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Cost-effectiveness analysis in the treatment of heavy menstrual bleeding in Spain

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ABSTRACT

Objective: To compare the effectiveness and costs associated with first-line medical treatments for chronic heavy menstrual bleeding (HMB) in Spain.
Study design: A cost-effectiveness analysis was conducted comparing the levonorgestrel-releasing intrauterine system (LNG-IUS) with the estradiol valerate/dienogest multiphase oral contraceptive (E2V/DNG), combined oral contraceptives (COC) and progestins (PROG). Study patients were fertile women diagnosed with HMB who initially wished to remain fertile. A Markov model based on reported clinical data and the opinion of a panel of experts was used. The time horizon of the analysis was 5 years. The analysis was conducted from the perspective of the Spanish National Health System (NHS), discounting both costs (€ 2013) and future effects at an annual rate of 3%. One-way sensitivity analyses and probabilistic sensitivity analysis were performed to test the robustness of the results.
Results: In the analysis at 5 years, the LNG-IUS was associated with a gain of 0.67, 2.22, and 3.53 symptoms free months (SFM) compared with E2V/DNG, COC and PROG, respectively. LNG-IUS contributed more quality-adjusted life months (QALM) than the other treatment alternatives (+1.74 *vs.* E2V/DNG, +3.33 *vs.* COC +3.53 *vs.* PROG). First-line LNG-IUS treatment resulted in savings of € 583, € 988, and € 1891 *vs.* E2V/DNG, COC and PROG, respectively. These cost benefits, coupled with the greater clinical benefits in terms of SFM and QALM, show that LNG-IUS is the dominant option (less costly and more effective).
Conclusion: LNG-IUS is the medical treatment of choice and cost-saving option for the control of HMB in Spain.

Introduction

In recent years, efforts have been made to reach a consensus definition of heavy menstrual bleeding (HMB), both in international organizations [1–3] and in Spain, in the framework of the Spanish Society of Gynaecology and Obstetrics (SEGO) consensus documents on menorrhagia [4]. According to the definition of the International Federation of Gynaecology and Obstetrics (FIGO) on abnormal bleeding, HMB is defined as excessive menstrual blood loss (>80 ml) that interferes with normal physical, emotional or social activity and worsens the quality of life of women [2,4].

There are no objective Spanish data on the prevalence of HMB, but globally it is estimated that between 8% and 27% of women suffer this disorder [4]. Despite generally being benign, HMB is common among fertile women, has important health implications, is a frequent complaint in primary care and generates a large number of gynecology referrals [4]. HMB also has important social

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implications, as it affects the quality of life, usually due to the possible development of anemia, which is objectively associated with HMB [4].

The alternatives proposed by the SEGO as first-line treatment in women diagnosed with HMB without contraindications to or rejection of hormones, are the levonorgestrel-releasing intrauterine system (LNG-IUS) and the newly approved regimen estradiol valerate/dienogest multiphasic oral contraceptive (E2V/DNG). Both alternatives are highly effective, achieving a reduction in bleeding of up to 94% and 89%, respectively [4] and are clearly superior in reducing bleeding to other alternatives such as other combined oral contraceptives (COC), progestins (PROG), tranexamic acid and nonsteroidal anti-inflammatory drugs, which achieve reductions in bleeding ranging between 35% and 68% [4]. Their priority use is recommended *vs.* surgery (hysterectomy or ablation/endometrial resection), which should only be used in the case of treatment failure or contraindication to medical treatment [4]. LNG-IUS and E2V/DNG are relatively non-aggressive and help to preserve fertility, an essential factor that should be taken into account when patient and physician agree on a treatment consensus.

The objective of this study was to analyze the effectiveness of current medical alternatives in the first-line treatment of chronic HMB in Spain.

Materials and methods

A cost-effectiveness analysis using a Markov model of 6-monthly cycles was performed to simulate the evolution of a cohort of women in reproductive age, with HMB initiating first-line medical treatment. The model compared costs and effects of different treatment patterns beginning from first line therapy until surgery and over a 5 year horizon (the time until LNG-IUS replacement is required).

