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Likelihood of conception with a single act of intercourse: providing benchmark rates for assessment of post-coital contraceptives

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Abstract

Emergency post-coital contraceptives effectively reduce the risk of pregnancy, but their degree of efficacy remains uncertain. Measurement of efficacy depends on the pregnancy rate without treatment, which cannot be measured directly. We provide indirect estimates of such pregnancy rates, using data from a prospective study of 221 women who were attempting to conceive. We previously estimated the probability of pregnancy with an act of intercourse relative to ovulation. In this article, we extend these data to estimate the probability of pregnancy relative to intercourse on a given cycle day (counting from onset of previous menses). In assessing the efficacy of post-coital contraceptives, other approaches have not incorporated accurate information on the variability of ovulation. We find that the possibility of late ovulation produces a persistent risk of pregnancy even into the sixth week of the cycle. Post-coital contraceptives may be indicated even when intercourse has occurred late in the cycle.

Keywords: Fertility; Emergency contraception; Menstrual cycle; Ovulation; Pregnancy

1. Introduction

Post-coital contraceptives reduce the risk of pregnancy, although their degree of efficacy is unclear. Placebo-controlled studies are unacceptable, and researchers have instead relied on indirect estimates of what a woman's probability of pregnancy might have been had she not been treated. We discuss methodological issues raised by these indirect approaches, and we use data from a prospective study to derive the (untreated) probability of pregnancy after a single act of intercourse on a given day of the cycle.

2. Materials and methods

Data are drawn from a prospective study of early pregnancy conducted in North Carolina [1]. Women (n = 221) who planned to become pregnant were enrolled at the time they discontinued use of any birth control. Women with known fertility problems were ineligible. Women were asked their usual cycle length, and whether their cycles were generally "regular" or "irregular." (Exact questions provided in Appendix.) Women collected daily first morning urine samples, and they recorded menstrual bleeding and unprotected intercourse daily. Most participants were white, well-educated women, with ages ranging from 21–42 (mean 30). All provided informed consent, which was approved by the NIEHS Institutional Review Board. Detailed descriptions of the study methods and participants have been provided elsewhere [1–3].

Day of ovulation was estimated on the basis of changes in daily patterns of urinary estrone-3-glucuronide (a major metabolite of estradiol) and pregnanediol-3-glucuronide (the major metabolite of progesterone). An algorithm based on the ratio of these steroid hormones provides a robust measure of the timing of ovulation. This ratio measure has been validated against the urinary peak of luteinizing hormone (LH) [4], which is one of the most accurate markers of ovulation [5]. Using the steroid ratio measure, we estimated day of ovulation in 696 cycles from 213 women.

We have estimated previously that the mean probability of a clinical pregnancy with a single act of intercourse is 0.04, 0.13, 0.08, 0.29, 0.27, and 0.08 for the 6 consecutive days ending with ovulation [6]. (Outside this 6-day interval,

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the estimated probability of pregnancy is <0.01.) In the present article, we extend these estimates by incorporating the variability in day of ovulation.

In assessments of post-coital contraceptives, the day of onset of subsequent menses is usually known (unless the woman becomes pregnant). However, post-coital contraceptives can delay the next menses [7,8], which would produce bias in fertility estimates using calculations of ovulation day counting backwards from subsequent menses. We, therefore, estimated pregnancy probabilities counting forward from the previous menses (i.e., the time from onset of menses to ovulation). Although this interval is admittedly more variable, it is less biased.

Estimation was as follows. The observed set of ovulation days (i.e., follicular phase lengths) for a given woman were weighted by the reciprocal of her total number of cycles, allowing all cycles to be included without over-representing less-fertile women. The empiric distribution of these weighted ovulation days was then smoothed by fitting a log-t distribution, assuming a zero probability of ovulation on the first 3 cycle days.

The resulting distribution of ovulation days also defines the probability that a given cycle day is one of the 6 consecutive fertile days ending with ovulation. This probability was multiplied by the probability that a clinical pregnancy would result from intercourse on that particular fertile day, thus apportioning the fertile contributions of the 6 fertile days across all menstrual cycle days.

In this calculation, we used as the denominator only those women whose cycle had not yet ended by that cycle day. This adjustment has little effect on pregnancy estimates during the first 4 weeks of the cycle, but provides more accurate estimates thereafter. After cycle day 28, fewer and fewer women are still awaiting their menses on any given day. Among this diminishing group, some had not yet ovulated (due to an unpredictably late ovulation). Such women were still potentially fertile, even though they may have thought menses was imminent. It is appropriate to base each cycle day's pregnancy estimate on the actual number of women still awaiting their next menses on that day.

