A randomized controlled trial of a cognitive-behavioural group intervention versus waiting-list control for women with uterovaginal agenesis (Mayer–Rokitansky–Küster–Hauser syndrome: MRKH)

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BACKGROUND: Uterovaginal agenesis (Mayer–Rokitansky–Küster–Hauser syndrome: MRKH) is a congenital abnormality of the female genital tract, characterized by the non-formation of the vagina and uterus. There is a widespread agreement that MRKH has a lasting negative psychological impact on women with this condition, but as yet little is known about how to conceptualize and manage this. We developed a cognitive-behavioural group treatment (CBT) of MRKH. The aim of the present study was to determine whether this intervention, compared to waiting-list control, improves psychosocial outcomes in women with MRKH. METHODS: After stratifying for age and type of MRKH (simple or complex), 39 women with MRKH were randomized to group CBT ($n = 19$) or waiting list ($n = 20$). Outcomes were assessed at pre-treatment, post-treatment (7 weeks) and at 3 months follow-up. The main outcome measure was the Symptom Check-List (SCL-90-R). Other outcomes included impact of event, self-esteem and interpersonal functioning. RESULTS: Participants allocated to group CBT showed significantly reduced psychological symptoms on the SCL-90-R and non-significant improvements on all secondary outcomes at the end of treatment and follow-up, whereas those on the waiting list remained unchanged. CONCLUSIONS: A group CBT intervention improves psychological outcomes in MRKH. This treatment may also be applicable to other gynaecological conditions.

Keywords: cognitive-behavioural therapy; group treatment; Mayer–Rokitansky–Küster–Hauser syndrome; randomized controlled trial; uterovaginal agenesis

Introduction

Uterovaginal agenesis (Mayer–Rokitansky–Küster–Hauser syndrome: MRKH) is a congenital abnormality of the female genital tract, resulting in non-formation of the vagina and the uterus, but with normal ovaries (Edmonds, 2000). The aetiology is thought to be polygenic multi-factorial; occasionally, the syndrome results from a genetic mutation or deletion of genes on chromosome 16 (Edmonds, 2003). MRKH occurs in ∼1 in 5000 female births and is typically diagnosed in mid-adolescence (Edmonds, 2000; Edmonds, 2003; Aittomaki et al., 2001). The treatment of choice for creation of a neovagina is dilation therapy (Frank, 1983; Nadarajah et al., 2005). All other approaches to creating a neovagina are surgically based and include using skin grafts (Alessandrescu dPeltecu et al., 1995), grafted peritoneum (Davidov, 1980) or bowel (Parsons et al., 2002).

We conducted a systematic literature review which addressed the question of the nature and severity of the psychological difficulties, these women experience (J.G.H.-B., unpublished data). Studies identified as part of the review agreed that MRKH has a significant and lasting negative psychological impact on women with this condition, with levels of psychological distress being high and self-esteem impaired even after successful creation of a neovagina. Most of the studies reviewed were of limited quality and contained qualitative, impressionistic and anecdotal evidence only, thus highlighting a distinct lack of knowledge about quantitative aspects of the psychological impact of this disorder and how to conceptualize and manage this. To remedy this, we conducted a cross-sectional study (J.G.H.-B., unpublished data), comparing women with MRKH ($n = 66$) with control women

recruited from the community ($n = 31$) of comparable age and socio-economic background. Women with MRKH fared significantly worse on several subscales of the Symptom Checklist (SCL-90-R) (Derogatis, 1992) a widely used measure of psychological distress and on the Rosenberg Self-Esteem Scale (RSE) (Rosenberg, 1965), but not on the short version of the Inventory of Interpersonal Problems (IIP-32) (Barkham et al., 1996). Contrasting these findings with relevant population norms for the SCL-90-R subscale scores, it appears that the scores of women with MRKH lie between the norms for non-patients and psychiatric outpatients.

