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Impact of group psychological interventions on pregnancy rates in infertile women

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Objective: To determine the efficacy of two different group psychological interventions on viable pregnancy rates in women experiencing infertility of less than 2 years' duration.

Design: Prospective, controlled, single-blind, randomized study.

Setting: Large tertiary-care teaching hospital.

Patient(s): One hundred eighty-four women who had been trying to get pregnant for 1 to 2 years.

Intervention(s): Participants were randomized into a 10-session cognitive-behavioral group, a standard support group, or a routine care control group. They were followed for 1 year.

Main Outcome Measure(s): Viable pregnancy.

Result(s): Seventy-three women discontinued participation in the study within the first year. There were a total of 47 in the cognitive-behavioral group, 48 in the support group, and 25 in the control group. There were statistically significant differences between participants in the two intervention groups versus the control group.

Conclusion(s): Group psychological interventions appear to lead to increased pregnancy rates in infertile women. (Fertil Steril® 2000;73:805–12. ©2000 by American Society for Reproductive Medicine.)

Key Words: Infertility, psychological interventions, support group, cognitive-behavior therapy, mind/body

The impact of psychological symptoms, such as depression and anxiety, on fertility remains controversial. Although it is widely accepted that infertility causes significant levels of psychological distress (1), the possibility that distress could cause or contribute to infertility remains a topic for debate.

Since biblical times, there has been a commonly held assumption that psychological distress could cause infertility. Psychogenic infertility was widely accepted by the medical community until the latter part of this century, when diagnostic abilities improved. The pendulum then swung in the opposite direction, with organic causes for infertility being identified in 95% of infertile couples. Psychological distress was seen solely as a result of the infertility experience.

However, recent research indicates that the relationship between stress and infertility is a complex one. One of the issues complicating research on the potential relationship has been the definition of stress. Until recently, most researchers interpreted stress as anxiety and used measures of anxiety in their search for a contributory factor to infertility. In fact, the relationship between anxiety and infertility is contradictory. Several studies have demonstrated that anxiety has a detrimental effect on fertility (2) and that anxiety reduction is associated with increases in pregnancy rates (3, 4). However, other research has failed to support a relationship between anxiety and fertility (5).

In the past 5 years, there has been a shift away from defining stress as anxiety, and several researchers have begun to investigate depression as well. This is not to say that depression is the only manifestation of stress. It is possible that earlier researchers who pursued anxiety as the sole potential psychological contributor to infertility were too limited in their approach.

Several recent studies indicate that there is a relationship between depression and infertility. One study suggested that depression could play an important role in the pathogenesis of infertility: Women with a history of depressive symptoms were nearly twice as likely as women without a history of such symptoms to report a subsequent history of infertility (6). Another study determined that women who had experi-

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enced at least one unsuccessful IVF cycle who were depressed before continuing IVF treatment experienced a 13% subsequent pregnancy rate, in contrast to a 29% pregnancy rate in women who did not experience depressive symptoms before their IVF cycle (5). A recent study confirmed this finding (7). Women with female factor infertility who had increased depressive symptoms on day 3 of their IVF cycle experienced significantly lower pregnancy rates than women who were not depressed.

A very recent study also supports the notion that depression may inhibit fertility (8). Women with severe levels of depression who attended a 10-session cognitive-behavior group program designed to decrease depression and anxiety experienced a 60% viable pregnancy rate within 6 months, in contrast to a 24% viable pregnancy rate in women who had low levels of depressive symptoms at program entry ($P<$ .035). This study supported an association between depression and infertility and showed that depressed women attending a program designed to reduce their depression experienced enhanced conceptions.