3. Results

The probability of pregnancy with one completely random act of unprotected intercourse was 3.1% in our data. Estimates can be substantially improved by including information on when intercourse occurred in the menstrual cycle. Fig. 1 shows the estimated probability of a clinical pregnancy with one act of intercourse during the cycle, estimated for each day of the cycle. (The dots show the probabilities calculated directly from the observed distribution of ovulation days, while the curve shows the probabilities based on the smoothed distribution of ovulation days.) Estimates based on the smoothed distribution are a reasonable approximation of the empiric results. The smoothed data are the basis of the remainder of the analysis.

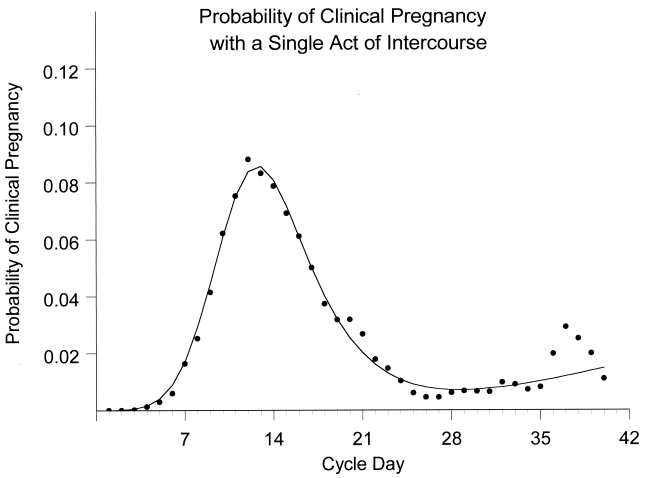

Fig. 1. Probability of clinical pregnancy with one act of intercourse relative to day of the menstrual cycle. (Dots are based on the empiric distribution of day of ovulation, while the line is based on the smoothed distribution of day of ovulation.)

The probability of conception is negligible during the first 3 days of the cycle. By day 7, the likelihood of pregnancy with intercourse is nearly 2%. This rises to a peak of nearly 9% on day 13. This probability declines thereafter but remains around 1% as late as day 40 and beyond.

We divided women according to whether they had reported regular (84%) or irregular cycles (16%), and repeated the analysis based on their separate patterns of ovulation. For women reporting regular cycles, the pattern of probabilities was little changed from the overall (Fig. 2 cf. Fig. 1). Women reporting irregular cycles had later and more irregular ovulation, with their peak probability of pregnancy occurring later in their cycle. Data from Figs. 1 and 2 are provided in the Table 1.

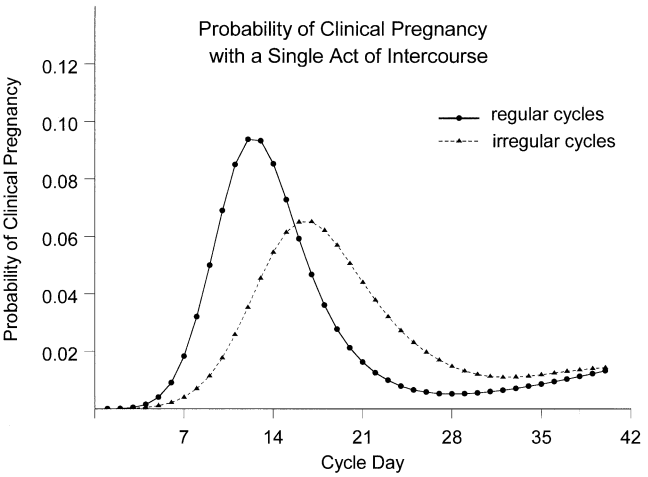

Fig. 2. Probability of clinical pregnancy with one act of intercourse relative to day of the menstrual cycle, for women who reported regular cycles, and for those who reported irregular cycles. (Based on the smoothed distribution of day of ovulation.)