We found only one small case series which reports on a group treatment programme for women with MRKH, albeit without specifying the underlying model or rationale (Weijenborg and ter Kuile, 2000). We, therefore, developed a cognitive-behavioural model and group treatment of MRKH, using the Medical Research Council's framework for the development of complex interventions to guide the process (MRC, 2000). Our psychological model of MRKH suggests that the core issue in MRKH is the major threat to these women's sense of themselves as fully-functioning, loveable adult women. This threat arises from various specific events associated with MRKH, starting with the clinical symptom of amenorrhoea through to diagnosis and treatment, together with a range of interpersonal influences (e.g. responses of doctors, family, friends and partners) which unfold during a developmentally sensitive time in adolescence, i.e. when the average young woman experiences her first sexual 'milestones' (e.g. first date, first kiss, first sexual intercourse). The model suggests that three psychological processes lead to and serve to maintain problematic adjustment to MRKH. These are: (i) a failure to adequately 'process' the diagnosis (e.g. by blocking out details or focusing on certain aspects only); (ii) the occurrence of idiosyncratic negative appraisals of MRKH-related events (e.g. 'I am not a proper woman', 'I am a freak', 'I am unloveable') which become incorporated into these women's sense of female identity; and (iii) a range of maladaptive cognitive and behavioural strategies (e.g. such as avoidance of intimacy, compensating for perceived defects by trying to be perfect and 'super-feminine') through which women attempt to reduce the sense of threat to their femininity and any accompanying emotional symptoms. Based on this model, we developed a CBT group treatment for MRKH. The aim of the present study was to test the efficacy of this intervention against waiting list. Our hypothesis was that women allocated to the CBT intervention would show improved psychosocial outcomes, whereas those on the waiting list would remain unchanged.

Materials and Methods

Design, setting and participants

A randomized controlled trial (RCT) of group CBT for MRKH versus waiting list was carried out at the UK National Centre for Adolescent and Adult Women with Congenital Abnormalities of the Genital Tract. Women aged 17 or above, with a diagnosis of MRKH (Type I—'simple' MRKH or Type II—'complex', i.e. with multiple congenital abnormalities) made or confirmed at the Centre, were eligible for the study. We excluded those with insufficient knowledge of English to participate in a group programme, those who were actively suicidal and women currently engaged in a psychological therapy. Recruitment took place between November 2004 and January 2005 and follow-ups were completed by June 2005. Women on the Centre's MRKH register were contacted by post with information about the study and an invitation to take part. Interested women were screened by the Centre's psychologist (J.H.B.) for inclusion, who also obtained written informed consent from those suitable for participation and enrolled them in the study.

Interventions

Study interventions were as follows:

Group CBT for MRKH

This intervention was designed to address the three key factors that maintain an unhelpful adjustment to MRKH. The intervention centres around a cognitive-behavioural case conceptualization which guides the therapy. As therapy progresses, each woman produces her own conceptualization tailored to her circumstances. Each session addresses a different MRKH-related topic. Treatment starts with a focus on the central life event of being diagnosed. Later sessions move on to dilator treatment, sexual and romantic relationships and mourning the losses of MRKH including infertility. These topics are used to help women process previously avoided thoughts and feelings, and to challenge unhelpful beliefs, including an exploration of societal scripts regarding women's roles and views on femininity; and to develop a more adaptive view of themselves, the world and their future. Participants are taught to identify unhelpful coping strategies and to replace them with more adaptive techniques. There is a focus on building interpersonal skills in romantic and sexual relationships (e.g. when and how to mention MRKH to a new partner). Finally, there is an attempt to help women find meaning in their experience.

In the sessions, the different perspectives and strengths of group members were used to brainstorm new ways of dealing with MRKH. Between sessions, women are instructed to complete homework assignments consisting of expressive writing (Pennebaker, 2004). Tasks relate to the themes of the sessions and were specifically constructed to enhance emotional processing of previously avoided material and to teach women to adopt more balanced perspectives on how they viewed themselves. At the end of the therapy patients are asked to produce a written good-bye letter so as to reflect on what they had learnt.

Groups had five to seven participants who met for seven once weekly sessions (each lasting 3 h), with one further session at 3 months' follow-up. Group sessions were led by a female psychologist (J.H.B.), who introduced the theme of each session, educated women about the model of therapy used and guided the interactions.

