

Appraisal of Core Therapy, Supportive Therapy, and Alternative Therapy in a Tertiary Care Rural Hospital of Vidarbha Region in Correlation to Plethora of Menopausal Problems

Priyanka Bharat Aglawe, Rajesh K. Jha, Vedprakash Mishra¹, Kamini M. Sakore², Aditya Chetan³, Deepti S. Shrivastava⁴

Departments of
Pharmacology and
¹Physiology, Jawaharlal
Nehru Medical College,
DMIMS (DU), ²Intern,
MBBS, Jawaharlal Nehru
Medical College, DMIMS
(DU), ⁴OBGY, Jawaharlal
Nehru Medical College,
Wardha, Maharashtra,
³Computer Science and
Applied Mathematics, Indian
Institute of Information
Technology, Delhi, India

ABSTRACT

Context: Menopause is a crucial phase of the women fraternity which marks the end of reproductive age. Mostly it is physiological; however, certain conditions may lead to premature menopause. Menopause has an extensive spectrum of symptoms which are extremely bothersome. An effective, empathetic, and rational treatment strategy is necessary. **Aim:** The present study was carried out to appraise the treatment strategies to tackle menopausal problems in Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha – a tertiary care hospital in rural Vidarbha. **Materials and Methods:** This monocentric hospital-based qualitative study was carried out on 330 menopausal women. Data were collected from in-depth interview of the health-care professionals of obstetrics and gynecology department and patients. **Results:** Of 330 participants, the incidence of natural menopause was 90.96% (2016) and 85.36% (2017); surgical menopause was 09.03% (2016) and 14.63% (2017). There was no incidence of chemotherapy-induced and pelvic radiation-induced menopause during the study. Pharmacotherapy (85.45%) and surgery (19.09%) were the mainstay treatments. The most common route of drug administration was oral (92.20%), followed by intravaginal (15.60%), topical (09.57%), and injectables (0.35%). Pharmacotherapy was categorized into core therapy (84.75%), supportive therapy (47.52%), and alternative therapy (03.19%). **Conclusion:** The present study concludes that there is a decline in the use of hormone replacement therapy for the management of menopausal complaints. There is lack of awareness of the complexity of menopausal symptoms and available treatment strategies in this rural population, and therefore, it is recommended to organize various awareness camps, so that a prompt and most suitable treatment can be provided.

KEYWORDS: Menopause, spectrum of symptoms, treatment strategies

INTRODUCTION

Menopause marks the end of reproductive age of the women fraternity. It is defined as the cessation of menstrual cycles for 12 consecutive months.^[1]

The history of menopause has several wayposts with regard to the development of treatment strategies. Testicular extract, crude ovaries, ovarian juice, and powdered ovarian tablets were used in the previous era, which followed the use of tranquilizers. The use of hormone replacement therapy (HRT) was only after

medicalization of menopause. Premarin was the first marketed estrogen as a treatment of menopause in the 1940s.^[2]

At present, HRT is the mainstay treatment.^[3]

Address for correspondence: Dr. Priyanka Bharat Aglawe, Department of Pharmacology, Jawaharlal Nehru Medical College, DMIMS (DU), Sawangi (M), Wardha, Maharashtra, India. E-mail: paglawe@gmail.com

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Nonhormonal treatments such as selective serotonin reuptake inhibitors, serotonin, and noradrenaline reuptake inhibitors,^[4] gabapentin, pregabalin, clonidine,^[5] phytoestrogens;^[6,7] herbal^[8,9] products; and various other nonpharmacological strategies are now in use.

Due to the availability of a wide range of treatment strategies, an in-depth study was required to appraise the recent prescribing trends in menopause.

The present study was carried out to assess the status of core therapy, supportive therapy, and alternative therapy in our tertiary care rural hospital of Vidarbha region – Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (Meghe), Wardha, in correlation to plethora of menopausal problems.

