ORIGINAL ARTICLE: ASSISTED REPRODUCTION

# Endometrin as luteal phase support in assisted reproduction

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**Objective:** To compare clinical pregnancy rate (PR) and live birth rate (LBR) between Endometrin monotherapy versus Endometrin and P in oil combination therapy in assisted reproductive technology (ART) cycles.
**Design:** Retrospective analysis.
**Setting:** Large private practice.
**Patient(s):** Patients undergoing autologous fresh IVF cycles, autologous frozen ET cycles, and fresh oocyte donor cycles were included for analysis.
**Intervention(s):** Endometrin as a single agent for luteal support, Endometrin monotherapy or Endometrin with P in oil used at least once every 3 days for luteal support, Endometrin combination therapy.
**Main Outcome Measure(s):** Clinical PR and LBR.
**Result(s):** A total of 1,034 ART cycles were analyzed. Endometrin monotherapy was used in 694 of 1,034 (67%) cycles and Endometrin combination therapy was used in 340 of 1,034 (33%) cycles. In all fresh cycles, clinical PR was not significantly different (IVF autologous: Endometrin monotherapy 46.9% vs. Endometrin combination therapy 55.6%; donor oocyte endometrin monotherapy 45.2% vs. Endometrin combination therapy 52.0%). Frozen ET cycles had a significantly higher clinical PR and LBR with combination therapy group compared with monotherapy (clinical PR 47.9% vs. 23.5%; LBR 37.5% vs. 17.3%).
**Conclusion(s):** Endometrin monotherapy was sufficient for the P component of luteal support and provided high PRs for fresh cycles in both autologous and donor oocyte cycles. Clinical PR and LBR in frozen ET cycles were significantly improved with the addition of IM P to Endometrin therapy. This may reflect the fact that lesser quality embryos are transferred in frozen ET cycles, and more intense P support is required for comparable PRs. (Fertil Steril® 2012;■:■–■. ©2012 by American Society for Reproductive Medicine.)
**Key Words:** IVF, ART, luteal phase support, progesterone, donor oocyte

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Progesterone (P) supplementation in the luteal phase for IVF has become standard practice due to iatrogenic disruption of normal corpus luteum (CL) function during oocyte retrieval. In an attempt to compensate for this detrimental effect, practitioners have supplemented the luteal phase using a variety of hormonal agents (1, 2). A meta-analysis by Soliman et al. (3) evaluated more than 30 randomized trials that addressed the need for luteal support and concluded that IM P or hCG was superior to placebo. Human chorionic gonadotropin is a highly effective means of luteal support but it carries the risk of ovarian hyperstimulation syndrome (OHSS) (4). Intramuscular P in oil results in high circulating serum P levels but the potential for pain and local reaction at the injection site may make this a less favored route of administration. Reduction in the number of injections from daily administration to twice weekly could mitigate inconvenience, pain, and risk of local reactions.

In addition to IM injection, P supplementation can also be given by oral or vaginal routes. Although oral formulations are convenient for the patient, two randomized controlled studies showed decreased implantation rates and pregnancy rates (PR) compared to IM or vaginal administration (5, 6). This was thought to be due to degradation from the first pass effect of hepatic metabolism (4). The vaginal preparations are better tolerated, more convenient, and have the ability to permit drug delivery directly to the uterus (7). Pooled data from several randomized controlled trials (8) have

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demonstrated that vaginal P is comparable to IM P for luteal phase support in fresh autologous IVF cycles.

Available vaginal preparations of P include pharmacy compounded suppositories, P in a bioadhesive gel, or as an oil-in-capsule formulation. All vaginal P forms were found to provide similar clinical PRs in fresh IVF cycles (9). More recently, a vaginal micronized P insert, Endometrin (Ferring Pharmaceuticals) was introduced and found to be safe and well-tolerated with comparable PRs in autologous fresh IVF cycles (10, 11).

At present, there are only four published large studies (11–14) specifically evaluating Endometrin for luteal support. These studies have compared Endometrin to vaginal P gel or Endometrin to IM P only in autologous fresh IVF cycles. When Endometrin was first introduced, several physicians in our group were not comfortable using Endometrin as a solo agent. They supplemented Endometrin therapy with a "boost" of IM P, given as a 50-mg IM injection administered at least once every 3 days. The aim of this retrospective study is to compare outcomes between the Endometrin monotherapy and Endometrin combination therapy groups to assess whether the addition of a small booster injection of IM P administered at least twice weekly improves outcomes. Furthermore, this study evaluates the efficacy of these two methods of P support in frozen ET cycles and donor oocyte cycles in addition to autologous fresh IVF cycles.

