Human Reproduction vol.13 no.6 pp.1502–1505, 1998

Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment

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Obesity affects ovulation, response to fertility treatment, pregnancy rates and outcome. In this prospective study, a weight loss programme was assessed to determine whether it could help obese infertile women, irrespective of their infertility diagnosis, to achieve a viable pregnancy, ideally without further medical intervention. The subjects underwent a weekly programme aimed at lifestyle changes in relation to exercise and diet for 6 months; those that did not complete the 6 months were treated as a comparison group. Women in the study lost an average of 10.2 kg/m^2, with 60 of the 67 anovulatory subjects resuming spontaneous ovulation, 52 achieving a pregnancy (18 spontaneously) and 45 a live birth. The miscarriage rate was 18%, compared to 75% for the same women prior to the programme. Psychometric measurements also improved. None of these changes occurred in the comparison group. The cost savings of the programme were considerable. Prior to the programme, the 67 women had had treatment costing a total of A$550 000 for two live births, a cost of A$275 000 per baby. After the programme, the same women had treatment costing a total of A$210 000 for 45 babies, a cost of A$4600 per baby. Thus weight loss should be considered as a first option for women who are infertile and overweight.

Key words: obesity/ovulation/pregnancy/self-esteem/weight loss

Introduction

The fertility of obese women compared to normal weight women is lower in natural cycles and infertility treatment cycles (Chong *et al.*, 1986; Hamilton-Fairley *et al.*, 1992; Zaadstra *et al.*, 1993; Crosignani *et al.*, 1994). Higher rates of miscarriage (Hamilton-Fairley *et al.*, 1992) and congenital anomalies (Waller *et al.*, 1994) are also reported for this group of women. In a previous paper (Clark *et al.*, 1995), we reported that even a small weight loss in anovulatory obese infertile women, achieved in a group setting over a 6 month period, resulted in an improvement in ovulation, pregnancy rate and pregnancy outcome, self-esteem and endocrine parameters. Ninety percent of the anovulatory women resumed ovulation and 45% had a spontaneous pregnancy. Of the remaining women who required treatment, the pregnancy rate per treatment cycle was >50% per cycle and the overall miscarriage rate was 25%, compared to 75% previously for the same women.

The aim of the current study was to apply the same principles to a larger group of women with mixed indications for fertility treatment, requiring a wider range of treatment options. We also wished to do a preliminary cost effectiveness assessment of the programme.

Materials and methods

Subjects

Patient inclusion criteria for the study were infertility for >2 years, body mass index (BMI) ⩾30 kg/m^2, being prepared to take 6 months 'time out' from conventional medical treatment for infertility and being able to attend a 3 h session once a week for 6 months. Subjects with the following attributes were excluded: presence of a medical condition that would compromise participation in an exercise programme, presence of an endocrine condition [other than polycystic ovary syndrome (PCOS)], such as hyperprolactinaemia, thyroid disease or Cushing's syndrome and a desire to continue conventional fertility treatment for the duration of the programme. A total of 120 women who met the criteria were approached with an information letter and a follow-up telephone call about the programme. Of these, 87 consented to take part in the study, which was conducted in four groups, each for 6 months. The subjects previously reported by Clark *et al.* (1995) are included in this report. Eighteen to 30 women started in each group. The characteristics of the subjects are shown in Table I. The women were patients at the Reproductive Medicine Unit at The Queen Elizabeth and Wakefield Hospitals. Of the 87 women, 20 were unable to complete the 6 month study programme due to work and other commitments ('drop-out' group) and were included for comparison with those who completed the group programme. There were no significant differences in age, BMI, length of infertility, PCOS or ovulation status between the two groups. However, those that 'dropped-out' had had significantly fewer treatment cycles than those who completed the 6 month programme. Causes of infertility covered a range of aetiology from anovulation to tubal disease and male factor infertility. Of the 87 patients, 69 were anovulatory at the commencement of the study and 53 of the subjects had some degree of male factor infertility as well.

Treatment, assessment and statistical analysis

These have been described previously (Clark *et al.*, 1995). The fitness testing and assessment of dietary change detailed previously was not carried out in this study.