MATERIALS AND METHODS

- Type of study: A monocentric hospital-based qualitative study
- Locus of administrative control: Department of Pharmacology, Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha
- Locus of study: AVBRH, Sawangi (Meghe), Wardha
- Study population: Females with menopausal symptoms coming to Obstetrics and Gynecology (OBGY) Outpatient department (OPD)/Inpatient department (IPD) of AVBRH, Sawangi (Meghe), Wardha
- Duration of the study: October 01, 2016–August 31, 2018
- Period of enrolment: October 01, 2016–December 31, 2017
- Period of analysis: January 01, 2018–August 31, 2018
- Sample size: 330.

The sample size of the study was calculated with reference to the parameter menstrual complaints,^[10] using the following formula:

Sample size formula for the difference between two proportions:

$$n = \frac{(2\alpha_{/2} + 2\beta)^2 (P_1 [1 - P_1] + P_2 [1 - P_2])}{(P_1 - P_2)^2}$$

Where

- $2\alpha_{/2}$ is the critical value of normal distribution at $\alpha_{/2} = 1.96$
- 2β is the critical value of the normal distribution at $\beta = 0.84$ (80% power)
- P_1 is the expected sample proportion of 1st group = 42.5%
- P_2 is the expected sample proportion of 2nd group = 44%.

Therefore,

$$n = \frac{(1.96 + 0.84)^2 (0.425 [1 - 0.425] + 0.44 [1 - 0.44])}{(0.425 - 0.44)^2}$$

$$n = 322.80$$

Ethical clearance

The research protocol was approved in the meeting held on July 9, 2016, by the Institutional Ethics Committee and the Letter of Approval was received on July 11, 2016 (Ref. No. DMIMS (DU)/IEC/2016-17/3016).

Study design

Inclusion criteria

- a. Women above 35 years of age who has been diagnosed with:
 - Natural menopause
 - Chemotherapy-induced menopause
 - Pelvic radiation-induced menopause
 - Surgical menopause.
- b. Menopausal women are presenting with menopausal complaints
- c. Menopausal women who are willing to participate in the study.

Exclusion criteria:

- a. Women below 35 years of age
- b. Women with a complaint of amenorrhea associated with polycystic ovarian syndrome
- c. Women with a history of malignancy.
 - Psychiatric disorder
 - Musculoskeletal disorder
 - Urogenital disorder.

Confidentiality

The identity and personal information of all the patients enrolled in the study was kept strictly confidential.

Statistical analysis

With the help of the statistician working in the Department of Community Medicine, JNMC, Sawangi (Meghe), Wardha, the collected data were statistically analyzed using descriptive and inferential statistics using Chi-square test to ascertain the clinical significance of the present study. The software used in the analysis was SPSS 22.0 version and GraphPad Prism 6.0 version (Armonk, NY: IBM Corp.) and $P < 0.05$ is considered as the level of statistical significance.

RESULTS

Incidence of different types of menopause

The incidence of natural menopause was found to be maximum which was followed by surgical menopause. In comparison to the year 2016, the incidence of natural

menopause was decreased, whereas surgical menopause was increased in the year 2017 [Table 1].

Treatment modalities

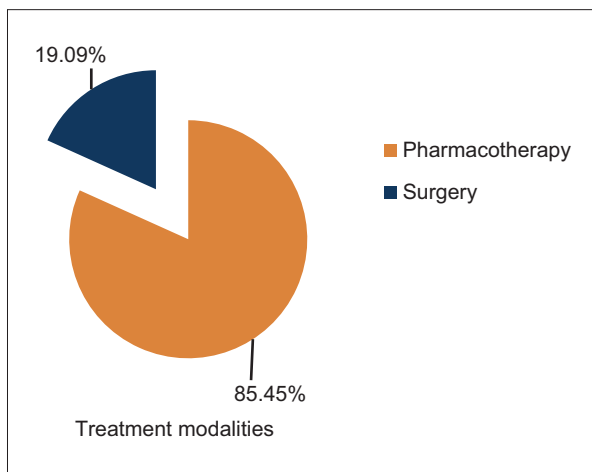
Pharmacotherapy and surgery were the main treatment modalities used to treat menopausal complaints of the patients visiting OBGY OPD of AVBRH, Sawangi (Meghe), Wardha [Graph 1].