If psychological symptoms such as depression inhibit conception, interventions that reduce these symptoms should be associated with increased pregnancy rates. In fact, there have been several studies that indicate that psychological interventions may lead to increases in pregnancy rates. These interventions range from structured interviews with secondary infertility patients (3), in which the experimental participants had a 60% pregnancy rate within 18 months compared to less than 10% of the control group, to cognitive-behavioral groups that teach relaxation and stress management strategies (8–10). Pregnancy rates in the cognitive-behavioral groups ranged from 33% to 44% within 6 months of completing the program. However, the reasons for the increased conception rates were not explored in any of these studies. Because the actual medical treatment received by the participants was not noted, it is possible that the increased conception rates in the experimental group was due to more aggressive medical treatment or increased compliance.

There have been no published, randomized, controlled, prospective trials to adequately assess the impact of group psychological interventions on subsequent pregnancy rates in infertile women. Psychological distress in infertile women increases with time (11), and depression peaks between the second and third year of infertility and does not return to the normal range until after 6 years of infertility (1). It is possible that a psychological intervention offered before the third year of infertility might prevent the surge in depression and could presumably lead to increased pregnancy rates.

The following study is part of a preventive intervention trial to look at the impact of group psychological interventions on several factors, including psychological status and viable pregnancy rates in infertile women who have been trying to conceive for less than 2 years. The psychological status data are currently being analyzed and will be presented at a later time.

The goal of this study was to determine whether psychological interventions could lead to increased pregnancy rates in infertile women. Presently, the two most common group interventions offered to infertile women are a support group or a cognitive-behavioral approach (mind/body group); therefore, these were the two interventions chosen to investigate.

The hypotheses of the study were as follows:

1. Women who participate in a cognitive-behavioral intervention will experience significantly more viable pregnancies than women who receive no psychological intervention
2. Women who participate in a support group intervention will experience significantly more viable pregnancies than women who receive no psychological intervention
3. Women who participate in a cognitive-behavioral intervention will experience significantly more viable pregnancies than women who participate in a support group intervention.

It was hypothesized that the cognitive-behavioral participants would have higher pregnancy rates than the support group participants on the basis of anecdotal data in the literature.

MATERIALS AND METHODS

Recruitment

Women who had been trying to conceive for 1–2 years were recruited for this study. Eligible women spoke English and were not currently practicing any relaxation technique; were not participating in any support group; were not in individual, group, or couples psychotherapy; were not currently taking any psychotropic medication; and were not clinically depressed.

Women with a history of pregnancy loss, single marital status, secondary infertility, or poor treatment prognosis were included. Each woman reported her infertility diagnosis at the time of recruitment, but diagnosis was disregarded as a criterion. The reason that diagnosis was disregarded was because many of the women were in the process of switching from their obstetrician/gynecologist to an infertility specialist, and the reported diagnosis was not definitive at the time.

Women were recruited from a variety of sources. Brochures that included a description of the study were placed in the waiting rooms of several local reproductive endocrinology group practices. A mailing was sent to appropriate patients from several collaborating physicians. Brochures were sent to all obstetricians/gynecologists from the hospital, public service announcements were distributed quarterly to local newspapers, paid advertisements were placed, and several local television stations carried stories on the study.

More than 2,000 women responded to the recruitment efforts. The vast majority of women who responded (90%) did not meet the criteria of trying to conceive for less than 2

years. This criteria had been established because this study is part of a large National Institute of Mental Health prevention study that mandated that women be trying to conceive for less than 2 years. Women who had been trying for more than 2 years and women who did not meet other criteria were referred to the Division of Behavioral Medicine mind/body clinical program (Beth Israel Deaconess Medical Center) (9, 10) as well as to Resolve for information about support groups.

This study was approved by the internal review board for the protection of human subjects at Beth Israel Deaconess Medical Center, Boston, Massachusetts. All women who were screened during their time 1 interview read and signed a written consent form.

Participants

A total of 212 women were screened for inclusion in the study and participated in a time 1 interview. Twenty-eight women did not qualify for the study because of the presence of clinical depression. One of the conditions for approval of this study by National Institutes of Mental Health and the internal review board was that women who were clinically depressed be referred for appropriate psychiatric care rather than possibly being randomized to the control group.

