Rates of medical or surgical treatment for women with heavy menstrual bleeding: the ECLIPSE trial 10-year observational follow-up study

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Primary conflicts of interest: Joe Kai is a member of the National Institute for Health and Care Research (NIHR) School for Primary Care Research board (2015 to present). Janesh Gupta has received consulting fees as clinical advisor for Femcare-Nikomed (Romsey, UK), and has provided expert testimony in the High, Crown and Coroner's Courts. Jane Daniels is a member of the NIHR Clinical Trials Unit standing advisory committee (2016 to present).

Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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Scientific summary

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Scientific summary

Background

Heavy menstrual bleeding (HMB) is a common problem that can significantly affect women's lives until menopause. Despite its high incidence and burden, many women do not seek medical help. The Clinical effectiveness and cost-effectiveness of levonorgestrel releasing intrauterine system in primary care against standard treatment for menorrhagia trial (ECLIPSE) randomised 571 women presenting to primary care with HMB to treatment with the levonorgestrel-releasing intrauterine system (LNG-IUS) or usual medical treatment (oral tranexamic acid, mefenamic acid, combined oral contraceptive pill or progesterone alone). The primary outcome was a patient-reported score of the burden of HMB, which was assessed over a 2-year period. This score improved significantly in both groups across all time points compared with baseline scores. At follow-up after 2 years, women in the LNG-IUS group reported significantly greater improvements than women assigned to the usual medical treatment group. By the 5-year follow-up, this benefit was reduced. There is a lack of evidence on longer-term outcomes, beyond 5 years, after seeking health care and treatment for HMB.

Objectives

The primary objective of this study was to assess continuation rates of medical treatments, and rates of ablative and surgical interventions, in women 10 years after initial management for HMB in primary care.

Additional secondary objectives were to develop a greater understanding of the natural history and treatment of HMB, in particular:

- an assessment of whether or not initial medical treatment (the LNG-IUS or usual medical treatments) influences women's trajectories
- an assessment of quality of life and sexual function experienced, and an evaluation of whether or not these are influenced by initial medical treatment
- a qualitative exploration of women's experiences of HMB, and decisions about treatments or surgical interventions, to provide insight into women's choices and what influences them, over this time period.

Design

This was a prospective observational cohort study, with a parallel qualitative study.

Participants

A maximum of 490 women who had participated in the ECLIPSE trial (ISRCTN86566246) were available to be re-approached. Of these women, 206 consented to providing outcome data via a questionnaire approximately 10 years after their original randomisation. A purposeful sample of 36 women, who had a range of ages, social diversity (socioeconomic, ethnicity and educational background), educational backgrounds, treatment experiences and trajectories, also participated in semistructured qualitative interviews.

Interventions

The allocation method of the ECLIPSE trial interventions and the distribution of the treatments used have been previously reported. The ECLIPSE trial randomised participants to either the LNG-IUS or usual medical treatment [oral tranexamic acid, mefenamic acid, combined oestrogen–progestogen or progesterone alone, chosen as clinically appropriate by general practitioners (GPs) and women]. Women could subsequently swap or cease their allocated treatment.

Main outcome measures

Data were collected directly from women on the use of treatments for HMB and the surgical interventions of hysterectomy and endometrial ablation as the primary outcomes for this observational study. Changes in treatment or cessation of treatment were also recorded. Generic quality of life was assessed using the Short Form questionnaire-36 items (SF-36), the EuroQol-5 Dimensions (EQ-5D) descriptive system and the EQ-5D visual analogue scale. The Sexual Activity Questionnaire (SAQ) measured the pleasure, discomfort and frequency of sexual activity. The primary outcome measure in the original trial was the patient-reported, condition-specific Menorrhagia Multi-Attribute Scale (MMAS) at 2 years' follow-up. As expected, few ($n = 13$) respondents completed the MMAS, so no data are reported for this outcome.

All semistructured telephone and face-to-face interviews were conducted by a female researcher. Interviews were audio-recorded and transcribed verbatim. The coding of interview transcripts was aided by the application of NVivo (QSR International, Warrington, UK) software, with the field researcher and a senior researcher each identifying emerging themes from the data and then developing these together. Data generation and thematic analysis were iterative until no new themes emerged, suggesting data saturation. A process of member checking was also undertaken.

Results

The baseline (prior to randomisation) characteristics of the reconsented responding women and those who were not followed up were very similar. The mean age of the women at follow-up was 53.7 years (standard deviation 5.1 years). Over the 10-year follow-up period, 60 out of 206 (29%) women had received a surgical intervention [hysterectomy, $n = 34$ (16.5%); endometrial ablation, $n = 26$ (12.6%)]. Between 5 and 10 years, 89 women (43.2%) had ceased all medical treatments and 88 (42.7%) continued to use the LNG-IUS alone or in combination with other oral treatments. Fifty-six women (28%) were using the LNG-IUS at 10 years [35% (38/110) of women originally allocated to the LNG-IUS and 19% (18/96) of women originally allocated to usual medical treatments]. There were improvements over time in SF-36 scores in both women who were initially allocated to the LNG-IUS and women who were allocated to usual medical treatment, with small and statistically insignificant differences between the two original allocation groups. Changes over time in the EQ-5D scores were very small and, again, no differences were seen between the original allocation groups. There was a clear deterioration in the discomfort domain of the SAQ, with no evidence of a difference between the allocation groups, but no changes were seen in the pleasure domain.

In the qualitative study, women reported wide-ranging debilitating impacts on their quality of life. Women had often normalised their HMB experience, reflecting wider societal and generational taboos around menstruation and low awareness that HMB is a treatable problem. Treatment decisions and experience were strongly positively or negatively influenced by the perceived quality of health-care interactions with clinicians. Other key influences on women's decisions about treatment for HMB over time included considerations in their lives in transition (e.g. changing personal relationships,

requirements for contraception or desire for children, and changes in work); the effects of treatment on fertility; their health concerns and knowledge, including that of family and peers; and their views about approaching menopause, or on avoiding premature menopause.

Limitations

Fewer than half of the original 571 participants contributed, but the cohort was demographically and clinically representative of the original trial population. A large proportion of women had, as expected, stopped having periods, owing to either the menopause or the surgical treatment, meaning that only a small number of women were able to report on the original primary outcome measure.

Conclusions

The study provides a helpful new indication of the expected proportions of women continuing to use or not use treatments for HMB, or progressing to surgical intervention, and of the significant proportion of women using the LNG-IUS, after a decade. Medical treatments for women with HMB can be initiated in primary care, with low rates of surgical intervention and improvement in quality of life observed 10 years later and with high likelihood of avoiding surgery. Clinicians should be aware of the considerable challenges that women with HMB experience over time, and the importance and value of patient-centred communication about treatment in this context.

Future work

Any further evaluation of treatments for HMB should include the long-term evaluation of outcomes and adherence. Further qualitative research might investigate the perspectives of health professionals, in particular GPs and nurse practitioners in primary care, alongside gynaecologists, to understand the challenges that they may experience seeing women with HMB and to elicit their perceptions of how care may be enhanced.

Trial registration

The original ECLIPSE trial was registered as ISRCTN86566246.

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