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Health Care Provider Hormonal Recommendations for Treatment of Menstrual Cycle-related Problems - A Vignette-based Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author JCP initiated the project. Author JCP is responsible for design and methodology. Author RC wrote the first and final drafts. Authors FB and SY performed statistical analysis. Authors TV and FB did data entry. Authors RC, FB, SY, TV, and JCP provided critical review and editing of the final document. All authors read and approved the final manuscript.

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ABSTRACT

Background: Combined hormonal contraceptives (CHC) are recommended for "non-contraceptive benefits" for menstrual cycle-related problems. But no evidence-based consensus exists. Our purpose was to assess the clinical choices of health care providers (HCP: pharmacists, physicians, nurses) for menstrual cycle-related scenarios.

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Methods: A 1-page questionnaire was provided to continuing professional education attendees at events across Canada. They suggested treatments for four common clinical scenarios each involving a different menstrual cycle-related problem. Each case was followed by five to six choices. All potential options included CHC and cyclic progesterone (P4) or medroxyprogesterone (MPA); HCP could choose multiple options.
Results: CHC was recommended by 84% of HCP for at least one of four scenarios; 64% chose cyclic P4/MPA at least once. For teenage menorrhagia, 63% chose CHC, 23% cyclic P4/MPA and only 31% ibuprofen. For the 35 year-old smoker with polycystic ovary syndrome (PCOS), 55% discontinued CHC, but 22% suggested switching to higher-dose anti-androgen CHC; 23% chose cyclic MPA, 32% spironolactone and 14% metformin. For a premenopausal fragility fracture, 34% recommended CHC and only 5% cyclic MPA; 17% chose a contraindicated aminobisphosphonate. For perimenopausal VMS, 10% chose CHC, 34% cyclic P4, 21% cyclic MPA.
Conclusion: There are significant variations among HCP disciplines for treatment of menstrual cycle-related problems. Contraindications and disadvantages of CHC-based therapies in these scenarios seem to not be recognized by HCP. Evidences for progesterone-based therapies have not been translated into current clinical practice. Few HCP suggested evidence-based non-hormonal treatments. Efforts are needed to translate research-based, physiological menstrual cycle treatments into safe and effective clinical practice.

Keywords: Menstrual-cycle disturbances; cycle-related problems; clinical practice; Combined Hormonal Contraceptives (CHC); cyclic progesterone therapy; evidence-based treatment; non-hormonal treatments.

1. INTRODUCTION

As many as 2.5 million women are affected each year by serious menstrual disorders requiring medical evaluation and treatment [1]. These have negative impacts on their quality of life [1-2]. Although menstrual cycle related disturbances may have many etiologies, fluctuations in endogenous estradiol (E2) and progesterone (P4) production as well as genetic factors are thought to contribute [2-4]. Thus, through their reproductive lives, menstrual cycle-related changes can lead to disturbing symptoms and problems for adolescents, pre- and perimenopausal women [2-4].

Given evidence for Hypothalamic-Pituitary-Gonadal (HPG) axis-related changes in menstrual irregularities [3,4] and other undesirable experience it seems appropriate to use hormonal therapies in the management of menstrual-cycle-related problems [3-5]. Combined Hormonal Contraceptives (CHC) containing both a synthetic estrogen and a progestin and formulated to be supra-physiological in order to provide birth control are commonly recommended for menstrual-cycle disturbances and related problems [6-9]; however current practice guidelines often differ [10-11]. Progestins such as Medroxy-Progesterone Acetate (MPA) are also traditionally used for problematic menstrual cycles because they act like progesterone to cause secretory endometrial changes and interact with endogenous estradiol in the reproductive system. Oral micronized P4 only became available in North America in the 1990s so less research is available using it. The approach, however, to treatment may differ among health care providers (HCP) depending on their disciplines, clinical experiences, judgements and understandings of the fundamental problems causing these symptoms [8-12].

Although physicians remain the leading care providers for patients with menstrual-related disorders, both pharmacists and nurses have or are gaining more important roles as the health-care system continues to evolve towards patient-centred multi-disciplinary collaborative care. In Canada, both professions are trained to assess and manage minor ailments in the community. Nurse practitioners have the authority to prescribe prescription medications and pharmacists who receive the most extensive training in pharmaceutical therapies, provide direct patient care in the community and are often consulted by physicians for recommendations on choosing pharmaceutical therapies.