Waiting list

Women allocated to this group were offered the opportunity to have group CBT after completing the follow-up period.

Treatment fidelity

A therapist manual for the intervention was produced. Sessions were tape-recorded and patients' writings were collected at each session. Regular supervision for the study therapist was provided.

Outcome measures

A number of widely used, well-validated self-report questionnaires were used. The main outcome measure was the global severity index (GSI) of the SCL-90-R (Derogatis, 1992). The SCL-90-R assesses a wide range of psychopathology and psychological distress

and has been shown to be sensitive to change in many different patient groups, including medical outpatient populations (score range: 0–128). The main reason for choosing this measure was that it was used as the main outcome in the only previous treatment study of MRKH (Weijenborg and ter Kuile, 2000). SCL-90-R has good reliability (test-retest and internal consistency) and validity (convergent and discriminant). The GSI is computed by first summing the scores on the SCL's nine symptom dimensions and a number of additional items. The sum is then divided by the total number of responses (score range 0–4).

Secondary outcomes included the following measures:
  (i) The Rosenberg Self-Esteem Scale (Rosenberg, 1965): this is a brief measure of global self-esteem (i.e. it measures overall feelings of worth or self-acceptance). We used this as most papers summarized in our systematic literature review (J.G.H.-B., unpublished data) highlighted low self-esteem in women with MRKH. The score range of the RSE is 10 to 40. It has been extremely and widely used across a large range of different populations of adolescents and adults and is generally considered the standard against which other measures of self-esteem are compared.
  (ii) The Impact of Events Scale (IES) (Horowitz et al., 1979): this assesses the impact of traumatic life happenings on a person. In the present study participants were asked to complete this scale in relation to being diagnosed with MRKH, which is often experienced as very traumatic. The IES has a score range 0–75. It has good validity and reliability and is highly sensitive to change, thus forming a good outcome measure for brief therapy.
  (iii) The short version of the Inventory of Interpersonal Problems (Barkham et al., 1996): this measures interpersonal distress. The IIP-32 has a score range of 0–128. The shortened version of the IIP-32 sacrifices little in terms of psychometric properties (reliability, validity), compared with the original IIP (127-item version).

Participants completed all measures at pre-treatment, post-treatment (7 weeks) and at three months' follow-up (week 19).

Sample size

We based our power calculation on the study by Weijenborg and ter Kuile (Weijenborg and ter Kuile, 2000), where the effect size for the change in SCL-90 from baseline to follow-up was 0.8. A sample size of 26 per group would give 80% power to detect an effect size of 0.8 using a 2-group t-test with a 0.05 two-sided significance level.

Randomization and blinding

The randomization codes were prepared by a researcher independent of the rest of the trial team using a table of random digits 0–9 (Pocock, 1983). Randomization was stratified by MRKH type (I and II) and age (17–25 years versus 26 years upwards). Randomization codes were concealed in consecutive, opaque, sealed envelopes. After a patient had completed their initial assessment the next available envelope was opened and the treatment allocation was conveyed to the patient by the psychologist (J.H.B.) in charge of the day-to-day running of the study. As she conducted the group CBT treatment and also the follow-up assessments, it was not possible to keep her blind to treatment allocation.

Statistical analysis

Primary and secondary outcomes were analysed in SPSS 13, using Linear Mixed Effects Random Intercept models (Landau and Everitt, 2004). All three measurement points, baseline, post-treatment

and follow-up were taken into account in the models. Baseline measures were used as covariates in the analysis, i.e. in each of the models fitted we included relevant baseline measurements (e.g. SCL-baseline for the SCL model etc.).

Effect sizes (Cohen, 1988) were calculated for all questionnaire outcomes as follows: (mean change score for CBT (from baseline to follow-up) minus mean change score for waiting list) divided by their pooled standard deviation.