Women who met the exclusion criteria for depression met one of the following conditions: a score >15 on the Beck Depression Inventory, a score >11 on the Hamilton Depression Test, or meeting the criteria for a clinical depression on the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition.* Thus, women with moderate to severe depression were excluded from the study.

One hundred eighty-four women were accepted into the study and were randomized, according to a computer-generated random numbers table, into a cognitive-behavioral group, a support group, or a routine care control group. There were two randomization procedures. When recruitment was very active, women were randomized into one of three groups (cognitive-behavioral, support, or routine care control). However, during slow periods, when there were not enough eligible women to fill the two intervention groups at the same time, women were randomized into control group versus intervention group, with the intervention group alternating between cognitive-behavioral and support.

During the second year of recruitment, as recruiting eligible women became more difficult, there were several occasions on which the randomization among the two intervention groups again had to be altered. Specifically, there were instances in which women had been randomized to one of the two intervention groups but were switched to the other intervention. The reason for this was that after women were randomized into one of the two intervention groups, there were not enough women to fill two different intervention groups if recruitment was slow. The interventions were conducted in a group setting (8–12 women per group). As such, it was possible that several women were randomized to a particular group but that the other members needed to begin that group had not yet been enrolled in the study. Rather than having members wait 6 or more months for that particular group to commence, several women were switched from one intervention group to another before the beginning of the group.

The basic issue was that at least 8 members per group was optimal, and slow recruitment made it difficult to fill groups in a timely fashion. Thus, a total of 15 women (10 support and 5 cognitive-behavioral) were switched to the other intervention group after randomization but before the intervention group began. There were never any subjects switched between intervention and control groups. All statistical analyses were conducted with the women's original group assignment (intention-to treat analysis).

Of the 184 women accepted into the study, 63 were randomized into the control group, 65 into the support group, and 56 into the cognitive-behavioral group. Thirty-eight (60%) of the 63 control women discontinued participation in the study during the first year because of dissatisfaction with group assignment. Fourteen joined a clinical behavioral medicine program, 6 joined a Resolve support group, 2 entered psychotherapy, 1 began biofeedback treatment, 3 did not like being part of a clinical trial, and 12 provided no specific reason for their withdrawal from the trial. A total of 25 control women were followed for the total year. Of the 65 support participants, 48 remained in the study at 12 months. The remainder did not participate because of dissatisfaction with group assignment or lack of interest in participating in the study. Of the 56 cognitive-behavioral participants, 9 did not participate because of various reasons, including low interest in group participation, the long drive to the hospital, and feeling discomfort because of secondary infertility. Forty-seven cognitive-behavioral participants were followed for the study year.

Methods

All participants were informed that they would be followed in the following fashion: monthly diaries to record all medical treatment for their infertility and two visits per year to the study psychologist (who was blinded to the participants' group assignments) for psychological testing to assess their level of distress.

All participants were provided with monthly fertility medication and treatment diaries. All participants were instructed to contact the research assistant (MF) if conception occurred. In addition, all participants were told that if they joined any sort of external individual, group, or couples psychological intervention, if they began taking psychotropic medication, or if they stopped trying to conceive, they would not be eligible to continue participating in the study. In addition, participants in the support and control groups were told that if they began any type of relaxation practice,

including yoga, they would become ineligible to continue as a study participant.

Participants who conceived during the study period were asked the method of conception (spontaneous conception by intercourse or the method of medical assistance) and the outcome of the pregnancy. The main outcome variable, viable pregnancy, was a live birth.

Participants who were randomized into either of the two intervention groups were given an appointment to meet with their group leader. Authors ADD and DC alternated leading the two different intervention groups to eliminate the possibility of leader bias. During this meeting, the participant's infertility, medical, and psychosocial history were reviewed. The schedule and format of the group was presented.