Our primary objective is to describe the hormone-based treatment recommendations for menstrual cycle-related problems of HCP including physicians, pharmacists, pharmacy and

nurse-clinician trainees, nurse-clinicians and public health nurses. The four vignettes each involved a different but common menstrual cycle-related problem occurring in different phases of women's reproductive lives including teen menorrhagia, polycystic ovary syndrome (PCOS) with worsening acne and flow despite CHC treatment, a premenopausal woman with hypothalamic menstrual irregularity and a fragility fracture and a regularly cycling women in her forties with night sweats. Once we analyzed the practice patterns, we could identify potential gaps in research, clinical practice, and professional education by comparing our results to the current evidence.

2. METHODS

Clinical vignettes were initially developed for our 2005-6 pharmacy survey [12] that interviewed a random sample of community pharmacists within one health administrative region. Each case was followed by five to six choices of possible hormonal and non-hormonal management options. Respondents were asked to indicate all appropriate options.

The one-page questionnaire containing these vignettes was provided to each continuing professional education attendee prior to a scheduled lecture relating to women's reproductive health that Dr. Jerilynn C. Prior had been invited to present. The lectures were offered in different times and places between 2007 and 2014.

Those completing the questionnaire were HCP with differing backgrounds and mostly practiced in Western Canada. In two situations the audience was of HCP trainees ─pharmacy students in a 3rd year class and nurse-practitioner students nearing graduation, both at the University of British Columbia. For ease of categorizing the HCP we have considered the trainees with their respective practicing colleagues; we have performed a sensitivity analysis and the responses of the trainees do not differ from the other members of their profession (data not shown).

All of the questionnaires were anonymous; willingness to complete the questionnaire and allow it to be collected were considered evidence of consent. The only demographic information that was collected was the respondents' HCP role (e.g. physician, pharmacist, nurse).

Data were entered into a Microsoft Excel spreadsheet as the questionnaires were obtained. These data were cross-checked for completeness and accuracy.

2.1 Statistical Analysis

Data were subcategorized by the respondents' HCP status. In making cross-disciplinary comparisons, those who noted no profession or were in other roles were omitted. Statistical comparisons between the subgroups were performed by Chi-Square Test. Statistical analyses used SPSS (statistical package for social sciences) Version 22 (Armouck, New York, USA). A probability value of $P \leq 0.05$ was considered to be statistically significant.

3. RESULTS

Three hundred fifteen survey responses were collected from respondents with different HCP roles as shown in Table 1. The largest HCP subgroup was pharmacists with 129 pharmacy students and 43 pharmacists totaling 172; there were 65 physicians and 31 nurses. For 41 surveys there was no HCP status provided and 6 surveys reported other HCP roles (e.g. physiotherapy). A synopsis of each case with survey results by the three main HCP categories of therapy suggestions is provided in Table 2.

Table 1. Demographics of survey respondents

Profession	Total (n = 315)
Pharmacist	54.6% (n=172)
Physician	20.6% (n=65)
Nurse	9.8% (n=31)
Other HCPs	1.9% (n=6)
Unknown	13% (n=41)

3.1 Case 1: Teenage Menorrhagia and Anemia

Approximately two thirds of HCP (62.9%) recommended CHC. Less than a quarter (23.2%) recommended cyclic P4 (16.8%), cyclic MPA (9.5%) or both. The majority, given her anemia, recommended iron supplements (67.3%). Ibuprofen, however, was recommended by less than a third (30.8%). Among HCP subgroups, physicians were more likely to recommend ibuprofen (53.8%) than nurses (32.3%) or pharmacists (19.2%), $P < .001$.