Table I. Characteristics of the patients recruited for the study before participation (values are means ± SD)

	Completed (n = 67)	'Drop-out' (n = 20)
Age (years)	31.6 ± 4.9	32.8 ± 5.0
Body mass index (kg/m^2)	37.4 ± 6.9	35.9 ± 4.1
Duration of infertility (years)	5.4 ± 2.5	6.2 ± 2.4
Previous fertility treatments (cycles)	3.7 ± 1.2	1.0 ± 0.5[a]
PCOS (%)	79	72
Anovulatory (%)	81	75

[a]$P < 0.001$.

PCOS = polycystic ovary syndrome.

Table II. Comparison between those who completed and those who did not complete the study

	Completed (n = 67)	'Drop-out' (n = 20)
Change in body mass index (kg/m^2)	−3.7 ± 1.6	−0.4 ± 1.4[a]
Resumed spontaneous ovulation (%)	90	0.0[b]
Pregnancy (%)		
Spontaneous	27	0.0[b]
Treatment	53	0.0[b]
Miscarriages (%)	18	0.0
Total women pregnant (%)[c]	77.6	0.0[b]
Total women with live birth (%)	67	0.0[b]

[a]$P < 0.001$.
[b]$P < 0.001$.
[c]Nine (13%) avoiding treatment.

Results

Weight loss

Women who attended the programme over the 6 months had significant weight loss (10.2 ± 4.3 kg, range 3.5–15; $P < 0.001$). Those who had not conceived 9 months after the end of the programme maintained this weight loss. In contrast, the 'drop-out' group had an insignificant weight loss (1.2 ± 3.6 kg, range +3.2 to –2.8) (Table II).

In assessing the women's progress in the Unit prior to starting the programme, it was noted that they had an average increase in BMI per year of 1 kg/m^2. This is 10 times the normal expected annual increase of 0.1 kg/m^2 (Rookus *et al.*, 1987).

Ovulation

At the beginning of the study, 69 (80%) of the women were anovulatory as judged by standard endocrine criteria. At the end of the 6 months, 90% of the previous anovulatory women in the study group were ovulating spontaneously compared to none of the 'drop-out' group. As previously noted the return to ovulation occurred after a small weight loss, with all women who resumed ovulation doing so by the fifth month of the programme, despite a mean weight loss at that time of 6.5 kg, which meant that all were still in the obese BMI range of >30 kg/m^2. The anovulatory women who attended >66% of the sessions all resumed spontaneous ovulation.

Table III. Pregnancies per cycle after participation in the programme and occurring simultaneously in non-study patients

	Completed group (n = 67) Post-programme	'Drop-out' group (n = 20) Post-programme	Average pregnancy rate in the Unit over same period Pregnancy rate (%)
OI	0/3 (0)	0/4 (0)	24
IUI	6/11 (55)	0/10 (0)	19
IVF	26/47 (55)	0/35 (0)	20

OI = ovulation induction, IUI = intrauterine insemination, IVF = in-vitro fertilization.
Values in parentheses are percentages.

Pregnancy

Of the 67 women who completed the study, 52 (77.6%) conceived, 45 (67%) achieving a live birth. Nine (13%) of the women elected not to proceed with further treatment cycles due to changes in their social or financial circumstances. Eighteen (32.7%) of the 55 pregnancies occurred spontaneously, the remainder following treatment. The subgroups of women in the study who did not do as well in terms of spontaneous and treatment pregnancies included smokers, those who attended less than two-thirds of the sessions over the 6 month programme or whose BMI was still >40 kg/m^2 at the end of the programme. All the women who did not achieve a spontaneous pregnancy or live birth were in one or more of these categories. Table III shows the women's pregnancy rates on treatment after the programme. Fewer ovulation induction cycles were carried out following the programme as it was principally the patients requiring that mode of treatment who spontaneously conceived. No pregnancies occurred in the 'drop-out' group, despite the majority continuing medical treatment. Of the 33 women who elected not to participate in the group (principally due to timing during the working day), but to be followed up, two pregnancies occurred on subsequent treatment cycles in the following 18 months, despite nine of the women achieving a 5–7 kg weight loss on their own. There were no spontaneous pregnancies in this group. Eighty percent of anovulatory women achieved a pregnancy (40% while in the study, 60% after the study), 63% of those with tubal factor [all on in-vitro fertilization (IVF) treatment] and 83% with male factor [50% on IVF or intracytoplasmic sperm injection (ICSI)].

Miscarriage

Prior to the programme, the 67 women who completed the study had achieved a total of eight conceptions, of which six miscarried (75% miscarriage rate). Following the programme, 10 of the 55 pregnancies miscarried [18% miscarriage rate, ($P < 0.01$)].