Table 1
Estimated mean probability of clinical pregnancy following a single act of unprotected intercourse on a given day of the menstrual cycle, conditional on reaching that day of the cycle

Cycle day	All women	Women with regular cycles	Women with irregular cycles
1	0.000	0.000	0.000
2	0.000	0.000	0.000
3	0.001	0.001	0.000
4	0.002	0.002	0.001
5	0.004	0.004	0.001
6	0.009	0.009	0.002
7	0.017	0.018	0.004
8	0.029	0.032	0.007
9	0.044	0.050	0.011
10	0.061	0.069	0.018
11	0.075	0.085	0.026
12	0.084	0.094	0.035
13	0.086	0.093	0.045
14	0.081	0.085	0.055
15	0.072	0.073	0.061
16	0.061	0.059	0.065
17	0.050	0.047	0.065
18	0.040	0.036	0.062
19	0.032	0.028	0.057
20	0.025	0.021	0.051
21	0.020	0.016	0.044
22	0.016	0.013	0.038
23	0.013	0.010	0.032
24	0.011	0.008	0.027
25	0.009	0.007	0.023
26	0.008	0.006	0.020
27	0.007	0.005	0.017
28	0.007	0.005	0.015
29	0.007	0.005	0.013
30	0.007	0.006	0.012
31	0.008	0.006	0.011
32	0.008	0.007	0.011
33	0.009	0.007	0.011
34	0.009	0.008	0.011
35	0.010	0.009	0.012
36	0.011	0.010	0.013
37	0.012	0.010	0.013
38	0.013	0.011	0.014
39	0.014	0.012	0.014
40	0.015	0.013	0.014

4. Discussion

A single act of unprotected intercourse can occur when intercourse is unplanned, when there has been a contraceptive failure (as with a broken condom), or when there has been sexual assault. In 1960, Tietze estimated that the chance of pregnancy with one completely random act of intercourse was 2% to 4% [9]. More recently, Holmes and her colleagues reported that the probability of pregnancy after rape was 5% in a national sample of US women [10]. (Criminal sexual assault is presumably random with regard to the menstrual cycle.) This study may have overestimated the probability of pregnancy because it could not exclude pregnancies conceived apart from the sexual assault. Our estimate of 3% is lower than reported by Holmes, but consistent with Tietze's estimate.

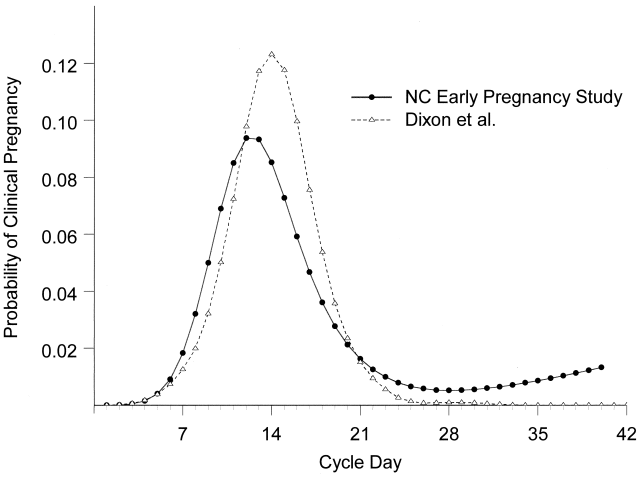

Fig. 3. Probability of clinical pregnancy with one act of intercourse for women with regular cycles, comparing data from the present study with data generated using the methods of Dixon et al. [12].

The probability of pregnancy can be estimated much more precisely if based on the day of intercourse relative to ovulation. Several studies have provided estimates for a single act of intercourse relative to ovulation [3,11,12]. Unfortunately, women do not ordinarily know when they ovulate, and there is no way to determine the ovulation day in retrospect. However, many women do know the day on which their previous menses began. When assessing the efficacy of post-coital contraception, investigators have used this information by converting pregnancy rates relative to ovulation into pregnancy rates relative to most recent menses.

The specific approach most often used for this purpose was suggested by Dixon et al. [13]. Dixon created a single set of pregnancy rates from several published studies [10, 11,14]. An arbitrary error distribution was added to account for the biologic variability of ovulation day. With Dixon's method, 14 days is subtracted from a woman's usual cycle length to estimate the "usual cycle day of ovulation". Dixon's pregnancy rates are then applied to the intercourse day relative to this inferred cycle day of ovulation. Women with irregular cycles are excluded.

To compare our results to Dixon's, we applied Dixon's pregnancy rates to the 171 women in our study who reported that they had regular cycles and who provided an "usual cycle length." Dixon advised subtracting 14 days from the usual cycle length, but 13 days provides a less biased estimate of the mean ovulation day [15], and is the number used here. The results are shown in Fig. 3.