For each treatment strategy, the model estimated the difference in costs, symptom-free months (SFM), surgery-free months (SuFM) and quality-adjusted life months (QALM). Comparison of the incremental results between treatment with LNG-IUS and other alternatives (E2V/DNG, COC and PROG) was made by calculating the incremental cost-effectiveness ratio (ICER), which was subsequently compared with the accepted cost-effectiveness threshold in Spain of € 2500/QALM [5].

The base case was conducted from the perspective of the Spanish National Health System (NHS), considering only direct medical costs and the ex-factory price of drug treatment. All costs were updated to 2013 according to the Consumer Price Index published by the National Statistics Institute [6]. Costs and clinical outcomes were discounted at an annual rate of 3% [7].

Model structure

The model simulates a hypothetical cohort of fertile women diagnosed with HMB who wished to preserve their fertility but, that at the time of starting treatment, did not wish to become pregnant. Thus, the health states of the model were defined combining HMB control and birth control (Fig. 1). All HMB patients entering the model initiate first line treatment with one of the options assessed. Patients remain on the same therapeutic alternative until there is a failure to control HMB or failure of birth control. In order to reflect all main events that could happen during the treatment, including pregnancy and abortion, treatment evaluations were made every 6 months, throughout the time horizon of the model (5 years). Those patients who fail controlling HMB (Fig. 2) or birth control (Table 1) switch to other alternative as a second-line therapy, according to current clinical practice in Spain.

Data collection

We conducted a systematic review of the literature in PUBMED, Cochrane and DARE to locate clinical studies or reviews (published in English and Spanish) that evaluated HMB and birth control efficacy, health related quality of life (HRQoL) and economic consequences of HMB and birth control. The search strategy included the following key words:

heavy menstrual bleeding, abnormal uterine bleeding, menorragia, hypermenorrhea, excessive menstrual loss, DUB, dysfunctional uterine bleeding, progestogen, progesterone, levonorgestrel, intra-uterine-device-medicated, IUS, LNG IUS, mirena, progestasert, birth control, oral contraceptives.

A panel of 14 clinical experts in HMB treatment, representative of the different Spanish Autonomous Communities (see Expert

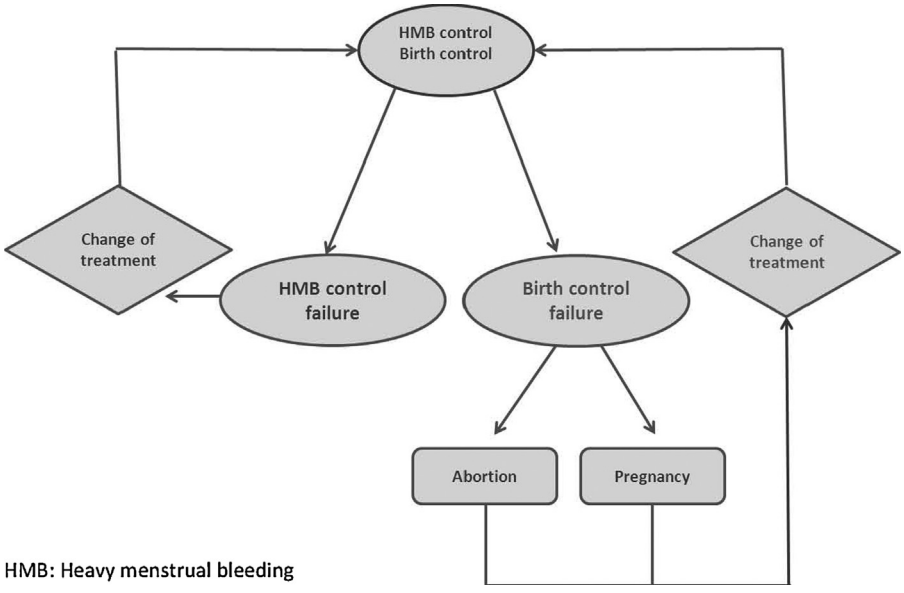

Fig. 1. Structure of the model.