Results

Patient flow and baseline characteristics

Fig. 1 shows a CONSORT diagramme detailing the participant flow through the study (Consort Group, 2001). Of 335 women contacted, 117 replied to the invitation to participate. Seventy eight declined participation and 39 agreed to be randomized. Non-participants were similar in age to participants, but no other sociodemographic information was available. However, 27 of the 78 women who declined participation in the study provided questionnaire data. Their baseline questionnaire scores (SCL-90-R, RSE, IES and IIP-32) did not differ from those of the study participants.

Of the 39 women who agreed to participate, 19 were randomized to group CBT-MRKH and 20 to waiting-list. Patients in both the CBT and waiting list groups were similar in terms of socio-demographic and medical characteristics (see Table 1). The mean number of sessions attended for all 19 participants allocated to group CBT-MRKH was 5.7 out of eight sessions.

Treatment outcomes

Treatment outcomes are presented in Table 2. On the global severity index of the SCL-90-R questionnaire scores of participants on the waiting list remained unchanged over time, whereas in the CBT group, participants' psychological symptoms were significantly reduced (CBT-group mean of GSI at baseline 0.93, 0.64 at post-treatment and 0.48 at follow-up ($P = 0.03$)). Exploring the SCL-90-R subscale scores, the picture was very similar, with CBT participants showing marked improvements on all subscales over time and waiting list participant remaining unchanged (details can be obtained on request from the authors).

On the RSE, there was a trend ($P = 0.07$) for improved self-esteem in the CBT group etc at follow-up (CBT group mean of 21.8 at baseline, 19.3 at post-treatment and 17.5 at follow-up).

On the other scales, CBT group scores also improved, but not significantly so. Associated effect sizes (from baseline to follow-up) were all between 0.74 and 1.14, i.e. mostly large (Cohen, 1988).

Treatment drop-outs had similar pre-treatment questionnaire scores to those who completed treatment.

Discussion

Our study is the first ever RCT of a psychological intervention for women with MRKH. In line with our hypothesis our study demonstrates that a brief and relatively inexpensive—but carefully designed and targeted—psychological intervention can
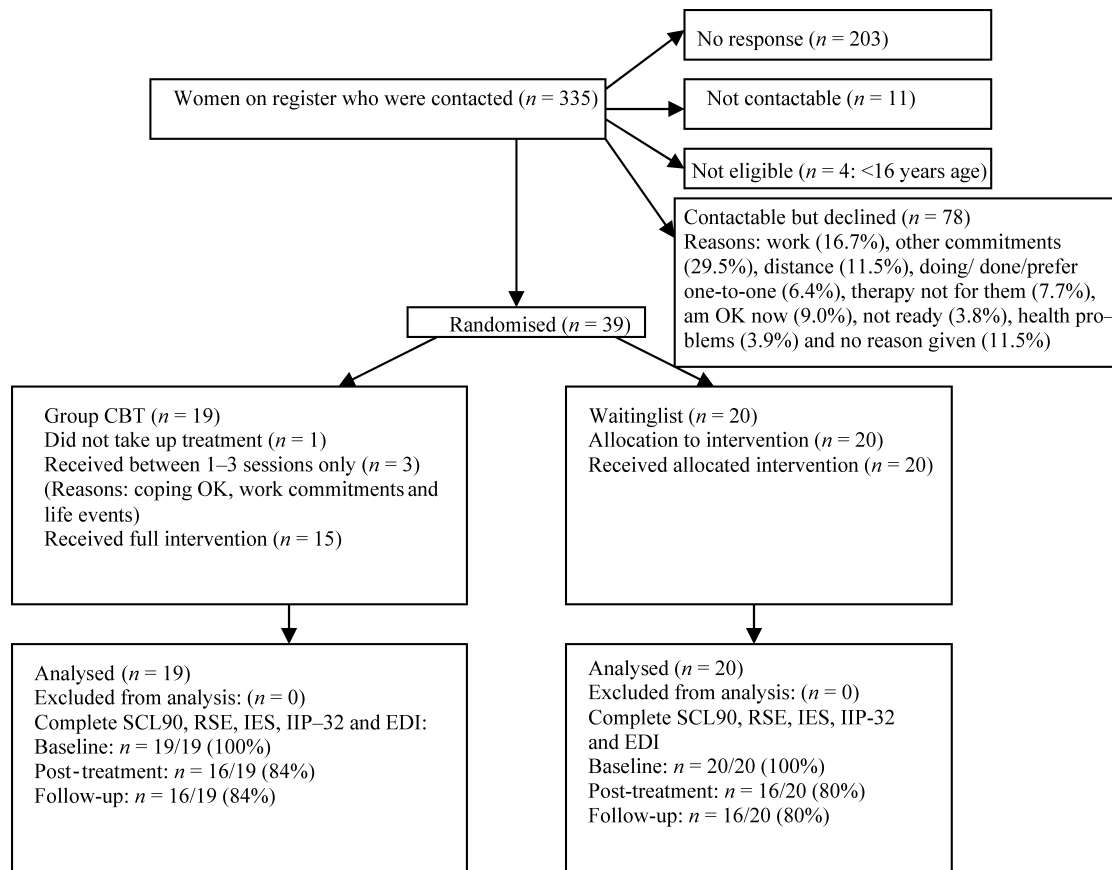
Figure 1: Participant flow through the study