The two curves are surprisingly similar, considering that our data are based on an empiric distribution of ovulation variability while Dixon's are based on a rough guess. Still, there are large differences on days 13–19. During these highly fertile days, Dixon's estimates are as much as 50% greater than those estimated here. If the single day of inter-

course that prompted treatment were randomly distributed across the menstrual cycle, then these differences would have little impact. However, women with unprotected intercourse may be more likely to seek emergency contraception during their mid-cycle, when they know they are at the highest risk of pregnancy. To the degree this selection occurs, Dixon's approach would produce inflated estimates of the *expected* pregnancy rate, and overestimate the efficacy of post-coital contraception.

In 1998, two papers [8,15] estimated the efficacy of emergency contraception using our published rates of pregnancy with intercourse relative to ovulation [3]. However, the authors did not take into account the natural variability of ovulation day in the cycle. The resulting probabilities of pregnancy are concentrated on too few days of the cycle, making the estimates too high in mid-cycle and too low on other days. As with Dixon's approach, this could lead to overestimation of the efficacy of treatment.

There is an additional problem with previous methods. They have incorrectly estimated that the probability of pregnancy is zero (or approaching zero) late in the menstrual cycle. Some women awaiting their menses are still preovulatory and thus at risk of pregnancy. While they are few in number, these women are not so few relative to the shrinking denominator of eligible ("surviving") women. Our survival-adjusted data suggest that the probability of pregnancy persists at around 1% for an extended time after day 28 (Figs. 1 and 2).

The routine exclusion of women with irregular cycles from past studies of emergency contraception deserves comment. If such women are receiving treatment, their inclusion in the analysis provides additional power at little additional cost, and makes the overall results more generalizable. Table 1 provides data that permit inclusion of these women.

There are limits to the use of any external standard of fertility. Such rates may not apply well to adolescents or to women in peri-menopause, both of whom have less regular cycles [16] and reduced fertility. More generally, there are many factors besides timing of intercourse that can affect a woman's probability of pregnancy. These include a woman's age, her smoking or other exposures to reproductive toxicants, her history of genital tract infections, and the man's fertility. For these reasons, the pregnancy probabilities shown here also provide poor estimates for any individual woman. For a given woman, it would be more useful to know the probability, on any particular day of her cycle, that she is within the 6 days of her fertile window [17].

No current method for assessing post-coital contraceptive efficacy takes these additional fertility factors into account. The ideal would be referent fertility rates from a large and diverse cohort of women for whom detailed information was available on the major factors that affect fertility. At present, no such data set exists. Finally, there are inherent problems in clinical studies of post-coital contraceptives due to the possibility that women may have more than one unprotected act of intercourse in the treated cycle [18]. This could lead to pregnancies falsely interpreted as failures of the post-coital contraceptive, and thus result in an underestimate of the true efficacy.

All available methods for assessing post-coital contraception assume that intercourse is independent of ovulation, i.e. that the time of ovulation is not influenced by intercourse, and conversely that the physiologic events leading to ovulation do not increase the probability of intercourse. One report has suggested that intercourse may be more common near ovulation, perhaps through pheromones or effects on the woman's libido [19]. While such correlations remain to be confirmed in humans, their presence could make conception more likely than shown by any current referent rates, leading to underestimates of contraceptive efficacy.

Finally, there may be women who would not seek emergency contraception following intercourse in the fifth week of their cycle or later because they believe they are not at risk of pregnancy. There is, in fact, a small but measurable risk. For a woman who needs maximum protection from pregnancy, post-coital contraception may be appropriate even with intercourse beyond the time she expects her next period.

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Appendix

Women were asked about their menstrual history as part of an interview conducted in person (usually in the women's home) at the time they were enrolled in the study. The exact questions on menstrual regularity and usual cycle length are shown below. A complete version of this questionnaire and other data collection instruments are available on the web (http://dir.niehs.nih.gov/direb/home_quest.htm).

"Generally speaking, are your periods regular or irregular? That is, is the length of time between your periods about the same each cycle?"

If a woman expressed uncertainty about the definition, the interviewer continued by saying, "*Regular* refers to the length of time between the first day of each period. We are not asking about amount of flow or the number of days the menstrual period lasts."

"What is your usual cycle length? That is, how many days is it from the first day of one menstrual period to the first day of your next menstrual period?"

The interviewer recorded the woman's response verbatim. Responses were later coded in the following way: if a

range of two consecutive numbers was given (e.g., 28–29), the lower number was used. If the women provided a wider range of days, the mean of the two numbers was used, rounding down from ½ if necessary.

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