Routes of drug administration

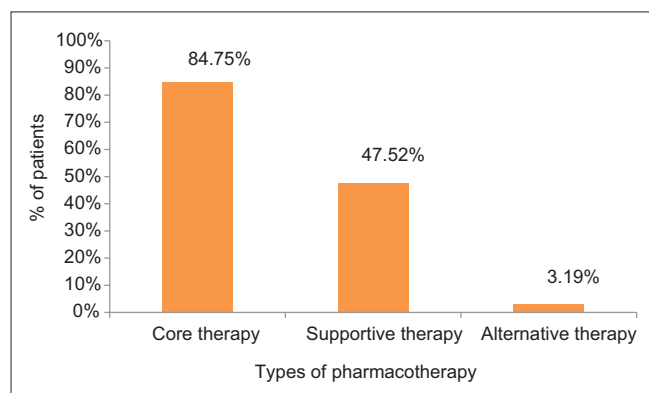
Drug administration in maximum number of patients was Oral, followed by Vaginal, Topical and Injectables [Graph 2].

Types of pharmacotherapy

Pharmacotherapy was further divided into core therapy, supportive therapy, and alternative therapy according to the type of drug. Drugs for treating the primary menopausal complaint were included in the core therapy; vitamins, supplements, and those drugs used to prevent the side effects of core drugs were included in the supportive therapy; whereas drugs other than allopathic were included under alternative therapy [Graph 3].



Graph 1: Treatment modalities for menopausal complaints

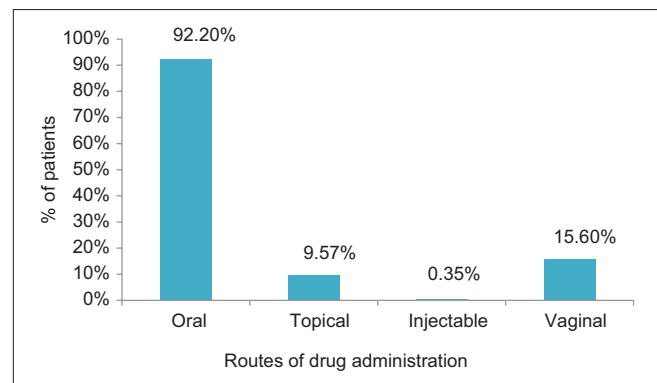


Graph 3: Different types of pharmacotherapy

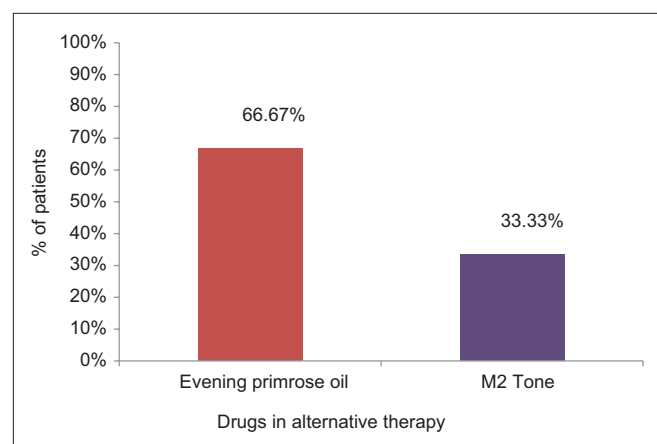
Core drugs (n – 239, % - 84.75)

The drugs used in core therapy were further classified according to the Anatomical Therapeutic Chemical (ATC) classification system [Table 2].

