as identified by the algorithm as a high value followed by two or more markedly lower readings. Data from the vaginal readings (VR) were standardized relative to the day of the VR Low.

The effectiveness of each approach (NFP evaluations and the OvaCue algorithm) in determining the fertility of each cycle was evaluated by comparing its identification of fertile days to the “fertile window” as defined by research performed at the National Institute of Environmental Health Sciences (Wilcox 1995). Wilcox and his colleagues studied 708 cycles contributed by 221 women, and concluded that, based on the day of ovulation defined by daily uLH assays,

“all conceptions resulted from intercourse that occurred during a six-day interval ending on the day of ovulation.”

The fertile window defined by the algorithm was taken to begin on the first day the OvaCue fertility status was ≥ 3 bars and to end on the day the

status returned to 3 bars, after days indicated as maximum fertility had occurred.

An effort to impose consistency among the differing NFP reports was made by coding the descriptors. A numerical code was applied to descriptions of mucus sensation (0-3) stretchiness (0-3) type (0-2) color (0-4) and texture (0-4) and to cervix texture (0-3) os character (0-3) and position (0-3). The code zero was applied to the ‘least fertile’ descriptor in each category, e.g., stretch code 3 indicated a spinn-barkheit of 1” or more, while 1 indicated $\frac{1}{4}$ ” to $\frac{1}{2}$ ”. a code score of more than 2 in any mucus category was taken as an indicator of fertility. The BBT shift was identified retrospectively as the first day of a sustained upward shift in BBT.

Results were evaluated against the following criteria (1) days within the ‘fertile window’ identified as infertile by the method and (2) days outside the “fertile window” identified as fertile by the method.

RESULTS

Data were collected from 53 cycles, of which 48 were usable. Four cycles were not included in the calculations because of incomplete data, and one cycle was not used because the cycle length was beyond the definitions of the study. The LH surge was determined in 33 of the 48 useable cycles.

Results of OvaCue algorithm-interpreted data were compared to conclusions made by each of the NFP methods. For determining the end of the fertile window, the OvaCue method correlated most highly with the sympto-thermal method ($r = 0.79$), and monitoring mucus symptoms ($r = 0.74$). In all cases the OvaCue method correlated higher in determining the end of the fertile window than the beginning (Table 1).

Table 1: Correlation of OvaCue method with NFP methods

Method	Fertile Window Start	Fertile Window End
Mucus	0.58	0.74
Sympto-thermal	0.60	0.79

The methods were also compared for effectiveness in determining the beginning and

end of the fertile window. The results of that comparison are shown in Table 2.

Table 2: Comparison of methods in determining the fertile window

Method	Fertile Window Start	Fertile Window End
Mucus	0.63	0.77
Sympto-Thermal	0.68	0.82
OvaCue	0.85	0.78

OvaCue and sympto-thermal data were then analyzed to determine the number of days in the fertile window that were interpreted as infertile (case 1) and the number of days outside the fertile window that were interpreted as fertile (case 2). Assuming an avoidance posture, the days in case 1 would be those that could lead to unintended pregnancy and in case 2 as those where abstinence

was recommended erroneously. Percentages were calculated based on the total number of days in the fertile window (33 cycles x 6 days in fertile window = 198 fertility days). Percentages for Case 2 were not calculated as total cycle days outside the fertile window for all cycles was not available. Results of the analysis are in Table 3.

Table 3: Effectiveness of methods for NFP use

Method	Case 1	% Effective	Case 2
OvaCue Algorithm	2 days	98.99	92 days
Sympto-Thermal	25 days	87.38	148 days

Using an OvaCue conception avoidance protocol of the first fertility sign (bar = 3) to the last high fertility (bar = 5), 2 fertile days out of 198 were mis-identified as infertile. Using sympto-thermal methods, 25 fertile days were mis-identified as infertile. In the same cycles, unnecessary avoidance occurred on 61% more days using sympto-thermal methods than the OvaCue method (148 vs. 92).

DISCUSSION

Participants reported that both the OvaCue and NFP methods were used without difficulty. After becoming acquainted with the basic menus and setup procedure of the OvaCue, users reported finding the OvaCue easy to use and understand. Oral readings are only required during the follicular and ovulatory phases of the cycle. Nevertheless, most subjects preferred developing the habit of taking an oral reading daily. Subjects reported that use of the vaginal sensor for a few days each cycle was not burdensome.

Self-evaluation of fertility signs using NFP methods is simple, easy-to-learn, and effective. While sufficient samples for statistical comparison between methods was not available, it was observed that many of the more experienced self-observers abstract the most relevant components from the NFP method initially learned. This was an interesting result of not specifying any particular method for use by these women. Some omitted BBT; some knew they did not need to begin observations before a certain cycle day; many did not use cervical characteristics; most discontinued observations once the fertile window had been recognized.

Although NFP methods have long been known to be effective, there are circumstances when a more objective means of evaluation is desirable. These would include women with irregular cycle lengths and those who incur fertility signs that are not readily apparent. Objective evaluation would be beneficial to those beginning NFP practice, and those desiring additional confidence in using NFP methods. Additionally, certain couples may find

the use of an automated fertility-monitoring device attractive.

It was determined that because the methods do not conflict from a procedural standpoint, the OvaCue could be used in conjunction with NFP methods without interference.

A benefit of this study has been to define more closely the protocol for any further investigations of the OvaCue/OvaGraph. In the future, a series of studies of which each cohort uses the same NFP method of self-observation would allow examination of the NFP method in relation to the Zetek electrolyte method.

CONCLUSIONS

Correlation among the OvaCue method and various NFP methods were varied. The closest relation exists between the Sympto-thermal method and the OvaCue method, with the methods being closer in determining the end of the fertile period and differing more in defining its end. Correlations of each method with the fertile window as defined by the LH surge led to the conclusion that the methods were similarly effective at determining the end of the fertile window, but the OvaCue was more effective for determining the beginning of the fertile window.

Based on the criteria of having no fertile days identified as infertile, the OvaCue algorithm correctly processed 46 of 48 cycles (96%). This result corresponds to conclusions made in earlier studies (Fernando 1988¹²).

In this study, the OvaCue/OvaGraph algorithm was effective at identifying the fertile window and has potential to be used as an adjunctive device in the learning and use of NFP methods.

Although a limited number of cycles were evaluated in this study, the initially positive results warrant a larger study. Goals for a future study would include further definition of the protocol for achieving or avoiding conception as well as to evaluate the efficacy of the automated method.

Improved data quality can be expected from coordinating the study participants through a centralized location. A requirement that participants use the same NFP method and be consistent and diligent in charting techniques and data reporting could also provide methodology improvements.

In the future, Zetek intends to complete a large-scale study in cooperation with one or more established NFP teaching centers in order to define more fully the efficacy and applications of the Electrolyte Method.

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