

Original article



Pharmacological Activity and Effectiveness of Electrohomoeopathy Medicine on Uterine Fibroids Individuals

Dr. Surendra Pandey ^{*1}, Dr. Harvinder Singh ²

¹Principal Secretary: EHF, Mumbai, India

²Research head: Alchemy research lab, Bathinda, Punjab, India

*Corresponding author: Dr. Surendra Pandey; suren02oct@gmail.com

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Abstract

Electropathy/Electrohomoeopathy is a comparatively modern medical technique that falls under the genre of complementary and alternative medicine. This medical technique was discovered in Italy in 1865 by Count Ceaser Mattei. Its drugs are composed entirely of herbal/medicinal plants and are manufactured with purified water and a sophisticated process of extracting spagiric essence from medicinal plants at room temperature. Uterine fibroids are noncancerous uterine growths that commonly arise during childbearing year. Uterine fibroids, also known as leiomyomas (lie-o-my-O-muhs) or myomas, aren't linked to an increased risk of uterine cancer and almost never turn cancerous. Fibroids range in size from microscopic seedlings that are undetectable to large masses that deform and expand the uterus. A single fibroid or a group of them can be present. Multiple fibroids can cause the uterus to enlarge to the point where it reaches the rib cage, causing weight gain. Uterine fibroids affect many women at some point in their life. However, because uterine fibroids rarely cause symptoms, people may be unaware that they have them. During a pelvic exam or a pregnancy ultrasound, fibroids may be encountered by chance. By the time they reach at the age 50, 20% to 80% of women experience fibroids. Women in their age forties and early fifties are the most susceptible to develop get fibroids. In this article we are going to discussed effectiveness of Electrohomoeopathy medicine on Uterine fibroids. How a new medical science which is totally plants-based source cost effective and accelerating its mechanism of action due to specialization of its unique fundamental principal and philosophy and satisfaction of patient due to the extraordinary result of Electrohomoeopathy medicine.

Keywords: *Electrohomoeopathy, Electropathy, Uterine fibroids, effectiveness of Electrohomoeopathy, Case study*

Introduction

It was observed that Fibroids don't really impact all women in the same way. Susceptible ladies who experienced symptoms are difficult to live with fibroids. Few women experience discomfort and heavy menstrual bleeding. Leiomyomas are benign uterine tumours that have no known cause in the several cases. In the cases lesions appear to be the outcome of myometrial change caused by certain physiological and pathological circumstances. The bulk of monoclonal estrogen-dependent uterine neoformations ^[1] affect predominantly women in their reproductive years, with 80 percent of them suffering for the rest of their lives ^[2]. The prevalence of uterine fibroids was assessed to be 33%, ultrasound scan used up to 50%, and histological testing of hysterectomy tissues showed 77% based on clinical data ^[3]. The disease's stated frequency varies greatly due to differences in study methodology. In reality, to determine the exact prevalence of fibroids, a good clinical investigation should include USG screening in a randomly

generated population ^[4]. A woman's risk of having fibroids might be increased by a number of circumstances.

Risk factor for fibroids and impact

Age: Fibroids become increasingly common as women become older, especially after menopause in their 30s and 40s. Fibroids normally diminish after menopause. History of the family: woman's more likely to get fibroids if having a family member who has them. If a woman's mother had fibroids, she has a three-fold increased risk of developing them herself. African-American women have the highest incidence of ethnic background fibroids than white women. Women who are obese are more susceptible to have fibroids. The danger is two to three times higher for very overweight women than for typical women. Habits of eating consuming a lot of red meat (such as beef) and ham has been related to an increased risk of fibroids. Women who eat a lot of green vegetables appear to be less likely to acquire fibroids.

The majority of fibroids develop in the uterine wall. Submucosal fibroids (sub-myoo-KOH-zuhl) invade the uterine cavity. Intramural fibroids (ihn-truh-MYOOR-uhl) are fibroids that grow within the uterine wall. Subserosal (sub-suh-ROH-zuhl) fibroids that grow on the exterior of the uterus. Many women with fibroids have no symptoms at all. The location, size, and number of fibroids can affect symptoms in persons who have them. The most common clinical symptoms of uterine fibroids in females who have them are listed here. Menstrual bleeding is really heavy. Menstrual cycles that last more than a week. Pelvic discomfort or pressure, urination on a regular basis, having trouble emptying the bladder, constipation and leg aches or a backache. When a fibroid outgrows its blood supply and begins to die, it can cause severe pain.