significantly ameliorate the psychosocial impact of this condition. This is evidenced by the significant between group differences on the global severity index and subscale scores of the SCL-90-R, with the group difference on the RSE featuring a trend in the same direction. Persistent psychological distress following diagnosis with MRKH and low self-esteem were mentioned in many of the papers contributing to our

systematic review as key features in the psychological response to MRKH. Our cross-sectional study (J.G.H.-B., unpublished data), conducted in parallel to the RCT presented here, confirmed this. Thus our finding of improvement in these two areas is particularly encouraging and clinically meaningful. On the IES and IIP-32 there also appeared to be some change in the active treatment group, but we may not have

Table 1: Baseline sociodemographic and medical data: social class was determined using the Hollingshead 2-factor model (Guy, 1976)

	CBT group ($n = 19$)		Waiting list ($n = 20$)		Total ($n = 39$)	
Age, mean (SD)	28.9	(10.0)	27.6	(7.1)	28.2	(8.6)
Age of diagnosis, mean (SD)	17	(2.0)	18.2	(1.9)	17.6	(2.0)
Years since diagnosis, mean (SD)	11.9	(10.3)	9.4	(7.2)	10.6	(8.8)
MRKH type, *n* (%)						
'Simple'	17	(89.5)	18	(90)	35	(89.7)
'Complex'	2	(10.5)	2	(10)	4	(10.3)
Social class, *n* (%)						
High	4	(21)	3	(15)	7	(17.9)
Medium to low	9	(47.4)	11	(55)	20	(51.3)
Student	5	(26.3)	6	(30)	11	(28.2)
Housewife	1	(5.3)	–	–	1	(2.6)
Relationship status, *n* (%)						
With current partner	13	(68.4)	11	(55)	24	(61.5)
No partner	6	(31.6)	9	(45)	15	(38.5)
Children, *n* (%)						
Yes	2	(10.5)	3	(15)	5	(12.8)
No	17	(89.5)	17	(85)	34	(87.2)
Ethnicity, *n* (%)						
White caucasian	13	(68.4)	16	(80)	29	(74.4)
Other	6	(31.6)	4	(20)	10	(25.6)

