

Natural procreative technology for infertility and recurrent miscarriage Outcomes in a Canadian family practice

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Abstract

Objective To study the outcomes of women with infertility or miscarriage treated with natural procreative technology (NaProTechnology or NPT), a systematic medical approach to promoting conception in vivo; and to compare the outcomes with those previously published from a general practice in Ireland.

Design Retrospective cohort study.

Setting An urban Canadian primary care practice in which the physician had a part-time practice in NPT.

Participants Couples with infertility or recurrent miscarriage who received treatment in the practice between August 2000 and July 2006.

Intervention All couples were taught to identify the fertile time of their menstrual cycles using the Creighton Model FertilityCare System (CrMS) and completed a standard NPT evaluation. Many also received additional medical treatment to enhance conception in vivo.

Main outcome measures Live birth was the primary outcome; secondary outcomes included conceptions, multiple births, low birth weight, and prematurity.

Results A total of 108 couples received NPT and were included in the analysis, of which 19 (18%) reported having 2 or more previously unexplained miscarriages. The average female age was 35.4 years. Couples had been attempting to conceive for a mean of 3.2 years. Twenty-two participants (20%) had previously given birth; 24 (22%) had previous intrauterine insemination; and 9 (8%) had previous assisted reproductive technology. The cumulative adjusted proportion of first live births for those completing up to 24 months of NPT treatment was 66 per 100 couples, and the crude proportion was 38%. The cumulative adjusted proportion of first conceptions was 73 per 100 couples, and the crude proportion was 47%. Of the 51 couples who conceived, 12 couples (24%) conceived with CrMS instruction alone, 35 (69%) conceived with CrMS and NPT medical treatment, and 4 (8%) conceived after additional surgical treatment. All births were singleton births; 54% were born at 37 weeks' gestation or later; and 78% had birth weights of 2500 g or greater.

Conclusion Natural procreative technology in a family physician's office was effective in treating infertility and miscarriage with outcomes that were comparable to those in an NPT general practice in Ireland. Larger multicentre prospective studies to compare NPT directly to other forms of infertility treatment are warranted.

In Canada, approximately 8% of heterosexual couples are infertile when measuring the inability to conceive after 1 year of attempts.^{1,2} This infertility prevalence nearly doubles when excluding the surgically sterile population, corresponding to 1 couple in 6 being unable to conceive in the first 12 months of trying.² The psychosocial effects of infertility and miscarriage include

emotional distress, depression, and marital dissatisfaction,^{1,3} all of which have implications not only for the couple but also for their extended families and society.

When first confronted with this issue, most couples will approach their family physicians for guidance. Hence, family physicians are in a unique position to provide comprehensive assessment and treatment of infertile couples.¹ However, these couples are increasingly referred to fertility specialists with only minimal, if any, investigation. There seems to be little emphasis on looking for hormonal or structural abnormalities that could be corrected without resorting to more complex and costly treatments, such as assisted reproductive technology or in vitro fertilization (IVF), which entail additional cost and pose additional risks for both the mother^{4,5} and her offspring.^{6,7}

A systematic primary approach to the diagnosis and treatment of infertility and miscarriage that can be applied by a family physician is an attractive alternative.¹ Natural procreative technology (NaProTechnology or NPT), based on the Creighton Model FertilityCare System (CrMS), is one such medical approach.⁸ The CrMS and NPT were developed based on a long history of methods used to identify ovulation and the fertile days of the menstrual cycle, known as *natural family planning* or *fertility awareness* methods.^{9,10} The first such approach used a woman's cycle length to arrive at fixed formulas for counting days of ovulation. However, owing to the variability of both the preovulatory (ie, follicular) and postovulatory (ie, luteal) phases, these methods are frequently inaccurate for prospectively identifying ovulation.¹¹ Recording the basal body temperature is another approach used to identify ovulation.¹⁰ While a rise in basal body temperature signals ovulation for most women, this biphasic shift usually occurs after ovulation and thus is not useful for predicting ovulation prospectively.¹²⁻¹⁵ Prospectively identifying the day of ovulation and the most fertile days of the menstrual cycle can be done with assessment of urinary luteinizing hormone or urinary estrogen metabolites, or by monitoring cervical secretions.^{12,14,16-22} The assessment of cervical secretions has a number of advantages with regard to fertility status, providing direct information about the environment for sperm survival.²¹⁻²³ Women's systematic vulvar observations from cervical secretions have been directly correlated with the probability of conception.²⁴ Standardized vulvar observation of cervical secretions is also one of the most accurate ways to identify the estimated time of ovulation, which is found to occur 3 days before and after the last day of fertile-type mucus in 99% to 100% of cycles.^{12,14,15,18-22}