Psychometric assessment

There was a significant improvement in all the psychological parameters measured, consistent with a global improvement in psychological health. In particular, the mean self-esteem

score for the study group rose from 19.3 to 21.3 ($P < 0.01$). The mean anxiety score for the study group was reduced from 6.7 down to 5.6 ($P < 0.01$). The mean depression score was reduced from 4.1 down to 2.2 ($P < 0.001$).

Group cohesion was very strong at the end of the programme, with all four groups maintaining informal exercise sessions and meetings throughout and after the course.

Costs

The total cost of running the 6 month programme (hours worked by each individual plus administration) was 8828 Australian dollars (A$). In comparison, the cost of one IVF cycle averaged A$4150 and one gonadotrophin ovulation induction cycle, calculated using the average number of ampoules used by these women, was A$1050. Therefore, the saving of two IVF cycles or eight ovulation induction cycles would have funded the programme in this Unit.

Prior to the programme, the 67 women who completed the study had had treatment totalling A$550 000 for two live births, a cost of A$275 000 per baby. After participation in the programme, the same 67 women had treatment costing A$210 000 for 45 live births, at a cost of A$4600 per baby.

Discussion

This study, which is an extension of a study previously reported involving women requiring ovulation induction, demonstrates that a group approach to the combined problem of obesity and infertility is associated with a marked improvement in pregnancy and ovulation rates and a reduction in the need for the use of high technology treatment. Obese infertile women, irrespective of their infertility diagnosis, appear to benefit. The outcomes in terms of pregnancy and ovulation rates were greater than could be expected based on the patients' past histories, and these changes, in combination with the significantly lowered miscarriage rate, indicate the programme is clearly cost-effective compared to starting conventional medical treatment for obese infertile women when they first present. There was a marked disparity in outcome between those women who failed to complete the programme and the study group who finished the 6 months despite having access to the same information during the 2–3 months they attended the programme. In addition, failure to attend more than two thirds of the sessions was associated with a less positive reproductive outcome.

The possible explanations for these results are still unconfirmed but recent publications on the impact of insulin indicate that this is likely to be a component. Lowering insulin resistance by weight loss or administration of an oral hypoglycaemic results in spontaneous ovulation (Velazquez *et al.*, 1994). In our preliminary study, we showed that women who reduced their weight had lower insulin concentrations. Others (Guzick *et al.*, 1994; Helmen *et al.*, 1996) have shown the same effect of weight loss on insulin concentrations and pregnancy rates. It is unclear whether reduction in insulin is the sole contributor to the change in reproductive outcome we found in this study.

Women who were unable to attend the programme but achieved a similar weight loss independent of the group did not have the same pregnancy results, suggesting that some other component of the group process of psychological changes also affects the results. Others have reported the positive benefits of improving psychological parameters in relation to reproductive outcome (Domar *et al.*, 1990; Thiering *et al.*, 1993), in contrast to Harlow *et al.* (1996), who assessed a group of women undergoing IVF treatment and found no difference in pregnancy outcome between those who registered higher concentrations of stress hormones compared to the rest of the IVF population. Stunkard *et al.* (1980) indicated that attempts at maintaining weight loss were much more successful when approached in a group situation than when the same information was given on a one to one basis. In addition, behavioural therapy was more successful than the use of drugs to lose weight.

This study was initiated by our concern for the long term physical and psychological health of obese infertile patients. We observed, as have others, that their pregnancy rates were reduced (Chong *et al.*, 1986; Zaadstra *et al.*, 1993; Crosignani *et al.*, 1994), their need for higher doses of medication was increased (McClure *et al.*, 1992) and their increase in weight, while patients of the Unit, was 10 times the average annual increase (Rookus *et al.*, 1987; Clark *et al.*, 1995). When starting the group, we believed that even if the women left the Unit without getting pregnant, if we had assisted in improving their long-term physical and psychological health, the programme would have been a success. The changes in reproductive outcome have been so striking that this study has been the basis for a randomized controlled trial of the effects of weight loss on fertility and treatment outcomes in a group situation. In the interim, these results continue to support the view that all who treat infertility should consider weight loss to be a prerequisite for obese women prior to any assisted reproduction programmes.

Acknowledgements

We thank Helen Holmes for typing this report. The Reproductive Medicine Unit and the University of Adelaide are acknowledged for initial funding.

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Received on August 26, 1997; accepted on February 23, 1998