## MATERIALS AND METHODS

### Study Design

Institutional Review Board approved analysis of patients undergoing fresh autologous IVF cycles, fresh donor oocyte cycles, and autologous frozen ET cycles from January 1, 2007 to December 31, 2008. Only patients who used either Endometrin monotherapy or Endometrin and IM P combination therapy were included in the analysis. All patients using other luteal support protocols or using a gestational carrier were excluded. Patients using autologous oocytes ranged in age from 21–44 years and patients using donor oocytes ranged in age from 30–49 years. The patient population was inclusive of a broad spectrum of diagnoses such as diminished ovarian reserve, endometriosis, male factor, tubal factor, and ovulatory dysfunction.

### Treatment

For autologous IVF cycles, the patients underwent down-regulation by midluteal phase GnRH agonist (GnRH-a) down-regulation with leuprolide acetate (LA; Lupron, Tap Pharmaceuticals) at a dose of 0.5 mg daily or with the use of a GnRH antagonist (Ganirelix Acetate, Organon or Cetrotide, Serono). The GnRH antagonist was initiated 6 days after stimulation or when the lead follicle was 12–14 mm. Antagonist was given as either 0.25 mg daily doses or a 3-mg dose followed by daily 0.25-mg injections after 96 hours. Controlled ovarian hyperstimulation (COH) with injectable gonadotropins was initiated after down-regulation was verified. Ovarian stimulation was carried out with recombinant FSH alone (Follistim, Organon or Gonal-f, Serono) or in a mixed protocol with hMG (Menopur, Ferring Pharmaceuticals). The stimulation protocol was decided by the physician of record and was based on age, antral follicle count, body mass index (BMI), and day 3 FSH levels. A standard starting dose of FSH 225 U or a mixed protocol with FSH and hMG 225 U total was initiated. Step-down or step-up protocol adjustments were made based on individual responses.

When two or more follicles had attained a minimum mean diameter of 18 mm, follicular maturation was achieved with either recombinant hCG 250 $\mu$g SC (Ovidrel, Serono) or urinary hCG 10,000 IU IM. Transvaginal ultrasound-guided oocyte retrieval was performed 36–38 hours after hCG injection.

The patients undergoing frozen ET and recipients of donor oocytes followed a standardized endometrial preparation protocol. Down-regulation was achieved with GnRH-a that was begun in either the midluteal phase of the preceding menstrual cycle or overlapped with oral contraceptive (OC) pills. Uterine preparation was carried out with transdermal $E_2$ patches (Vivelle Dot Noven Pharmaceuticals) for 14 days or until the uterine lining reached a minimum of 7 mm with a trilaminar appearance. If the $E_2$ level was $<$150 pg/mL or the lining was $<$6 mm, transvaginal $E_2$ (Estrace, Barr Laboratories) was administered. Cycles were cancelled if, despite the addition of $E_2$, the endometrial lining failed to develop. The GnRH-a was discontinued upon initiation of P therapy. All included frozen ETs were at the blastocyst stage. Standard laboratory protocols were followed for IVF, donor oocyte, and frozen ET cycles, including intracytoplasmic sperm injection (ICSI), assisted hatching for cleavage stage embryos, and extended culture for blastocyst transfer, as clinically appropriate.

Ultrasound-guided transfer was performed, and all patients received luteal phase P supplementation administered as Endometrin 100-mg vaginal inserts three times daily, Endometrin monotherapy, or a combination of Endometrin (3 times a day) with a booster injection of P in oil (50 mg IM) at least once every 3 days. Serum hCG levels were measured 15 days after retrieval, and a clinical pregnancy was defined as the presence of a gestational sac on ultrasound.

### Assessments

The primary end point assessed was clinical PR. The secondary end points included spontaneous abortion rates, biochemical pregnancy losses, and live birth rates.

### Statistical Analyses

A detailed statistical analysis was performed using JMP Software, version 9.0 (SAS Institute). Continuous variables were analyzed by one- and two-classification analysis of variance, with the later including an interaction term. If the interaction was not statistically significant, the analysis was rerun without the interaction term. Differences between mean values were assessed by Tukey's honestly significant different tests. Categorical variables were analyzed by nominal logistic regression using an analogous strategy. A probability of $<.05$ was considered to be significantly different.