Two systematic approaches to teaching women to monitor ovulation and the fertility (menstrual) cycle include the Billings Ovulation Method (BOM) and the CrMS. The BOM, developed during the 1960s in Australia, relies on self-observation and description of cervical fluid characteristics.^{9,10,25} The CrMS was introduced in 1976 by obstetrician-gynecologist Dr Thomas Hilgers, based on research conducted at St Louis University and Creighton University.^{9,10} It is similar to the BOM, but has more standardized protocols for observing, describing, and evaluating vulvar observations of cervical secretions, as well as vaginal bleeding.^{21,24,26} The CrMS is taught by trained CrMS instructors throughout North America and in other parts of the world (North America: www.fertilitycare.org; Europe: www.fertilitycare.net; Asia and Australia: www.fertilitycare.com.au).²⁷ Multiple training programs for instructors of the CrMS are conducted worldwide, including in Canada.²⁸ All CrMS instructors must be affiliated with FertilityCare Centers of America or FertilityCare Centers International (both nonprofit organizations) in order to use CrMS instructional materials, although they may be employed by an organization or be self-employed.²⁷

Based on the standardized menstrual cycle data available from the CrMS, Dr Hilgers and colleagues have conducted applied clinical research over the past 35 years to develop a series of medical protocols to evaluate possible causes of infertility, and to apply fertility treatments to enhance the probability of conception in vivo. These protocols are known as *natural procreative technology*, *NaProTechnology*, or *NPT* and are described in detail in a textbook published in 2004.²⁹ Guided by the biomarkers of the CrMS charting, physicians trained in NPT use targeted hormonal tests to evaluate patients' menstrual cycles and identify factors that might be inhibiting natural fertility. The treatments used in NPT to enhance fertility in vivo include standard fertility medications and surgeries, but in NPT their application and adjustment is guided by the biomarker monitoring of the CrMS.³⁰ Response to treatment is assessed objectively by luteal hormonal testing and the improvement of

biomarkers in the CrMS chart. In addition, any potential contributing factors from the male partner are investigated and corrected to the extent possible. Once a pregnancy is achieved, progesterone levels are obtained serially³¹; if they are found to be deficient, natural progesterone supplementation is provided.³² Currently, the only comprehensive continuing medical education course for NPT is conducted annually by the Pope Paul VI Institute for the Study of Human Reproduction, affiliated with Creighton University School of Medicine, in Omaha, Neb. Many hundreds of physicians from around the world have been trained through this course.

A recent study found that NPT practised by trained generalist physicians in an Irish clinic resulted in live birth rates comparable to cohort studies of more invasive treatments.³³ Our study was conducted to assess the outcomes of NPT treatment in infertility and miscarriage in a single family practice in Ontario. We hypothesized that the primary outcome of live births and the secondary outcomes of conceptions and multiple births would be comparable to those in the Irish study.

METHODS

This retrospective cohort study took place in an urban Canadian medical practice where approximately 80% of patients were seen for general family medicine and 20% for NPT during the study years. The NPT patients were referred by centres that teach the CrMS or were self-referred. We included all patients who sought NPT treatment for infertility or recurrent miscarriage from August 2000 to July 2006 (inclusive). *Infertility* was defined as inability to conceive for at least 1 year with random intercourse, or for at least 6 months with fertility-focused intercourse using the CrMS to identify the fertile period of the menstrual cycle. Patients with a history of 2 or more miscarriages were also eligible. We excluded patients who failed to complete the initial investigations or return to discuss the results.