Table 2. Approaches to menstrual related problems by healthcare provider status of survey respondents

Treatment options	Total (n=274)	Physician (n=65)	Pharmacist (n=172)	Nurse (n+31)	*P - value*
Case 1: 13 year old girl with regular but heavy menstrual flow and anemia					
One iron tablet a day	67.3% (n=212)	64.6% (n=42)	69.8% (n=120)	51.6% (n=16)	*P* = .12
Ibuprofen 200 mg every 4 hours during flow	30.8% (n=97)	53.8% (n=35)	19.2% (n=33)	32.3% (n=10)	*P* < .001
Prometrium® 300 mg at bedtime days 12-27 of cycle	16.8% (n=53)	13.8% (n=9)	23.3% (n=40)	6.5% (n=2)	*P* = .05
Low dose oral contraceptive	62.9% (n=198)	64.6% (n=42)	64.5% (n=111)	51.6% (n=16)	*P* = .36
Medroxyprogesterone 10 mg BID days 12-27 of cycle	9.5% (n=30)	7.7% (n=5)	10.5% (n=18)	9.7% (n=3)	*P* = .80
Case 2: 35 year old woman smoker with 15 years of oral contraceptive use for irregular periods and hirsutism has worsening acne and heavy flow					
Change to 35 μg EE-cyproterone oral contraceptive	21.9% (n=69)	23.1% (n=15)	16.3 (n=28)	38.7% (n=12)	*P* = .02
Medroxyprogesterone 10 mg BID, cycle days 9-27	22.9% (n=72)	24.6% (n=16)	22.1% (n=38)	22.6% (n=7)	*P* = .93
Spironolactone	32.1% (n=101)	49.2% (n=32)	29.1% (n=50)	16.1% (n=5)	*P* = .002
Topical antibiotic-retinoic acid once a day	30.2% (n=95)	16.9% (n=11)	43.6% (n=75)	6.5% (n=2)	*P* < .001
Metformin	13.7% (n=43)	30.8% (n=20)	4.1% (n=7)	6.5% (n=2)	*P* < .001
Discontinue oral contraceptives	55.2% (n=174)	53.8% (n=35)	63.4% (n=109)	29.0% (n=9)	*P* = .002
Case 3: 25 year old physically active woman who is thin and irregularly menstruating but is otherwise healthy, has had a fracture of her wrist. She fell while walking					
An oral contraceptive	33.7% (n=106)	35.4% (n=23)	39.5% (n=68)	6.5% (n=2)	*P* = .002
Medroxyprogesterone 10 mg 14 days a month	5.4% (n=17)	7.7% (n=5)	3.5% (n=6)	3.2% (n=1)	*P* = .34
Estradiol patch with cyclic oral micronized progesterone	11.7% (n=37)	21.5% (n=14)	8.1% (n=14)	16.1% (n=5)	*P* = .02
Calcium from food and supplements totaling 2000mg/day	73.3% (n=231)	78.5% (n=51)	66.9% (n=115)	90.3% (n=28)	*P* = .007
Alendronate-aminobisphosphonate	17.1% (n=54)	10.8% (n=7)	20.3% (n=35)	12.9% (n=4)	*P* = .17
Vitamin D 400 IU/day	83.8% (n=264)	78.5% (n=51)	86.6% (n=149)	80.6% (n=25)	*P* = .27
Case 4: 42 year old woman with regular flow every 26 days says she is getting very sore breasts and wakes up soaked with sweat several times during the night before flow starts.					
Compounded progesterone cream 20 mg twice a day	27.9% (n=88)	21.5% (n=14)	29.1% (n=50)	32.3% (n=10)	*P* = .52
An oral contraceptive	10.2% (n=32)	7.7% (n=5)	11.6% (n=20)	3.2% (n=1)	*P* = .29
Medroxyprogesterone 10 mg, cycle days 14-27	20.6% (n=65)	23.1% (n=15)	20.3% (n=35)	6.5% (n=2)	*P* = .14
Oral micronized progesterone 300 mg at bedtime, cycle days 14-27	33.7% (n=106)	47.7% (n=31)	35.5% (n=61)	6.5%(n=2)	*P* < .001
Vitamin E 400-800 IU/day	6% (n=19)	7.7% (n=5)	4.1% (n=7)	6.5% (n=2)	*P* = .51
Oral micronized estradiol with medroxyprogesterone	21.6% (n=68)	18.5% (n=12)	22.7% (n=39)	41.9% (n=13)	*P* = .03