The formats of the two different types of intervention groups were identical and differed only in terms of the actual content of the sessions themselves. Both kinds of groups met on a weekly basis for 10 weeks for 2 hours on a weekday evening. Husbands or partners were not invited to attend. All sessions were tape recorded, and a random sample was reviewed by an experienced psychologist to ensure that the group leaders maintained the integrity of the contents (i.e., that relaxation techniques were not discussed in any support sessions). Compliance with maintaining session content was 100%.

Participants in the cognitive-behavioral group received relaxation training, cognitive restructuring, methods for emotional expression, and nutrition and exercise information as they apply to infertility (8–10). The relaxation techniques included meditation, progressive muscle relaxation, imagery, autogenic training, and yoga. Several sessions were dedicated to cognitive restructuring in which participants learned to identify recurrent negative thought patterns and how to separate truth from fear. For example, a participant who reported thinking "I will never have a baby" might restructure the thought to "I am doing everything I can to try to get pregnant." The cognitive-behavioral program was modified for this study so that the format of each intervention was identical; only the actual content of the sessions was different. Thus, for this study, both the cognitive-behavioral and support programs were exactly 2 hours each week, with no visitors or modifications to the schedule.

Support participants spent the first hour of each session "checking in" with the group. This included an update on medical visits or treatments, issues that may have occurred with family or friends regarding infertility, and a summary of how each participant was feeling. The second hour was spent on a different topic each week, including the impact of infertility on participants' self-esteem; their relationship with their partner, family, and friends; spirituality; and job or career.

All participants were followed for 1 year. Information on conception was obtained from participant report, as was pregnancy outcome.

Statistical Analysis

The primary outcome was defined before the study began. The following characteristics in the cognitive-behavioral, support, and routine care control groups were compared: age, highest educational level, months of attempted conception, current medical treatment, and types of medical treatment. Demographic characteristics were compared by using analysis of variance or the χ^2 test. Kaplan-Meier survival analyses were used to compare the overall time to viable pregnancy for all three groups, and post hoc paired comparisons were used to detect differences among the groups. Logistic regression analysis was performed for additional analyses regarding the relationship between age or diagnosis and viable pregnancies. All analyses were performed by using SPSS software (SPSS, Inc., Chicago, IL).

RESULTS

Sample Characteristics

The demographic characteristics of the study sample are summarized in Table 1. There were no statistically significant differences among the three groups in age, highest education level, months of infertility, or whether or not participants were receiving medical treatment at the time of randomization. Table 2 shows that there were also no significant differences in type of treatment among the three groups ($P=.960$). Across all three groups, a total of 44% of the participants were not receiving active treatment, 22% were receiving clomiphene citrate, 12% were receiving gonadotropin therapy, 4% were receiving intrauterine inseminations without medications, 16% were undergoing advanced reproductive technology treatment, and 2.2% were receiving "other" treatment (i.e., bromocriptine or Estrace).

Time to Viable Pregnancy

A Kaplan-Meier survival analysis (12, 13) of time to viable pregnancy within 12 months was statistically significant ($P=.0044$). This analysis included all participants, and it was known that women discontinuing participation were not pregnant at the time of disenrollment. According to standard procedures, participants were followed as long as possible and their status on the last day of follow-up were recorded. Data from all randomized participants were included in the survival analysis until they either discontinued participation or became pregnant. Post hoc paired comparisons were significant for group assignment. The cognitive-behavioral participants had significantly different viable pregnancy rates than the control women ($P=.001$), and support participants had significantly different viable pregnancy rates than the control women ($P=.0146$). There were no significant differences between the cognitive-behavioral and support study participants ($P=.2016$).

Overall Viable Pregnancies

Viable pregnancies in the participants who remained in the study for the full year were as follows: 55% of the

TABLE 1

Demographic characteristics for 184 women who tried to get pregnant for 1 to 2 years.