Uterine Leiomyoma Pathogenesis

Even while many health issues for uterine fibroids have been related to estrogen and progesterone levels and metabolism in epidemiologic research, other processes are also involved in their formation. The precise role of female hormones (estrogens and progesterone) in the formation and multiplication of uterine fibroids has recently been challenged [5]. The researchers tracked the growth of fibroids in black and white women with clinically meaningful fibroids utilizing MRI scanning. They discovered that fibroids in the same woman often grow at different rates despite sharing the same hormonal environment. Fibroids in the same patients varied in size, regressed, or remained stable. The size and location of the tumour appear to have minimal effect on fibroid growth, suggesting that each tumour will have its own fundamental rate of growth. This research opened up new possibilities for investigation, validating prior results that fibroids are monoclonal in origin and have a wide range of genetic characteristics [6]. In uterine leiomyomata, ethnic disparities in expression of dysregulated proteins were also discovered. Variation in molecular markers has been linked to tumour size and it is hypothesised that the molecular variances reflect differences in tumour growth rates. Furthermore, molecular markers may differ between black and white cancers [7]. Myomas are more common in African-Americans than in Caucasians and Hispanics, according to popular belief [8]. Although the explanation of black women's increased incidence is unknown, variations in circulating oestrogen levels have been discovered [9]. It's uncertain if these ethnic variances are caused by genetic differences or by documented differences in hormone metabolism, food, or environmental variables. A statistically significant inverse association between blood 25-(OH) Vit D levels and the prevalence of fibroid in black people was recently discovered by many researchers. [10]. A positive feedback loop between extracellular matrix production and cell proliferation participates in fibroid underlying etiology, which vitamin D may help to disrupt [11]. Myomas and keloids, all much more prominent in black women, share similar genetic characteristics. Moreover, it is well known that family history is a crucial causative factor, with first-degree relations of female patients having a 2.5-fold increased risk of developing fibroids [12]. Such bias, however, would render self-reported family history ineffective as a predictor of fibroid risk, as Saldana et al. recently demonstrated [13]. Several studies have found a rapid increase in the incidence of fibroid beyond the age of 30. This could be due to hormonal changes over time or an increase in symptomatology from fibroids that were already present. Furthermore, the high incidence of fibroids in the perimenopausal period could be to blame for the rise in gynecologic surgery rates among women who have reached the end of their reproductive years [14]. According to one study, the risk

of myomas increased by 21% for every 10 kg rise in body weight and a higher BMI [15]. Similar findings were observed in women with more than 30% body fat [16]. Although adipose tissue converts androgens from the adrenal and ovarian glands to estrogens, obesity lowers the synthesis of sex hormone binding globulin in a variety of ways. As a result, a rise in myoma prevalence and/or growth in obese and overweight women may be due to an increase in physiologically available estrogens. Furthermore, an in vitro model was employed to study the connection between obesity-related chronic inflammation and the development and progression of uterine leiomyoma utilising representative adipocyte cell lines and human uterine leiomyoma cells. They showed that coculturing adipocytes with uterine leiomyoma cells promotes leiomyoma cell proliferation, and they also showed that TNF-treatment boosts human uterine leiomyoma cell proliferation in a concentration-dependent way [17]. It's unknown whether certain foods, such as red meat, ham, green vegetables, or fibre, influence the growth of myomas. Because there have only been a few observational studies on the subject, it's also difficult to determine the precise impact of physical activity on the development of uterine myomas [18]. By blocking aromatase and decreasing the conversion of androgens to estrone, smoking has been demonstrated in various studies to reduce the occurrence of myomas. Smoking has a substantial stimulating effect on the 2-hydroxylation route of estradiol metabolism, resulting in decreased bioavailability in oestrogen target tissues [19]. Menarche before the age of ten has been linked to an increased risk of uterine myomas, whereas menarche after the age of sixteen has been linked to a lower risk [20]. Increased parity has been linked to a lower incidence and number of clinically evident myomas in some studies [21]. This could be linked to ECM remodelling and a specific expression of peptide and steroids hormone receptors caused by pregnancy and parturition. Hormone therapy does not appear to be a significant stimulator of fibroid growth in postmenopausal women [22]. Similarly, the evidence for a relationship between oral contraceptives (OC) and the growth of leiomyomas is contradictory. This could be due to the fact that each OC formulation contains varying levels of estrogens and progesterone types [23]. Increased oestrogen and progesterone levels may cause an increase in mitotic rate, which may be the cause of somatic mutation. In specific parts of the nonneoplastic myometrium of the uterine myomatous, discovered an elevated concentration of oestrogen receptors (ER) [24].

Genetic Pathways in Fibroids Etiology

According to cytogenetic surveys, approximately 40percent of uterine fibroids are chromosomally modified and have cytogenetic abnormalities that are shared by a various cancers. Investigations have revealed translocations between chromosome 12 and 14, trisomy 12, translocations between chromosome 6 and 10, and deletions between chromosomes 3 and 7 [25].