1. Imidazole and triazole derivatives of topical antifungals: Candid cream (Clotrimazole) was used topically in 2.09% of menopausal women on core therapy
2. Combination of topical corticosteroid with antibiotics: Candid B cream (Clotrimazole + Beclometasone) was used topically in 8.37% of menopausal women on core therapy
3. Imidazole derivative of gynecological anti-infectives and antiseptics: Tablet Candid V pessary (Clotrimazole) was used intravaginally in 3.77% of menopausal women on core therapy
4. Gynecological anti-infective drugs: Tablet Clid V pessary (Clindamycin + Metronidazole + Clotrimazole + Lactobacillus sporogens) was used intravaginally in 14.23% of menopausal women on core therapy
5. Plain preparation of natural and semisynthetic estrogens: Estrogen cream (Estradiol) was used topically in 0.84% of menopausal women on core therapy



Graph 2: Routes of drug administration



Graph 4: Alternative drug preparations used in menopausal women

Table 1: Incidence of natural menopause, chemotherapy-induced menopause, pelvic radiation-induced menopause, and surgical menopause

Year	Natural menopause, n (%)	Chemotherapy-induced menopause, n (%)	Pelvic radiation-induced menopause, n (%)	Surgical menopause, n (%)
2016	151 (90.96)	0	0	15 (09.03)
2017	140 (85.36)	0	0	24 (14.63)

2.48, $P=0.11$, NS, $P>0.05$. NS: Not significant

6. Progesterone and estrogen fixed combinations: OC pills (Levonorgestrel + Ethinylestradiol) were taken orally by 1.67% of menopausal women on core therapy
7. Progesterone derivatives: Tablet Primolut – N (Norethisterone) was taken orally by 0.42% of menopausal women on core therapy
8. Triazole derivative of systemic antimycotics: Tablet Flucos (Fluconazole) was used orally in 0.84% of menopausal women on core therapy
9. Fluoroquinolone group of antibacterial drugs: Tablet Norflox (Norfloxacin) was used orally in 6.28% of menopausal women on core therapy
10. Tetracycline group of antibacterial drugs: Tablet Doxy (Doxycycline) was used orally in 39.33% of menopausal women on core therapy
11. Other antibacterial drugs: Tablet Metro (Metronidazole) was used orally in 35.56% of menopausal women on core therapy
12. Third-generation cephalosporins: Tablet C Tax–O (Cefixime) was used orally in 3.77% of menopausal women on core therapy
13. Combinations of antibacterials: FAS 3 kit tablets (Fluconazole + Azithromycin + Secnidazole) were used orally in 0.42% of menopausal women on core therapy
14. Nitrofur derivative of antibacterial drugs: Tablet Nitrofur (Nitrofurantoin) was used orally in 1.26% of menopausal women on core therapy
Tablet Norflox TZ (Norfloxacin + Tinidazole) was used orally in 1.67% of menopausal women
15. Urologic drugs: Syrup Cital and Syrup Citralka (Disodium hydrogen citrate) were used orally in 17.57% of menopausal women on core therapy
16. Belladonna alkaloids, semisynthetic, quaternary ammonium compounds: Tablet Buscopan and Tablet Hyocimax (Hyoscine butylbromide) were used orally in 13.39% of menopausal women on core therapy
17. Propionic acid derivatives of nonsteroidal anti-inflammatory and antirheumatic products: Tablet Brufen (Ibuprofen) was used orally in 1.67% of menopausal women on core therapy
18. Opioid group of analgesic drugs: Tablet Tramadol was used orally in 2.09% of menopausal women on core therapy
19. Combination of antispasmodic with analgesic drugs: Tablet Meftal spas (Dicyclomine + Mefenamic acid)

- were used orally in 2.51% of menopausal women on core therapy
20. Analgesic and antipyretic drugs: Tablet PCM (Paracetamol) was used orally in 0.42% of menopausal women on core therapy
21. Antifibrinolytic drugs: Tablet Pause (Tranexamic acid) was used orally in 10.04% of menopausal women on core therapy
22. Piperazine derivative of antihistaminics for systemic use: Tablet Ceriz (Cetirizine) was used orally in 0.84% of menopausal women on core therapy
23. Gynecological antiseptics: Tablet Betadine pessary (Povidone iodine) was used intravaginally in 0.42% of menopausal women on core therapy.