## RESULTS

Between January 1, 2007 and December 31, 2008, a total of 1,034 assisted reproductive technology (ART) cycles were available for analyses (Fig. 1). Endometrin monotherapy was used in 694 of 1,034 cycles (67%), whereas Endometrin combination therapy was used in 340 of 1,034 cycles (33%). In the Endometrin combination group, more than 75% of patients were supplemented with IM P every 3 days, whereas the remaining patients were supplemented with IM P every other day. Age was not significantly different between patients treated with Endometrin monotherapy or Endometrin combination therapy for the IVF autologous and frozen ET groups (Tables 1 and 2). Patients in the donor oocyte group (Table 3) treated with Endometrin alone were older than the patients treated with Endometrin combination therapy; however, clinical PR and live birth rates were not significantly different between the two groups. Other parameters, such as etiology of infertility and BMI, were not significantly different between treatment groups (BMI data not shown).

The number of embryos transferred was similar for all treatment groups. There was not a statistically significant difference between biochemical, spontaneous abortion, and live birth rates in all treatment groups.

The clinical PRs, implantation rates, and live birth rates were not significantly different for patients treated with Endometrin monotherapy and Endometrin combination therapy in the IVF autologous and donor oocyte groups (Tables 1 and 2). In the frozen ET group (Table 3), clinical PRs, implantation rates, and live birth rates were lower for the group treated with Endometrin monotherapy than the group that had the addition of IM P to Endometrin.

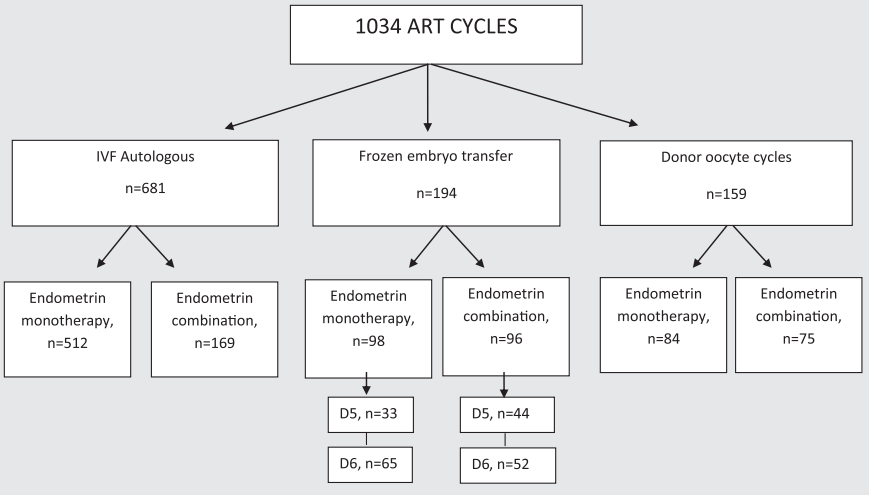
To further examine why the clinical PR was lower in the Endometrin monotherapy group for frozen ETs, the individual record was examined and reanalyzed between those embryos that were frozen and transferred on day 5 versus day 6 (data not shown) as some studies have shown a higher PR from embryos vitrified on day 5 compared with day 6 (15). For both Endometrin monotherapy and combination therapy (Supplemental Figure 1), we observed a higher PR with embryos transferred on day 5 compared with day 6 (Endometrin monotherapy day 5 clinical PR, n = 33 with 9/33 [27.3%] compared to day 6 clinical PR, n = 65 with 14/65 [21.5%] and Endometrin combination therapy clinical PR day 5, n = 44 with 26/44 [59.1%] compared to day 6 clinical PR, n = 52 with 20/52 [38.5%]). Overall, when comparing groups, Endometrin combination therapy was superior for frozen ETs to Endometrin monotherapy and the patients with the best outcomes were those on combination therapy with an embryo that was vitrified on day 5.