Mechanical Transduction and the Extracellular Matrix Play a Factor

As a result of study into the pathophysiology of fibroids and abnormal extracellular matrix (ECM), a profibrotic growth factor, transforming growth factor (TGF-), was discovered [26]. TGF-3 and its signal mediators are overexpressed in leiomyomas relative to normal myometrium [27]. In addition, inhibiting the TGF-pathway reduces the mRNA expression of various ECM genes in uterine leiomyomas [28].

MicroRNA and Estrogens: The growth of uterine leiomyoma is intimately linked to estrogens and their receptors. The levels of mRNA and protein expression, as well as the concentration of ER-Alfa and ER-Beta, are all higher in leiomyoma than in normal myometrium, according to several studies [29]. Progesterone, Growth Factors, Cytokines and Chemokines, and Extracellular Matrix Components all have a part in uterine leiomyoma progression. The "endometrial sub-endometrial myometrium unit disruption illness" should be considered a different entity from adenomyosis. The pathological thickness or abnormalities of the subendometrial myometrium, which is the likely source of submucosal and intramural fibroids, is the most common manifestation of this disorder.

Electrohomeopathy and its role in Uterine fibroids

Materials and methods

This study period was from May-2019 to Jan-2021 in the outpatient department in the Electrohomeopathy clinic patient 10

patients included for the data while 7 patient data available while 3 patient data not included due to treatment interruption and limitation of scanning data. This is kind of prototype study model related to specify female patients with uterine fibroids. The study group having all the adult female with an average of (26.06±1.11) years; course of disease 1-8 months with an average of (4.52±0.94) months. Effectiveness of all the patient with Electrohomeopathy medicine was measured

1. Selection of Electrohomeopathy medicine

The Electrohomoeopathy remedies collected from the Alchemy research Bathinda Punjab, Electrohomoeopathy remedies has been mixed and formulated under the supervision of qualified person Dr. Harvinder Singh (M. Pharm Pharmaceutics) HOD of the lab along with others Pharmacist and technical qualified associate. The below plants collected, authenticated and formulated and used during this study. All the groups randomly collected from Alchemy-38 Kits there batch and expiry mentioned as per the below table.

Table 1: Electrohomeopathy remedies and combination groups used during the study

Electrohomoeopathy Medicine used during the study	Plants used in the group	Batch	Expiry
A3	Arnica Montana, Artemisia abrotanum, Avena sativa, Hydrastis Canadensis, Malva sylvestris, Pulsatilla vulgaris and Sanguinaria Canadensis	A3-002	Jun-21
S5	Berberis vulgaris, Cochlearia officinalis ou) pinulbog, Hydrastis canadensis, Matricaria chamomilla, Nasturtium officinale, Scrophularia nodosa, Smilax medica, Tussilago farfara and Veronica officinali	S5-002	Jun-21
C1	Caulophyllum thalictroides, Conium maculatum, Pimpinella saxifrage, Rhus toxicodendron and Vincetoxicum officinale	C1-002	Jun-21
WE	Achillea millefolium, Agaricus muscarius, Anthemis nobilis, Arnica Montana, Avena sativa, Cimicifuga racemosa, Genista scoraria, Guaiacum officinale, Menyanthes trifoliata, Petroselinum sativum, Ruta graveolens, Sanguinaria canadensis, Sanguisorba officinalis, Taraxacum officinale, Taxus baccata and Viscum album	WE-002	Jun-21
C5	Conium maculatum, Phytolacca decandra, Pimpinella saxifrage, Rhus toxicodendron and Vincetoxicum officinale	C5-002	Jun-21
F1	Aconite napellus, Aesculus hippocastanum, Berberis vulgaris, Cetraria islandica, Cinchona calisaya, Cinchona sucirubra, Erythraea centaurium, Salix alba and Sambucus nigra	F1-002	Jun-21
RE	Aconite napellus, Rhododendron ferrugineum, Rosa canina, Rosmarinus officinalis, Vitis vinifera (Common Grape Vine)	RE-002	Jun-21
Womb Cure	Alchemy formulation with Combo EH remedies	WC-002	Jun-21

S-Scrofoloso, A-Angiticos, C-Canceroso, F-Febrifugo, RE-Red Electricities and WE-White Electricities

2. Selection of dose

All the patients which enrolled during the study period started therapy with Electrohomeopathy remedies as mentioned in the

table: 2 in the initial dilution of D6 from the Alchemy spagiric kit have been used. Selection of dose depend on the severity of the patients and monitored during the follow up visit.