Supportive therapy (n – 134, % - 47.52)

The drugs used in supportive therapy were further classified according to the ATC classification system [Table 3].

Multivitamin combinations

Multivitamin with minerals

Multivitamin tablets and injections (Vitamin A, B1, B2, B3, B5, B6, B7, B12, C, D3, E, Calcium, Iron, Cu, Mn, Zn, Magnesium oxide, P, Sodium molybdate, and Boron) were used in 5.97% of the menopausal women who were on supportive therapy to improve their general health.

Multivitamin with other combinations

B-colen NS syrup (Pine bark extract, carbohydrates, sugar, Vitamin C, B3, B5, B1, B2, B12, and B6, lysine, zinc sulfur, and copper sulfate) was used orally in 16.42% of patients on supportive therapy.

Drugs for peptic ulcer and gastroesophageal reflux disease

Rantac (Ranitidine) was prescribed to 63.43% of menopausal women on supportive therapy.

Iron preparations

Iron tablets were used in 10.45% of menopausal women on supportive therapy.

Mineral supplements

Calcium tablets were used in 18.66% of menopausal women on supportive therapy.

Vitamin D preparation

Vitamin D granules (Cholecalciferol) were used in 04.48% of menopausal women on supportive therapy.

Table 2: Taxonomic profile of the core drugs used in menopausal women

Drugs	NPN	Dosage form	ROA	Dose	FOA	DOT	ATC code	Number of patients	Percentage of patients
Candid cream	Clotrimazole	Ointment	Topical	1%	BD	7 days	D01AC01	5	02.09
Candid B cream	Clotrimazole + Beclometasone	Ointment	Topical	0.025% + 1%	BD	7 days	D07CC04	20	08.37
Candid V pessary	Clotrimazole	Tablet	Vaginal	200 mg	HS	7 days	G01AF02	9	03.77
Clid V pessary	Clindamycin + Metronidazole + Clotrimazole + Lactobacillus sporogens	Tablet	Vaginal	100 mg + 100 mg + 100 mg + 150 million spores	HS	7 days	G01A	34	14.23
Estrogen cream	Estradiol	Ointment	Topical	0.1 mg/1g	BD	7 days	G03CA03	2	0.84
OC pills	Levonorgestrel + Ethinyl estradiol	Tablet	Oral	0.15 mg + 0.03 mg	OD	3 months	G03FA11	4	01.67
Primolut - N	Norethisterone	Tablet	Oral	5 mg	BD	5 days	G03DC02	1	0.42
Flucos	Fluconazole	Tablet	Oral	150 mg	HS	1 days	J02AC01	2	0.84
Norflo	Norfloracin	Tablet	Oral	400 mg, 100 mg	1/w	4 weeks	J01MA06	15	06.28
Doxy	Doxycycline	Tablet	Oral	100 mg	BD	7 days	J01AA02	94	39.33
Metro	Metronidazole	Tablet	Oral	400 mg	TDS	7 days	J01XD01	85	35.56
C Tax - O	Cefixime	Tablet	Oral	200 mg	BD	7 days	J01DD08	9	03.77
FAS 3 kit	Fluconazole + Azithromycin + Secnidazole	Tablet	Oral	150 mg + 1000 mg + 1000mg	OD	1 days	J01RA07	1	0.42
Nitrofur	Nitrofurantoin	Tablet	Oral	100 mg	TDS	7 days	J01XE01	3	01.26
Norflo TZ	Norfloracin + Tinidazole	Tablet	Oral	400 mg + 600 mg	BD	7 days	J01RA13	4	01.67
Cital	Disodium hydrogen citrate	Syrup	Oral	1.37 g/5 ml, 1.53 g/5 ml	10 ml BD	7 days	G04BX	42	17.57
Buscopan	Hyoscine Butylbromide	Tablet	Oral	100 mg, 10 mg	BD	3 days	A03BB01	32	13.39
Hycimax	Ibuprofen	Tablet	Oral	400 mg	BD	3 days	M01AE01	4	01.67
Brufen	Tramadol	Tablet	Oral	400 mg, 100 mg	BD	3 days	N02AX02	5	02.09
Tramadol	Dicyclomine + Mefenamic acid	Tablet	Oral	10 mg + 250 mg	BD SOS	3 days	A03D	6	02.51
Meftal spas	Paracetamol	Tablet	Oral	500 mg	BD	3 days	N02BE01	1	0.42
PCM	Tranexamic acid	Tablet	Oral	500 mg	BD TDS	5 d 3 d	B02AA02	24	10.04
Pause	Cetirizine	Tablet	Oral	10 mg	HS	3 days	R06AE07	2	0.84
Ceriz	Povidone iodine	Tablet	Vaginal	200 mg	HS	5 days	G01AX11	1	0.42
Betadine pessary									