## DISCUSSION

The results in this study were consistent with the findings of the majority of other published reports showing comparable PRs in autologous fresh cycles when comparing vaginal micronized P to IM P (11–14). This study demonstrated that Endometrin monotherapy was sufficient for the P component of luteal support and provided high PRs in both fresh autologous IVF cycles and fresh oocyte donor cycles. Our findings are in contrast to a recent prospective trial that demonstrated higher live birth rates with vaginal P (Crinone, Fleet Laboratories) compared to IM P (16) in fresh autologous IVF cycles. That study was the first to demonstrate superiority of a vaginal preparation compared with P in oil, although the dose of P in oil was low at 25 mg daily in women less than 40 years old. Further trials are needed comparing the efficacy of the varied vaginal P preparations.

A novel finding of our study was that in frozen ET cycles, the addition of P in oil to Endometrin therapy was superior to Endometrin used alone. This may reflect the fact that lesser quality embryos are transferred in frozen ET cycles, and more intense P support is required for comparable PRs. However, it should be noted that combination therapy may have

## FIGURE 1




Flow chart of patient participation. ART = assisted reproductive technology; D5 = day 5; D6 = day 6.

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## TABLE 1

**IVF autologous cycles.**

| Parameter | Endometrin alone | Endometrin + IM P | *P* value |
|---|---|---|---|
| Age (y) | 33.0 ± 3.8 | 32.6 ± 4.4 | .33 |
| Cycles (n) | 512.0 | 169.0 | |
| Embryos transferred (n) | 2.0 ± 0.7 | 2.1 ± 0.8 | .25 |
| Endometrial thickness (mm) | 11.2 ± 2.4 | 11.40 ± 2.4 | .59 |
| Positive hCG (%) | 56.8 | 67.4 | .014 |
| Implantation rate (%) | 37.0 | 41.0 | .28 |
| Clinical pregnancy rate (%) | 46.9 | 55.6 | .05 |
| Biochemical pregnancy rate (%) | 9.4 | 7.1 | .36 |
| Spontaneous abortion rate (%)[a] | 6.1 | 13.1 | .004 |
| Live birth rate (%)[a] | 40.6 | 42.3 | .07 |

*Note:* Data are expressed as mean ± SD or percentage (frequency).
[a] Patients lost to follow-up are excluded from analysis: Endometrin alone = 2, Endometrin + IM P = 1.

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## TABLE 3

**Frozen ET autologous.**

| Parameter | Endometrin alone | Endometrin + IM P | *P* value |
|---|---|---|---|
| Age (y) | 34.5 ± 4.0 | 35.1 ± 4.6 | .41 |
| Cycles (n) | 98.0 | 96.0 | |
| Embryos transferred (n) | 1.8 ± 0.7 | 1.9 ± 0.6 | .34 |
| Endometrial thickness (mm) | 9.5 ± 2.2 | 9.5 ± 2.4 | .34 |
| Day 5 blastocyst transfer (n) | 33.0 | 44.0 | |
| Day 6 blastocyst transfer (n) | 65.0 | 52.0 | |
| Positive hCG (%) | 33.7 | 60.4 | .0002 |
| Implantation rate (%) | 15.3 | 35.8 | .0001 |
| Clinical pregnancy rate (%) | 23.5 | 47.9 | .0004 |
| Biochemical pregnancy rate (%) | 10.2 | 10.4 | .96 |
| Spontaneous abortion rate (%) | 6.1 | 9.4 | .40 |
| Live birth rate (%) | 17.3 | 37.5 | .0015 |

*Note:* Data are expressed as mean ± SD or percentage (frequency).

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subtle clinical advantages such that the overall clinical PR appears to be higher but did not quite reach statistical significance.

Further analyses of frozen ET cycles were performed to help clarify this finding. Clinical PRs were found to be higher with day 5 blastocyst transfers compared to day 6 blastocyst transfers. The difference between groups, however, could not be explained by having a higher proportion of the more favorable group in the combination therapy arm. For both day 5 and day 6 transfers, clinical PRs and live birth rates were higher in the Endometrin combination therapy compared with the Endometrin monotherapy group.

One retrospective cohort analysis (17) of frozen ET cycles compared P vaginal suppositories and IM P versus IM alone found a higher PR with IM alone, but this may have been related to the higher number of embryos transferred. A Cochrane Review (18) that included 22 randomized trials found that there was no statistically significant benefit of vaginal versus IM P administration for women undergoing ETs with frozen embryos or embryos derived from donor oocytes. Although no published articles have directly compared Endometrin to IM P in frozen ET cycles, the preponderance of studies in the literature have demonstrated no difference in vaginal compared with IM P supplementation in frozen ET cycles.