3.2 Case 2: 35 Year Old Smoker on CHC with PCOS, Worsening Acne and Menorrhagia

For this woman with polycystic ovary syndrome (PCOS; also called anovulatory androgen excess (AAE) [12], over half recommended that she discontinue CHC (55.2%). However, 21.9% wanted her to switch to 35 μg ethinyl estradiol-cyproterone acetate, since it is includes an anti-androgenic progestin. In total, 46.7% opted for CHC. Cyclic MPA was recommended by 22.9%. Recommendations for other therapies varied considerably; spironolactone was recommended by 32.1%, topical antibiotic with retinoic acid by 30.2 % and metformin by 13.7%. HCP analysis showed physicians being more likely to suggest metformin (30.8%, pharmacists 4.1%, nurses 6.5%, $P < .001$) and spironolactone (49.2%, pharmacists 29.1%, nurses 16.1%, $P = .002$) respectively.

3.3 Case 3: 25 Year Old with Irregular Menstruation and Fragility Fracture

For her treatment, more HCP chose CHC (33.7%) than chose menopausal hormone therapy-type estradiol patch with cyclic oral micronized progesterone (11.7%). Cyclic MPA use was advised by only 5.4%. For non-hormonal recommendations, the majority of HCP recommended 400 IU of Vitamin D (83.8%) and up to 2,000 mg/d of calcium supplementation (73.3%). The aminobisphosphonate, alendronate, was recommended by 17.1%.

3.4 Case 4: 42 Year Old with Regular Cycles, Night Sweats and Breast Tenderness

Cyclic P4 was recommended by 33.7%, compounded P4 cream by 27.9%, oral micronized estradiol with MPA by 21.6%, cyclic MPA by 20.6% and CHC by 10.2%. In HCP subgroup analysis, physicians were the most likely to recommend cyclic P4 (47.7%) followed by pharmacists (35.5%) and nurses (6.5%), $P < .001$.

3.5 Summary of Hormonal-based Therapies

For the purpose of evaluating the use of hormone-based therapies, we compiled the recommendation rates of CHC, cyclic P4, and cyclic MPA from all four vignettes and analyzed them. The second case included two different CHC options. A response of "Change to ethinyl estradiol-cyproterone acetate oral contraceptive" or to not choose to "Discontinue oral contraceptives" were all counted as recommending CHC. Vignettes related to teenage menorrhagia and perimenopausal night sweats both included options for both cyclic P4 and MPA. Choosing either one or both was counted as a recommendation for P4/MPA therapy.

The majority of HCP (83.8%) recommended CHC for at least one of the four cases (Fig. 1). More than half of HCP (51.5%) chose CHC for two or more cases. HCP subgroup differences were statistically significant ($P = .05$). More nurses (93.5%) recommended CHC for at least one case followed by physicians (84.6%) and pharmacists (79.7%); more physicians (56.9%) and pharmacists (51.8%), however, recommended CHC for multiple cases than did nurses (38.7%). Nearly two-thirds (64.1%) of HCP recommended cyclic P4/MPA therapies for at least one of the four cases with 24.7% recommending it for two or more cases (Fig. 2). Chi-Square testing did not demonstrate a statistically significant P4/MPA recommendation difference among HCP disciplines ($P = .11$).

4. DISCUSSION

This vignette-based 2007-2014 study describes 315 Canadian health care providers' clinical practice decisions for menstrual cycle-related treatments. Overall results suggest that there remain significant variations [12,13] in the treatment choices for menstrual related disorders among HCP. There are widely varying rates of recommendations for hormonal options with CHC being most prevalent. Although it is a more physiological and often evidence-based option, cyclic P4 or MPA was chosen less frequently, especially for menorrhagia, premenopausal osteoporosis and PCOS/AAE. In addition, therapies such as cyclic MPA with evidence-base data on increased bone mineral density for hypothalamic cycle and ovulatory disturbances are thus relevant for premenopausal fragility fracture [5]. Ibuprofen for heavy flow [14,15], spironolactone for androgen excess [16,17] and metformin for insulin resistance in PCOS/AAE [18] for which there are data on effectiveness, are significantly underutilized.