Data were extracted from the patient medical records that were maintained by the family physician. Extracted information included data from the initial NPT consultation for infertility and miscarriage, all subsequent follow-up visits, and all telephone contacts. Each included patient was assigned an identification number so only de-identified data abstracted from their medical records were entered into a computerized database. Institutional review board approval was obtained from the William Osler Health System, Etobicoke Hospital Site, in Toronto, Ont.

Data abstracted from the clinical records included age, race, number of pregnancies in the lifetime, length of time trying to conceive, gynecologic diagnoses before and after NPT evaluation, NPT treatments, pregnancies, live births, prematurity, low birth weight, and multiple births. Any missing information was obtained by telephone follow-up.

The NPT evaluation began with the couple charting the menstrual cycle using the CrMS, followed by hormonal and ultrasound tests timed to the menstrual cycle. Women continued to chart using the CrMS throughout their NPT treatment (range 1 to 24 cycles). After evaluation, if indicated, medications were given to enhance cervical mucus production (such as vitamin B6, guaifenesin, amoxicillin, erythromycin, or clarithromycin given during the follicular phase)^{30,33-35} or to increase luteal hormones (eg, oral, vaginal, or transbuccal progesterone or human chorionic gonadotropin injections).^{30,33,36} Clomiphene was frequently used to enhance ovulation. Semen analyses were performed, and the male partner was treated for any potential contributing factors or was referred to a urologist. Surgical treatments such as laparoscopy were also obtained by referral when necessary. Treatments were adjusted from cycle to cycle by reviewing the response of the biomarkers within the CrMS chart, such as improved cervical mucus production or the disappearance of abnormal bleeding.^{29,33} Additional monitoring was done by measuring midluteal estradiol and progesterone levels. The couple was instructed to use the fertile time for intercourse and was advised that it might take up to 24 months for optimization of their cycles for conception leading to a live birth.^{30,33}

Given that this study was based on a descriptive analysis of outcomes of an existing practice, we did not conduct sample size or power calculations. The primary outcome was the cumulative proportion of couples experiencing conception or conception leading to live birth, assessed at 6, 12, and 24 months after entering the study. We employed life-table analysis to adjust for

dropout from treatment.³⁷ Crude proportions were also calculated. Proportions of multiple, low-birth-weight, and premature births were also assessed.

RESULTS

Between August 2000 and July 2006, 232 couples were seen for initial consultation for NPT. We excluded 104 couples who were seen for conditions other than infertility or recurrent miscarriage, such as ovarian cysts and premenstrual syndrome, or because they did not undergo the initial standard investigations. We excluded an additional 20 couples whose patient records were unavailable. The final study cohort consisted of 108 couples, of whom 99 (92%) met the inclusion criteria for infertility, and an additional 9 (8%) were included because of a history of 2 or more miscarriages.

Women, on average, were 35.4 years old (SD = 5.0 years) and most were white (80%) and nulligravida (56%). The mean (SD) length of time that couples had attempted to conceive before NPT assessment was 3.2 (3.7) years, with 81 (75%) trying to conceive for more than 1 year before NPT treatment (Table 1).

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Table 1

Characteristics of couples beginning treatment with natural procreative technology

A high proportion of women reported having unexplained infertility (40%) and at least 1 unexplained miscarriage (29%) before starting NPT. With NPT evaluation, it was found that only 1% had unexplained infertility and 2% had unexplained miscarriages, while 62% of the women had low progesterone, 50% had low luteal estrogen, 50% had low follicular estrogen, and 9% had limited cervical mucus. Also, more women were identified as having anovulation and polycystic ovary syndrome (14% vs 2% and 6% vs 3%, respectively) after NPT evaluation than before therapy (Table 2).

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Table 2

Diagnoses of couples before and after NPT evaluation: $N = 108$; couples could have multiple diagnoses.