Variable	Study group			*P* Value
	Cognitive behavioral (n = 56)	Support (n = 65)	Control (n = 63)	
Mean (±SD) age (y)	33.96 ± 4.32	33.71 ± 4.65	35.19 ± 4.84	.16
Mean (±SD) level of education (y)	16.91 ± 2.02	16.29 ± 1.63	16.98 ± 2.38	.11
Mean (±SD) duration of infertility (mo)	18.68 ± 3.66	17.99 ± 4.11	17.44 ± 3.36	.20

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cognitive-behavioral and 54% of the support group participants experienced a viable pregnancy, in contrast to 20% of the controls. These percentages are provided only for summary purposes and were not analyzed separately from the survival analysis because such an analysis would be statistically inappropriate owing to the disproportionate number of dropouts in the control group.

Medically Assisted Viable Pregnancies

Table 3 shows the number and proportion of participants who had a viable pregnancy by virtue of medical assistance. A χ^2 test indicated that there were no significant differences in the number of viable pregnancies that occurred as a result of medical interventions that cycle.

Thus, although 42% of the cognitive-behavioral pregnancies were a result of spontaneous conception, compared to spontaneous conception rates of 11% and 20% in the support and control groups, respectively, this did not reach statistical significance. It also means that the significantly increased overall pregnancy rates in the two intervention groups were not due to increases in medical interventions.

DISCUSSION

Women who participated in a group psychological intervention had significantly increased viable pregnancy rates compared to women who did not participate in any psychological intervention. This difference was not due to any group demographic differences, including age and duration of infertility, nor was it because of group differences in medical interventions.

There were a number of limitations in the methods of this study. The first was that the participants were not a classic infertility subgroup; they had been trying to conceive for 12–24 months. Because a main aim of this study was to determine whether psychological interventions could prevent the surge of depressive symptoms that are typically seen in the second to third year of infertility (1), participants were recruited before the appearance of these symptoms. Thus, the results of this study may not be applicable to patients with longer durations of infertility.

The second limitation of the study was the disproportion-

TABLE 2

Treatment in 184 women who tried to get pregnant for 1 to 2 years.

	Study group						*P* Value
	Cognitive-behavioral (n = 56)		Support (n = 65)		Control (n = 63)		
	No.	Percentage	No.	Percentage	No.	Percentage	
Current medical treatment							
Yes	28	50	39	60	36	57	.53
No	28	50	26	40	27	43	
Type of medical treatment							
Unassisted	28	50	26	40	27	43	.96
Clomiphene citrate	12	21	13	20	15	24	
Gonadotropins	5	9	9	14	9	14	
Only intrauterine insemination	2	4	3	5	2	3	
Advanced reproductive technologies	8	14	13	20	8	13	
Other	1	2	1	2	2	3	

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TABLE 3

Viable pregnancies resulting from medical interventions.

Variable	Study group						*P* Value
	Cognitive-behavioral (n = 26)		Support (n = 26)		Control (n = 5)		
	No.	Percentage	No.	Percentage	No.	Percentage	
Viable pregnancies from medical interventions							
Assisted	15	58	22	85	4	80	.120
Unassisted	11	42	3	11	1	20	
Missing	0	0	1	4	0	0	

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ate number of dropouts from the control group. Thirty-eight control women, 16 support participants, and 9 cognitive-behavioral participants discontinued the study; none of these participants were pregnant at the time of discontinuation. It would not be methodologically accurate to include the discontinued control women's pregnancy rates because many of them left the study specifically to join the clinical mind/body program, a Resolve support group, or other forms of therapy, thus contaminating their control status. However, the statistical analysis employed, the Kaplan-Meier survival analysis, was designed for this type of situation.

Although there were significantly more dropouts in the control group, all participants were included in the survival analysis until they reached one of two end points: study discontinuation or viable pregnancy. Thus, the statistical significance reached when comparing the two intervention groups to the control group was legitimate and reflected a real and true difference between the groups.