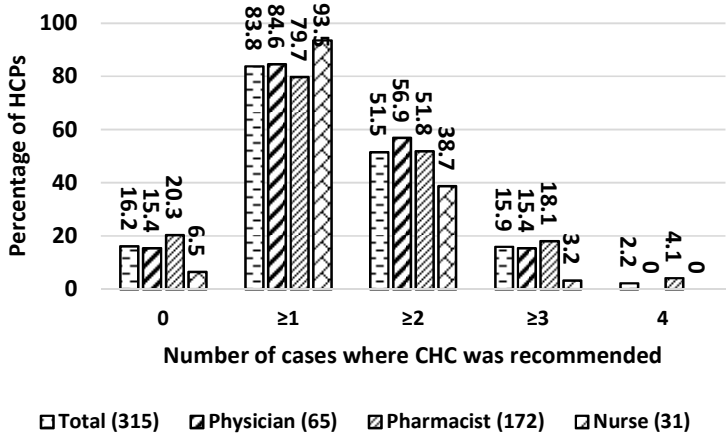

Fig. 1. CHC recommendation rates by health care providers from all four vignettes

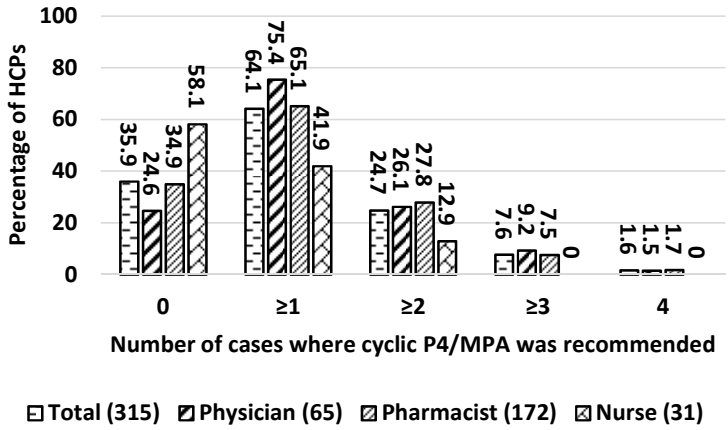

Fig. 2. Cyclic Progesterone (P4)/Medroxyprogesterone (MPA) recommendation rates by health care providers from all four vignettes

4.1 Case 1: Teenage Menorrhagia and Anemia

In the first vignette, we presented a 13 year old with anemia secondary to menorrhagia. Our results showed that HCP favoured CHC over cyclic P4/MPA. Although high dose (30-35 µg Ethinyl estradiol CHC tablets/day) for a week was effective for menorrhagia in adults [19], the evidence that CHC is effective for teenaged menorrhagia is lacking [15]. The origin of heavy flow in teens is usually anovulation with higher estradiol levels (population-based endometrial hyperplasia in teens [20]), thus higher dose or longer duration P4 or MPA would be more reasonable than high dose estrogen treatment. A Cochrane meta-analysis showed oral progestin (primarily norethisterone which is metabolized in part into estrogens) taken for 10-12 days during the luteal phase can help produce regular uterine shedding but is less effective than NSAIDs in decreasing the amount of flow [21]. Long cycle (e.g. cycle days 5-26) progestin is as effective for heavy flow in adults as the levonorgestrel-releasing IUD [22]. Given evidence strongly suggesting that CHC use in adolescents impedes peak bone mass [23,24], and that it is without proven effectiveness, CHC should be avoided in a teenager with menorrhagia not needing contraception. In addition, NSAIDs have been proven to effectively reduce flow volume by 20-50% [14,15] in menorrhagia by improving the balance of endometrial prostaglandin synthesis, leading to vasoconstriction [25,26]. However, our results showed surprisingly low ibuprofen recommendation rates (30.8%).