The most common treatments given to women included folic acid and vitamins (67%), medications (vitamin B6, guaifenesin, amoxicillin, erythromycin, or clarithromycin) to enhance cervical mucus production (49%), luteal progesterone (49%), luteal human chorionic gonadotropin (47%), and clomiphene (37%). Surgical interventions included laparoscopy (7%) and other procedures (5%). Among couples who conceived ($n = 51$), 12 (24%) used only CrMS fertility charting and optimally timed intercourse, 35 (69%) conceived with CrMS and NPT medical treatment, and 4 (8%) conceived after additional surgical treatment (Table 3).

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Table 3

The NPT treatments used among all couples and among those who conceived within 24 months

As shown in Table 4, there were 51 clinically recognized conceptions by 24 months after starting NPT treatment, with an adjusted cumulative live birth proportion (accounting for withdrawals from treatment, loss to follow-up, and continuing treatment at the end of the study follow-up period) of 66 per 100 couples at 24 months.

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Table 4

Cumulative outcomes per 100 couples in NPT evaluation and treatment: $N = 108$ couples.

For first conceptions regardless of outcome, the adjusted cumulative proportion was 73 per 100 couples at 24 months. Out of the 41 live births within 24 months, 17 (41%) conceptions occurred within the first 3 months, 26 (63%) occurred within the first 6 months, and 35 (85%) occurred within the first 12 months. The median time to conception leading to a live birth was 4 months.

Table 5 shows the birth outcomes of all live births observed. There were no twin or higher-order births; 54% were born at 37 weeks' gestation or later; and 78% had birth weights of 2500 g or greater. There were 57 couples who had not conceived after 24 months, and 56 couples who had not conceived after 36 months. Of those who did not conceive, 30 (54%) were lost to follow-up, 11 (20%) decided to try other treatment, and 8 (14%) transferred to another NPT physician. Other exit reasons included adoption, separation or spousal death, too far to travel, poor sperm count after vasectomy reversal, and premature ovarian failure.

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Table 5

Outcomes for NPT live births: $n = 41$.

DISCUSSION

In this cohort of couples with infertility or recurrent miscarriage, most (66%) couples who continued treatment conceived and had live births within 2 years with NPT in life-table analysis. Of those who conceived, 24% were able to conceive before any NPT evaluation using only timed intercourse during the fertile phase, but most (76%) had a diagnosis guiding subsequent NPT treatment designed to enhance conception *in vivo*. Of all couples beginning NPT treatment, including those who dropped out of treatment, 38% had live births. In infertile couples with no treatment, conceptions within 2 years leading to live births have been found to be about 42% for a population in the Netherlands with a mean female age of 29.1 years and mean duration of infertility of less than 2 years,³⁸ and about 20% for a Canadian population with a mean female age of 29.5 years, and mean duration of infertility of 3.5 years.³⁹ Thus, this NPT cohort, with a mean female age of 35.4 years and a mean duration of infertility of 3.2 years, had a substantially higher live birth rate.

Defining *infertility* as not having conceived after 1 year of trying for pregnancy is conventional but arbitrary. Some authors have suggested that 6 months should be the cutoff for when the fertile window is definitively identified and used consistently for timing intercourse.^{40,41} We used either definition for inclusion in this study.

Compared with outcomes from the recent study of NPT in the treatment of infertility in an Irish general practice, both the crude cumulative proportion of first live births after 24 months (38.0% vs 25.5%) and the proportion of conceptions (47.2% vs 33.0%) were higher. While the mean female age was similar in both studies, the average length of time that couples tried to conceive before starting NPT was much longer in the Irish study (5.6 years vs 3.2 years). Also, 33% of couples had previous assisted reproductive technology in the Irish study compared with only 8% in this study. Thus, the infertile cohort in this study had a better initial prognosis than that in the Irish study. Diagnoses and treatments, as well as low rates of multiple births and preterm births, were similar in both studies.³³