The third limitation of the study was the issue with randomization. The randomization schedule was altered midstudy from a three-group randomization to a two-group randomization. In addition, a total of 15 participants were switched from one intervention group to the other after randomization but before the intervention group began. These issues do not cloud the statistical differences between the two kinds of intervention groups with the control group. However, they would interfere with any attempt to compare the two intervention groups. In fact, there were no differences between the two intervention groups with the conservative but appropriate intention-to-treat analysis. In addition, at the end of the data analysis phase, the analysis was performed by actual group attendance. The pattern of results was similar regardless of which statistical approach was used.

The published literature contains numerous references that describe various psychological interventions for infertile women, most of which contain pregnancy rates and many of which suggest that these interventions lead to higher than anticipated pregnancy rates (14). Possible explanations for these increased pregnancy rates include the following theories:

1. Psychological factors, such as depression, could hamper fertility, and psychological assistance relieves these symptoms
2. Women who receive supplemental psychological assistance may feel more prepared to pursue medical treatment that carries a greater likelihood of conception
3. Women who receive supplemental group psychological assistance may hear from others of newer technologies and pursue these treatments
4. Pregnancy rates are actually not higher but are what would be expected of women who aggressively pursue treatment.

The data from this study suggest that the significantly increased viable pregnancy rates in the women who received group interventions was not due to external factors, such as more aggressive medical treatment, because the three groups were equivalent in the amounts and types of medical treatments received, and there were no significant differences in spontaneous versus medically obtained pregnancies. Thus, the second, third, and fourth possible explanations can be excluded.

It appears that both interventions contained some component that affected participants' fertility, supporting the first theory. In fact, the design of the study, which specifically excluded clinically depressed women, actually could have prevented even greater differences between the groups of participants. If depression can hamper fertility, excluding women with moderate to severe symptoms decreases the possibility of achieving a significant treatment effect. However, a statistically significant group effect was discovered, suggesting a powerful intervention effect.

It remains to be determined how attending a 10-session group psychological intervention can affect conception. Recent research supports the theory that psychological distress can have effects on multiple systems, including inhibition of hypothalamic GnRH, activation of the hypothalamic-pituitary-

adrenal axis, and alterations of the immune system (15, 16). The impact of these perturbations by psychological stress and depression could then in turn adversely affect ovulation, fertilization, tubal function, or implantation.

A recent study of 10 depressed and 13 normal women indicated that depression is associated with abnormal regulation of luteinizing hormone (17). Activation of the hypothalamic-pituitary-adrenal axis can profoundly inhibit reproductive function. This inhibition of reproductive function can be at many levels, ranging from inhibition of hypothalamic GnRH to possible direct actions on the ovary and endometrium in a manner that could prevent pregnancy. Furthermore, stress and depression alters immune function and specific cytokines (18), which in turn could adversely affect reproductive function.

Further research is necessary to determine whether psychological interventions have an impact on pregnancy rates in women with infertility for more than 2 years and whether they are effective in women undergoing advanced reproductive technology treatment, because this is the most costly and invasive option. In addition, research is needed to determine whether psychological interventions, when offered in their original design, have differing effects: for example, the impact that the cognitive-behavioral program might have if it were offered according to the clinical model, with several extended sessions, husbands or partners attending three sessions, an so on. It would also be interesting to determine the efficacy of a combination group: that is, a program that would include both cognitive-behavioral as well as support time.

Group psychological interventions are efficient and cost-effective. The psychological preprogram and postprogram scores from this study are in the analysis stage; therefore, the psychological benefit of these particular interventions cannot be documented yet. However, there is clear evidence that patients achieve psychological benefit from attending similar programs (3, 4, 9, 10, 14).

The authors of a recent study on depression and IVF outcome suggested that because mind/body programs are effective in reducing negative emotions that may impair IVF success, patients should be offered such a program in conjunction with IVF (7). The results of this study suggest that psychological interventions may affect pregnancy rates at an earlier point and should perhaps be implemented in conjunction with initial medical treatment.

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