4.2 Case 2: 35 year old Smoker on CHC with PCOS/AAE Worsening Acne and Menorrhagia

The second vignette illustrated a 35 year old smoker with PCOS/AAE currently taking CHC but experiencing worsening hirsutism, irregular and heavy flow. CHC are recommended as first-line therapies in PCOS/AAE, but are contraindicated in smokers over the age of 35 due to increased risk for venous thromboembolism (VTE) [11,27]. Cyclic MPA is an effective agent for endometrial protection in women with PCOS [28]. In addition a 6-month RCT showed cyclic MPA significantly decreased serum levels of luteinizing hormone and total testosterone, as well as free androgen index, and acne and seborrhea scores [29]. Nearly half (44.8%) of the HCP continued CHC in spite of its known elevated VTE risk in a smoker ≥35 years old; one fifth (21.9%) switched to an even higher dose CHC (35 µg EE) because its progestin is the androgen receptor blocker, cyproterone acetate. Not many HCP (22.9%) recommended cyclic MPA which would have been an appropriate CHC alternative in PCOS/AAE with less risk for VTE [30]. Metformin is a helpful non-hormonal agent to increase insulin sensitivity as well as to decrease androgen production and potentially restore ovulatory menses [31-34]. Metformin was chosen by only 13.7%; it was the least recommended therapy in this vignette. Spironolactone is an effective androgen receptor blocker for treating hirsutism [35-38], yet less than one third (32.1%) chose spironolactone.

4.3 Case 3: 25 Year Old with Irregular Menstruation and a Fragility Fracture

In the third scenario, a physically active 25 year old woman who is otherwise healthy has menstrual irregularity and a fragility fracture, which suggests hypothalamic disturbance. CHC was the most favoured hormonal option and recommended by one third of HCP (33.7%). Although CHC and menopause-type hormone therapies have traditionally been used for osteoporosis in perimenopausal and postmenopausal women [39,40], evidence in premenopausal women is lacking Both neutral and negative effects on BMD from premenopausal CHC use have been reported [41,42,23,24]. A systemic review in 2006 demonstrated only fair BMD evidence supporting CHC in premenopausal women with oligo-amenorrhoea [43]. Basic science and clinical evidence supports progesterone as an important factor in promoting osteoblastic bone formation [44,45]; MPA acts similarly to P4 *in vitro* through the progesterone osteoblast receptor [46]. Benefits of improved spinal bone density with MPA 10 mg/day for 10 days each month in physically active women with hypothalamic cycle and/or ovulatory disturbances have been demonstrated in an RCT [5]. However, rarely did HCP recommend cyclic MPA (5.4%). There are no data with either CHC or cyclic P4/MPA showing fracture prevention. In fact, past CHC use is associated with increased fracture risks in multiple studies [47-49]. Bisphosphonates are beneficial in the treatment of osteoporosis in menopausal women and in men, but they are not indicated in premenopausal women [50-52]. Given potential fatal fetal effects, bisphosphonates need to be used with caution in women of childbearing age [53,54]. Approximately one sixth (17.1%) of HCP recommended alendronate for the 25 year old woman with irregular cycles and a fragility fracture. She was not noted to be using contraception.

4.4 Case 4: 42 Year Old with Regular Cycles, Cyclic Night Sweats and Breast Tenderness

The final vignette presented a woman in her 40s with regular cycles but experiencing night sweats accompanied by premenstrual breast soreness [55]. She is in very early perimenopause based on shorter cycles, sore breasts and vasomotor symptoms [56]. Symptoms such as breast tenderness suggest she is experiencing higher estrogen levels and may have a “luteal out of phase” cycle, as recently described [57]. This and the inconsistent effects of exogenous estrogen to suppress higher endogenous perimenopausal E2 production [58] plus RCT evidence that CHC is not more effective than placebo for perimenopausal hot flushes [59] make estrogen-based therapies not suitable. Oral micronized P4 has been shown by RCT to be effective for hot flushes and night sweats in healthy early postmenopausal women [60] and does not cause a rebound increase in vasomotor symptoms (VMS) when discontinued [61]. High-dose progestin therapies (megestrol, depot MPA and norethindrone acetate) have also demonstrated comparable benefits in treating hot flushes in RCT to estrogen-based therapies in women with breast cancer and with fewer adverse-effects [62-66].

The overall responses to this vignette displayed HCP reluctance to recommend hormone based

therapies for perimenopausal VMS as none of the treatment options was recommended by more than 34% of respondents. However, higher recommendation rates for P4/MPA therapies were observed over therapies containing estrogen. A combined 46.7% of the HCP recommended either cyclic P4 or cyclic MPA therapy. CHC (10.2%) was the least recommended of all hormonal options.