The overall live birth rate for large cohorts of patients using IVF is in the range of 50% after 1 year of treatment.^{38,42,43} A small randomized trial and 2 simulation studies suggest that conservative treatment (such as NPT) might have cumulative rates of live birth that over time are similar to more invasive treatments like IVF.⁴³⁻⁴⁵ However, all comparisons must be made cautiously,

because the underlying characteristics of couples (including women's age, previous pregnancies, length of time attempting pregnancy before treatment, and previous treatments attempted) affect the probability of live birth and can vary greatly between different study populations.^{42,45,46} The Cochrane systematic review of IVF for unexplained infertility states that the effectiveness of IVF for unexplained infertility remains unproven because of the lack of good cohort studies.⁴⁷ Further cohort studies for all types of infertility treatment are needed,^{37,47} and we hope this study will help stimulate further cohort-based evaluation of fertility treatments. With regard to neonatal outcomes, it is important to note that there were no multiple gestations in this study. With IVF, multiple gestations are common (eg, 28% in Canada).⁴⁸

Limitations

One limitation of this study is the limited sample size within a single family practice. Consequently, this study was not able to examine any subgroup effects. Also, 48% (52 out of 108) of couples exited the NPT program before a full 24-month course of treatment. This is similar to the dropout rate in the Irish study, as well as in most studies of fertility treatments.⁴³ Finally, it is possible that couples who choose NPT might somehow be different than those who choose other treatments. However, the characteristics of woman's age, length of time trying to conceive, previous pregnancy, and previous treatments are the main factors that are known to affect the probability of conception with or without treatment.^{40,42,46,49,50} These characteristics are reported in this study to allow for assessment of the applicability of these results to other populations.

Conclusion

In the treatment of infertility and miscarriage, the current study showed that NPT in a single family physician's office resulted in cumulative proportions of live births and initial conception that were comparable to those in an NPT general practice in Ireland. The low proportions of multiple and preterm births were also similar. The approach of NPT is such that it is readily integrated into a general family practice in Canada, improving timely access to couples seeking infertility treatments. Further larger multicentre prospective studies to compare NPT to other forms of infertility treatment are warranted.

Acknowledgments

We thank **Vania Branker**, the research assistant who verified and entered data in the database, and **Dr Francis Sem** for his review of the first draft of the manuscript.

Notes

EDITOR'S KEY POINTS

- This research examines outcomes of natural procreative technology (NaProTechnology or NPT), a systematic medical approach for treating infertility and miscarriage, in a family physician's office.
- Natural procreative technology is based on the Creighton Model FertilityCare System, which helps a woman identify her fertile phase and the likely day of ovulation through daily observations of vaginal discharge of cervical fluid. Preovulatory estradiol and postovulatory estradiol and progesterone levels (and sometimes follicular ultrasound) are used to diagnose hormonal deficiencies or ovulatory defects.
- This study shows that NPT in a single family physician's office resulted in cumulative live birth and conception proportions comparable to those in an NPT general practice in Ireland. There were no multiple births.

POINTS DE REPÈRE DU RÉDACTEUR

- Cette étude voulait connaître les issues d'une technique de procréation naturelle (NaProTechnology ou NPT), une méthode

médicale systématique pour traiter l'infertilité et les fausses couches à partir du bureau d'un médecin de famille.

- La technique de procréation naturelle est basée sur le Creighton Model FertilityCare System qui aide les femmes à identifier leur phase fertile et le jour probable de leur ovulation grâce à l'observation quotidienne des sécrétions du col qui s'écoulent du vagin. On utilise les niveaux préovulatoires d'oestradiol et les niveaux post-ovulatoires d'oestradiol et de progestérone (et parfois l'échographie du follicule) pour diagnostiquer les déficiences hormonales et l'absence d'ovulation.
- Cette étude montre que l'utilisation de la technique NPT au bureau d'un seul médecin de famille a entraîné des proportions cumulatives de naissances vivantes et de conceptions comparables à celles d'une clinique de NPT en Irlande. Il n'y a eu aucune naissance multiple.

Footnotes

This article has been peer reviewed.

Cet article a fait l'objet d'une révision par des pairs.

Contributors

Dr Tham contributed to the concept of the study and the quantitative data collection, directed the writing, and approved the final version of the manuscript. **Dr Schliep** was responsible for data analysis, participated in the writing, and approved the final version of the manuscript. **Dr Stanford** contributed to the concept of the study, guided the analysis, edited the manuscript, and approved the final version of the manuscript.

Competing interests

None declared

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