The strengths of this study included the sample size that encompassed a broad spectrum of typical infertility patients presenting for ART. More than 1,000 cycles were analyzed, and to our knowledge, this is the first study to include donor oocyte and autologous frozen ETs comparing Endometrin monotherapy to Endometrin combination therapy.

This study is limited by its retrospective design and by its lack of randomization. Some providers in our group chose to add IM P to their patients receiving Endometrin, whereas other physicians did not. In general, the providers who chose to add IM P did so consistently for all patients, reducing bias. The Endometrin combination therapy group was somewhat heterogeneous, more than 75% of patients were supplemented with IM P every 3 days whereas the remaining patients were supplemented with IM P every other day. These "booster" injections of P, even in the form of every 3-day administration, in combination with Endometrin may be sufficient to sustain steady serum levels of P.

The smaller number of cycles in the frozen ET groups limits the analysis when further divided into day 5 and day 6 ETs and may prevent more meaningful interpretation of the data. The lack of smoking history also limits this study as smoking can impact implantation and miscarriage rates.

In summary, this study showed Endometrin monotherapy was sufficient for the P component of luteal support and provided high PRs in both autologous IVF cycles and donor oocyte cycles. The addition of IM P was superior to Endometrin monotherapy in autologous frozen ET cycles. This may reflect the fact that the best quality embryos are transferred in the original fresh cycle and lesser quality embryos are transferred in frozen ET cycles, thus more intense P support is required for comparable PRs. Additional larger prospective trials are warranted to determine the optimum luteal phase supplementation in ART cycles.

## TABLE 2

**Donor oocyte cycles.**

| Parameter | Endometrin alone | Endometrin + IM P | *P* value |
|---|---|---|---|
| Age (y) | 41.9 ± 3.6 | 39.4 ± 5.1 | .0004 |
| Cycles (n) | 84.0 | 75.0 | |
| Embryos transferred (n) | 2.2 ± 0.7 | 2.1 ± 0.6 | .12 |
| Endometrial lining (mm) | 9.4 ± 2.3 | 9.4 ± 2.0 | .77 |
| Positive hCG (%) | 61.9 | 61.3 | .94 |
| Implantation rate (%) | 32.0 | 35.0 | .63 |
| Clinical pregnancy rate (%) | 45.2 | 52.0 | .39 |
| Biochemical pregnancy rate (%) | 16.7 | 9.3 | .17 |
| Spontaneous abortion rate (%)[a] | 6.0 | 6.8 | .82 |
| Live birth rate (%)[a] | 39.3 | 43.8 | .56 |

*Note:* Data are expressed as mean ± SD or percentage (frequency).
[a] Patients lost to follow-up are excluded from analysis: Endometrin alone = 2, Endometrin + IM P = 1.

*Feinberg. Endometrin as luteal phase support in assisted reproduction. Fertil Steril 2012.*

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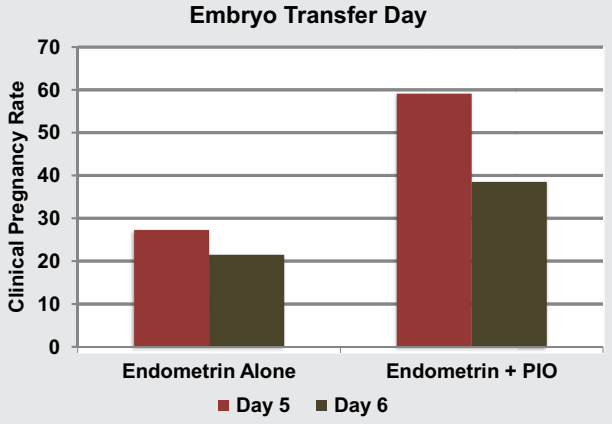
## REFERENCES