4.5 Hormone-Based Therapies

To elucidate what HCP understand about, and how they use, CHC and progesterone in current practice, we presented scenarios in which estrogen-containing therapies are inappropriate or can potentially be harmful. Our results, however, displayed an overall higher preference for using estrogen-dominant CHC than cyclic P4/MPA therapies. Only 16.2% of the HCP avoided CHC use in all four vignettes compared to 35.9% who never recommended cyclic P4/MPA. Over eight of 10 (83.8%) recommended CHC for at least one scenario. More than half (51.5%) recommended CHC for multiple vignettes, two times the number so choosing cyclic P4/MPA (24.7%). Even for the woman with apparent hypothalamic irregular cycles and fracture, a situation for which cyclic MPA is evidence-based [5], only 5.4% recommended it, perhaps because systematic reviews did not quote that randomized controlled trial (RCT) [67,68] and clinical guidelines did not recommend it [68].

4.6 Gaps between Research Evidence and Practice

Results from our HCP survey suggest significant gaps between research-based evidence and current clinical practice. CHC was the most frequently recommended hormonal treatment for scenarios in which CHC-specific evidence of Level I effectiveness is lacking. CHC is also not officially indicated for these conditions. Contraindications to and disadvantages of oral estrogen-based therapies in many cases (such as in a smoker of age 35) have not been recognized. On the other hand, recent evidence related to hormonal therapies for menstrual disturbances, especially the potential benefits of cyclic P4/MPA (http://www.cemcor.ubc.ca/resources/cyclic-progesterone-therapy) have not been translated into clinical practice. Cyclic P4/MPA was rarely chosen for teenage menorrhagia, PCOS/AAE or for irregular cycles and fragility fracture (although for the later we have RCT evidence that it increased bone mineral density) [5].

In addition, non-hormonal medications that have traditionally been used in other conditions are not being utilized for the conditions for which they have been proven effective in menstrual cycle-related problems. Few HCP recommended evidence-based ibuprofen for menorrhagia, or metformin and spironolactone for PCOS. Furthermore, we observed a 17.1% recommendation rate for a strong nitrogen-containing bisphosphonate in a childbearing aged woman in whom it is contraindicated.

Subgroup analysis showed that physicians are significantly more likely to recommend evidenced-based non-hormonal agents such as ibuprofen for menorrhagia (53.8%) than pharmacists (19.2%), and spironolactone and metformin for PCOS/AAE. (49.2% and 30.8%) than pharmacists (29.1% and 4.1%) and nurses (16.1% and 6.5%) respectively. Many of these practice issues were noticeably amplified in the pharmacist group that was largely composed of 3rd year pharmacy students (74.6%). This may also suggest gaps between research evidence and what is being taught in current professional training programs.

One limitation to this study was potential selection bias. Participants of the current study were attendees at continuing professional education lectures relating to women's reproductive health. It is possible that attendees at these events have more interest in menstrual cycle-related topics and reproductive health than HCP in general. However, it is difficult to deduce whether the participants' knowledge is more or less compared to their peers, as they could be attending the lectures either due to lack of knowledge or due to increased interest. In addition, deciding the treatment in practice may differ among HCP depending on patients' desires and expectations related to their life style or religious attitudes.

5. CONCLUSION

The overall results of this vignette-based survey study suggest significant variations among healthcare providers in managing menstrual cycle related disorders. Research-based data supporting the use of P4/MPA treatments are not yet translated into clinical practice. CHC remains the most frequently used hormone-based treatment despite a lack of evidence for Level I effectiveness in these scenarios.

Contraindications to and disadvantages of CHC in these cases appear to be unrecognized by HCP. Evidence-based non-hormonal treatments are considerably underutilized for their proven indications in menstrual cycle disturbances. Future efforts are needed to translate research-based, physiological treatments for menstrual cycle-related problems into safe and effective clinical teaching and practice.

ETHICAL APPROVAL

This confirms that this study is not against the public interest, and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported. JcP the founder and scientific director of the University of British Columbia Centre for Menstrual Cycle and Ovulation Research (www.cemcor.ca) is also the author but receives no honouraria for the book Estrogen's Storm Season—stories of perimenopause 2005, reprinted 2007 available http://www.cemcor.ubc.ca/resources/estrogen%E2%80%99s-storm-season.

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