Table 2: Primary and secondary outcomes

Variable (score range)	CBT BL (n = 19)	CBT post (n = 16)	CBT FU (n = 16)	Waitlist BL (n = 20)	Waitlist post (n = 16)	Waitlist FU (n = 16)	Effect size BL to FU	Estimated CBT group effect	95% CI	P
SCL-90-R (GSI) (0–4)	0.9 (0.6)	0.6 (0.5)	0.5 (0.3)	1.0 (0.8)	0.9 (1.0)	1.0 (1.0)	0.74 (0.01 to 1.44)	−0.40	−0.77 to −0.03	0.03
RSE (10–40)	21.8 (4.7)	19.3 (4.3)	17.5 (4.6)	22.2 (6.0)	21.1 (5.3)	20.4 (6.2)	0.92 (0.17 to 1.63)	−2.34	−4.89 to 0.20	0.07
IES (0–75)	29.1 (16.4)	24.8 (15.2)	16.6 (13.5)	27.3 (20.8)	20.1 (18.8)	25 (19.7)	1.14 (0.37 to 1.86)	−8.38	−20.4 to 3.64	0.17
IIP-32 (0–128)	41.6 (18.1)	33.3 (15.2)	30.8 (17.6)	38.3 (19.9)	38.7 (16.2)	36.6 (19.3)	0.72 (−0.01 to 1.42)	−5.66	−14.0 to 2.71	0.18

Mean questionnaire scores (and SD) at baseline, post-treatment and follow-up, effect-sizes - at follow-up (with 95% Confidence Intervals [CI]) and estimated CBT group effects with P-values and 95% CI. Models fitted for each questionnaire used the respective baseline value as a covariate. BL = baseline, FU = follow-up. On all questionnaires higher scores denote more pathological scores.

had enough power for this to translate into statistically significant differences.

The study has a number of strengths. It describes an exploratory trial with a theoretical and model development phase having led to the intervention in an iterative process. The intervention and its components are clearly defined and its content and delivery was standardized and reproducible. Through its inclusion of expressive writing, the study also contains a qualitative component, which enriches our understanding of these women's plight, what might be helpful components of therapy and the way in which through treatment they come to re-evaluate their difficulties. A separate analysis of these writings is planned.

Limitations of the study are that the sample size is small and the study is likely to have been underpowered to detect significant differences on some of the outcomes. Multiple outcomes were assessed and given the exploratory nature of the trial, no corrections for multiple testing were made. This increases the risk of type I error. The response rate was low, which raises questions about the representativeness of our sample and the possibility of selection bias. For example, more motivated, psychologically minded or particularly unwell women may have preferentially chosen to participate. However, we do know that non-respondents were similar in age to participants and the baseline questionnaire scores of study participants compared with a sub-sample of the women who decided to not participate were very similar. This goes some way to reassure that study participants were representative of the total population of MKRH women on the register.

One reason for the low response rate may have been that we approached potential participants by letter. This postal method of recruitment may not have been optimal and more individualized approaches (e.g. via telephone or face to face in the clinic) might have yielded better results.

We chose a small number of well-validated and widely used outcome measures to allow comparability with previous studies. It would have been desirable to also include some measures focusing more specifically on the targets of the intervention (e.g. coping and negative appraisals). However, available measures of coping and cognitive appraisals may not be specific enough to tap what goes on in MRKH and we did not want to overload our participants with generic measures.

The person who conducted the therapy also administered the self-report questionnaires and was thus not blind to group allocation. We did not formally measure treatment fidelity, e.g. by using a cognitive-therapy rating scale. Moreover, the design does not allow us to identify what the effective components of the intervention were, i.e. whether improvements were due to the specific techniques based on the model or whether it was due to non-specific factors such as having group support or therapist factors.

The study raises broader issues about how a small study such as ours can inform clinical practice and future research and about the development, evaluation and dissemination of complex interventions for relatively rare disorders such as MRKH. Clinically, the findings of this study are of relevance to practitioners in general practice, paediatrics, gynaecology, endocrinology, psychology and psychiatry as women with MRKH may come into contact with any of these specialities. Moreover, the psychological treatment developed here may serve as an exemplar for the development of interventions in other areas of gynaecological–psychological medicine, as it could easily be adapted for conditions such as Complete Androgen Insensitivity Syndrome (CAIS), Premature Ovarian Failure or early onset Endometrial Cancer, all of which may have a psychological impact not dissimilar to MRKH.

Thinking about future research, given the rarity of MRKH it will be exceptionally difficult to mount a more definitive large study on this topic. Thus, our small preliminary trial may be the best available evidence in this area for a long time to come. Perhaps future studies should include women with a range of disorders with similar psychological impact, although this might somewhat dilute the specificity of the approach.

Acknowledgements

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