1. Hubayter ZR, Muasher SJ. Luteal supplementation in in vitro fertilization: more questions than answers. Fertil Steril 2008;89:749–58.
2. The Practice Committee of the American Society of Reproductive Medicine. Progesterone supplementation during the luteal phase and in early pregnancy in the treatment of infertility: an educational bulletin. Fertil Steril 2008;90:S150–3.
3. Soliman S, Daya S, Collins J, Hughes EG. The role of luteal phase support in infertility treatment: a meta-analysis of randomized trials. Fertil Steril 1994; 61:1068–76.
4. Pritts EA, Atwood AK. Luteal phase support in infertility treatment: a meta-analysis of the randomized trials. Hum Reprod 2002;17:2287–99.
5. Licciardi FL, Kwiatkowski A, Noyes NL, Berkeley AS, Krey LL, Grifo JA. Oral versus intramuscular progesterone for in vitro fertilization: a prospective randomized study. Fertil Steril 1999;71:614–8.
6. Friedler S, Raziel A, Schachter M, Strassburger D, Bukovsky I, Ron-El R. Luteal support with micronized progesterone following in vitro fertilization using a down-regulation protocol with gonadotrophin-releasing hormone agonist: a comparative study between vaginal and oral administration. Hum Reprod 1999;14:1944–8.
7. Miles RA, Paulson RJ, Lobo RA, Press MF, Dahmoush L, Sauer MV. Pharmacokinetics and endometrial tissue levels of progesterone after administration by intramuscular and vaginal routes: a comparative study. Fertil Steril 1994; 62:485–90.
8. Zarutskie PW, Phillips JA. A meta-analysis of the route of administration of luteal phase support in assisted reproductive technology: vaginal versus intramuscular progesterone. Fertil Steril 2009;92:163–9.
9. Polyzos NP, Messini CI, Papanikolaou EG, Mauri D, Tzioras S, Badawy A, et al. Vaginal progesterone gel for luteal phase support in IVF/ICSI cycles: a meta-analysis. Fertil Steril 2010;94:2083–7.
10. Ng EH, Chan CC, Tang OS, Ho PC. A randomized comparison of side effects and patient convenience between Cyclogest suppositories and Endometrin tablets used for luteal phase support in IVF treatment. Eur J Obstet Gynecol Reprod Biol 2007;131:182–8.
11. Doody KJ, Schnell VL, Foulk RA, Miller CE, Kolb CA, Blake EJ, et al. Endometrin for luteal phase support in a randomized, controlled, open-label, prospective in-vitro fertilization trial using a combination of Menopur and Bravelle for controlled ovarian hyperstimulation. Fertil Steril 2009;91: 1012–7.
12. Khan N, Richter KS, Newsome TL, Blake EJ, Yankov VI. Matched-samples comparison of intramuscular versus vaginal progesterone for luteal phase support after in vitro fertilization and embryo transfer. Fertil Steril 2009; 91:2445–50.
13. Mitwally MF, Diamond MP, Abuzeid M. Vaginal micronized progesterone versus intramuscular progesterone for luteal support in women undergoing in vitro fertilization-embryo transfer. Fertil Steril 2010;93:554–69.
14. Blake EJ, Norris PM, Dorfman SF, Longstreth J, Yankov VI. Single and multidose pharmacokinetic study of a vaginal micronized progesterone insert (Endometrin) compared with vaginal gel in healthy reproductive aged female subjects. Fertil Steril 2010;94:1296–301.
15. Shapiro BS, Richter KS, Harris DC, Daneshmand ST. A comparison of day 5 and day 6 blastocyst transfers. Fertil Steril 2001;75:1126–30.
16. Silverberg KM, Vaughn TC, Hansard LJ, Burger NZ, Minter T. Vaginal (Crinone 8%) gel vs. intramuscular progesterone in oil for luteal phase support in in vitro fertilization: a large prospective trial. Fertil Steril 2012;97:344–8.
17. Graziano V, Check JH, Dietterich C, Choe JK, Yuan W. A comparison of luteal phase support in graduated estradiol/progesterone replacement cycles using intramuscular progesterone alone versus combination with vaginal suppositories on outcome following frozen embryo transfer. Clin Exp Obstet Gynecol 2005;32:93–4.
18. Glujovsky D, Pesce R, Fiszbajn G, Sueldo C, Hart RJ, Ciapponi A. Endometrial preparation for women undergoing embryo transfers with frozen embryos or embryos derived from donor oocytes. Cochrane Database Syst Rev 2010:CD006359.

## SUPPLEMENTAL FIGURE 1




Clinical pregnancy rates (PR) for frozen embryo transfers by day of transfer, day 5 or day 6. Clinical PR by day of ET for Endometrin monotherapy or Endometrin + Progesterone in oil (PIO). Statistical analysis: Endometrin alone versus Endometrin + PIO: *P*=.0008; day 5 versus day 6 transfer: *P*=.051; interaction: *P*=not significant (NS).

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