NPN: Nonproprietary name, DOT: Duration of therapy, FOA: Frequency of administration, ROA: Route of administration, ATC: Anatomical therapeutic chemical, BD: Twice a day, HS: Bedtime, TDS: Three times a day, OD: Once a day

Alternative therapy (n = 9, % - 3.19)

- Herbal preparation: Evening primrose oil in the form of tablets and capsules were used orally in 66.67% of patients on alternative medicine
- Ayurvedic preparation: Syrup M2 Tone is an Ayurvedic medicine which contains Ashoka, Ashwagandha, Cedrus Deodara, Kasisa Bhasma, Lodhra, Mesua Ferrea, Nardostachys Jatamansi, and Shatavari as active ingredients. It was used Orally in 33.33% of patients on alternative medicine [Graph 4].

DISCUSSION

The incidence of natural menopause decreased in the year 2017 as compared to 2016, which can be explained by the finding of increased incidence of surgical menopause.

During the literature search, no studies with similar results were found as the number of studies evaluating the incidence of various types of menopause has not been conducted yet. However, a research conducted by

Table 3: Taxonomic profile of supportive drugs used in menopausal women

Drugs	NPN	Dosage form	ROA	Dose	FOA	DOT	ATC code	Number of patients	Percentage of patients
Multivitamin	Vitamin A, B1, B2, B3, B5, B6, B7, B12, C, D3, E, Calcium, Iron, Cu, Mn, Zn, Magnesium oxide, P, Sodium molybdate, and Boron	Tablet Injection	Oral I.V.	10 ml	OD BD Stat	30 days 15 days 1 day	A11AA	8	05.97
B-colen NS	Pine bark extract, carbohydrates, sugar, vitamin C, B3, B5, B1, B2, B12 and B6, lysine, zinc sulfur, and copper sulfate	Syrup	Oral	10 ml	BD	1 month	A11AB	22	16.42
Rantac	Ranitidine	Tablet	Oral	150 mg	OD BD	3 days 7 days	A02BA02	85	63.43
Iron	Iron	Tablet	Oral	200 mg 100 mg	OD	1 month	B03A	14	10.45
Calcium	Calcium	Tablet	Oral	1 g 500 mg	OD	1 month	A12AA	25	18.66
Vitamin D	Cholecalciferol	Granules	Oral	50000 IU	1/week	1 month	A11CC55	6	04.48

NPN: Nonproprietary name, DOT: Duration of therapy, FOA: Frequency of administration, ROA: Route of administration, ATC: Anatomical therapeutic chemical, BD: Twice a day, HS: Bedtime, TDS: Three times a day, OD: Once a day

the Study of Women's Health Across the Nation roughly estimated that 5% of women belonging to the age group of 40–45 years, whereas 25% of women in 45–55 years' experience natural menopause.^[11]

Unni^[12] and Syamala and Sivakami^[13] also showed similar finding that the incidence and prevalence of premature menopause including surgical menopause is increasing at an alarming rate in India, especially in the states such as Andhra Pradesh, Gujarat, and Karnataka.

During the study, there was no incidence of chemotherapy or pelvic radiation-induced menopause. However, the study by Shuster *et al.*^[14] is suggestive of an increased incidence of chemotherapy and pelvic radiation-induced menopause, which they associated it to the increased and better treatment strategies of cancer in all the age groups of women, and exposure to higher doses of alkylating agents and higher doses of radiation to the ovaries during cancer therapy makes women more likely to experience ovarian failure.

Pharmacotherapy and surgery were the main treatment modalities used for menopausal complaints of the patients visiting OBGY OPD of AVBRH, Sawangi (Meghe), Wardha.

During the study, the use of hormonal therapy was very less; Estradiol cream 0.84%, Levonorgestrel + Ethinyl estradiol oral contraceptive pills 01.67%, and Norethisterone 0.42%. Estradiol cream was used as monotherapy and in combination for urogenital

symptoms such as increased frequency of micturition, burning micturition, and itching in the vulva region. Levonorgestrel + Ethinyl estradiol oral contraceptive pills were used for abnormal uterine bleeding and dysfunctional uterine bleeding as a monotherapy; whereas norethisterone was used for dysfunctional uterine bleeding as a monotherapy.

These findings are in contrast to the findings by Hackley and Rousseau,^[15] Santoro *et al.*,^[16] and Panay *et al.*,^[17] which showed the maximum use of HRT to manage various urogenital symptoms such as hot flashes and musculoskeletal symptoms. However, Rousseau^[18] in her study revealed that the primary care physicians showed a lower rate of hormonal therapy recommendations.

Similarly, Hersh *et al.*^[19] in their study revealed that the use of HRT has considerably declined.

During the study, the maximum drugs used in core therapy had a symptomatic cure approach with an effort to minimize the use of HRT. Maximum drugs used were antibiotics of various groups.

Multivitamin, Iron, Calcium, and Vitamin D were used for pain in the abdomen, white discharge, backache, dysfunctional uterine bleeding, abnormal uterine bleeding, uterine prolapse, vaginal erosions, and menorrhagia as a supportive therapy. Ranitidine was prescribed as a supportive drug along with antibiotics and pain killers, so as to reduce the gastrointestinal side effects of these drugs.

A herbal preparation of evening primrose oil (66.67%) in the form of tablets and capsules; and an Ayurvedic preparation Syrup M2 Tone (33.33%) was used as alternative medicines for the treatment of menopausal symptoms.

Evening primrose oil was used in combination with calcium and Vitamin D supplements for hot flush, mastalgia, white discharge, and pain abdomen.

Syrup M2 Tone was used as a monotherapy for abnormal uterine bleeding in two patients and in combination with tablet Pause (Tranexamic acid) in one patient.

Ohn Mar *et al.*^[20] in their study on the use of alternative medications showed a similar finding that evening primrose oil is the most used alternative medication (18.1%) which is followed by use of soy-based products (12.3%), green tea (6.8%), and ginkgo (5.8%).

Mehrpooya *et al.*^[21] in their study concluded that herbs such as black cohosh and evening primrose oil are effective in reducing the severity of hot flashes, but black cohosh is more effective than evening primrose oil.

Limitation of the study

- As the present study was carried out in a rural setup, there was lack of awareness in females about the various clinical manifestations of menopause, and therefore, there was underreporting of few categories of symptoms in our study
- Due to time constraint, no follow-ups were conducted in the present study. Therefore, assessment of the status outcome after the treatment was out of scope
- As the data of the present study were collected only from the OBGY Department of AVB Rural Hospital, Sawangi (Meghe) Wardha, patients bypassing the OBGY department to other department according to the type of menopausal complaint could not be addressed.

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Conflicts of interest

There are no conflicts of interest.

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