Table 2: Group and Dosing regimen

Prophylactic Electrohomoeopathy medicine	Dilution	Dose	Frequency
Medicine protocol-I (before meal) in 100 ml normal water			
A3	D6	10 drops	Tid
S5	D6	10 drops	Tid
C1	D6	10 drops	Tid
WE	D6	10 drops	Tid
Medicine protocol-I (after meal) in 100 ml normal water			
C5	D6	10 drops	Tid
F1	D6	10 drops	Tid
RE	D6	10 drops	Tid

3. Selection of Patient

The initial symptoms decreased in the first follow up within 2 weeks as per the OPD record.

The study group having all the adult female with an average of (26.57 ± 1) years; course of disease 6-8 months. Effectiveness of all the patient with Electrohomeopathy medicine was measured.

Inclusive criteria

In line with the diagnostic criteria for uterine fibroids as per the ultrasonography report. The course of disease is more than 3 months. The vital signs are stable, and the mental health is normal. The patients and their families have agreed for the treatment already taken conventional treatment with no effect or aggravation of treatment. Patient ready to follow the line of protocol along with precautionary advised.

Exclusion criteria

Patients who received any relevant surgery for disease specific before the study. Patients who receiving concomitantly any conventional medicine or alternative medicine. Patients who withdraw from this study halfway. Patients with concurrent history of pregnancy or unwilling for the treatment. Patients with untrue and incomplete clinical data. Patients require emergency hospitalization or severity and comorbidity require attention of higher medical instituted.

Characteristic of patients during OPD enrollment

All the patient included in the study most common symptoms observed her symptoms included Low back pain, Chronic vaginal discharge, increased abdominal distention Constipation, Excessive or painful bleeding during your period (menstruation), Bleeding between your periods, A feeling of fullness in your lower abdomen/bloating. Frequent urination (this can happen when a fibroid puts pressure on your bladder) and Pain during sex.

4. Patient details diagnosis at the time of enrolment

Case study 1: A 26-year, female patient with initial RJ history of right-side abdominal pain underwent USG abdomen pelvis scanning on 28-Sep-2019 patient detail included. A hemorrhagic cyst measuring $33.7 \times 27.0 \times 28.2$ mm seen in the right adnex arising from the right ova. Mild free fluids seen in the pelvis mud pelvic vessel congestion. Forward peristalsis is seen. As per the impression of the report showed right ovarian hemorrhagic cyst. Features or mild PID (Pelvic inflammatory disease) and Right renal calculus. No hydronephrosis.

5. Table 3: Summary of Patients investigator and study details

Patient Details		Description						
Gender		Female						
Investigator details		Dr. Varinder Singh						
Place		CCIM.EH Bathinda Punjab						
Observation period		Approximately 6 months+						
Age in year		26	32	32	20	26	31	19
USG Scanning Center Initial place		Dr. Valaiti Ram Memorial Scanning Center, Bathinda- Punjab	Dr. Valaiti Ram Memorial Scanning Center, Bathinda- Punjab	Dr. Valaiti Ram	Satyam Scan	Garg Diagnostic	Kiran Diagnostic	MD Hospital/Scan
USG Scanning Center final			Sarasw Imaging Center- Sirsa- Haryana	Sindhu Hospital/Scan	Satyam Scan	Garg Diagnostic	Dr. Mohinder Singh Scan, Bathinda	Dr. Valaiti Ram
Treatment start date	30-Sep-19	Oct-20	Jul-20	Aug-20	Nov-20	Apr-19	Jan-19	
Treatment end date	15-Jan-20	Mar-21	Jan-21	Dec-20	Feb-21	Jul-20	Dec-2020 (OG)	

Result and discussion

After the treatment with Electrohomoeopathy medicine mentioned in table: 2

All the patients received Electrohomeopathy remedies as mentioned in the table: 2 symptoms were gradually decreased in the week 2-4 depend on the severity of the patients (table: 4).

Table 4: Symptomatic effect of Electrohomoeopathy medicine

Symptoms	Treatment duration (2-4 weeks)	Treatment duration (4-8 weeks)	Treatment duration (8-16 weeks)	Treatment duration (16-24* weeks)
Low back pain.	++	+++	+++	+++
Chronic vaginal discharge.	+	+	++	+++
Increased abdominal distention	+	+	+	+++
Constipation.	++	++	++	+++
Excessive or painful bleeding during your period (menstruation).	+	+	+	+++
Bleeding between your periods.	-	+	+	+++
A feeling of fullness in your lower abdomen/bloating.	+	+	+	++
Frequent urination (this can happen when a fibroid puts pressure on your bladder).	+	++	++	+++
Pain during sex.	+	+	++	++

(+: mild intensity effect) (++ moderate intensity effect) (+++: severe intensity effect)

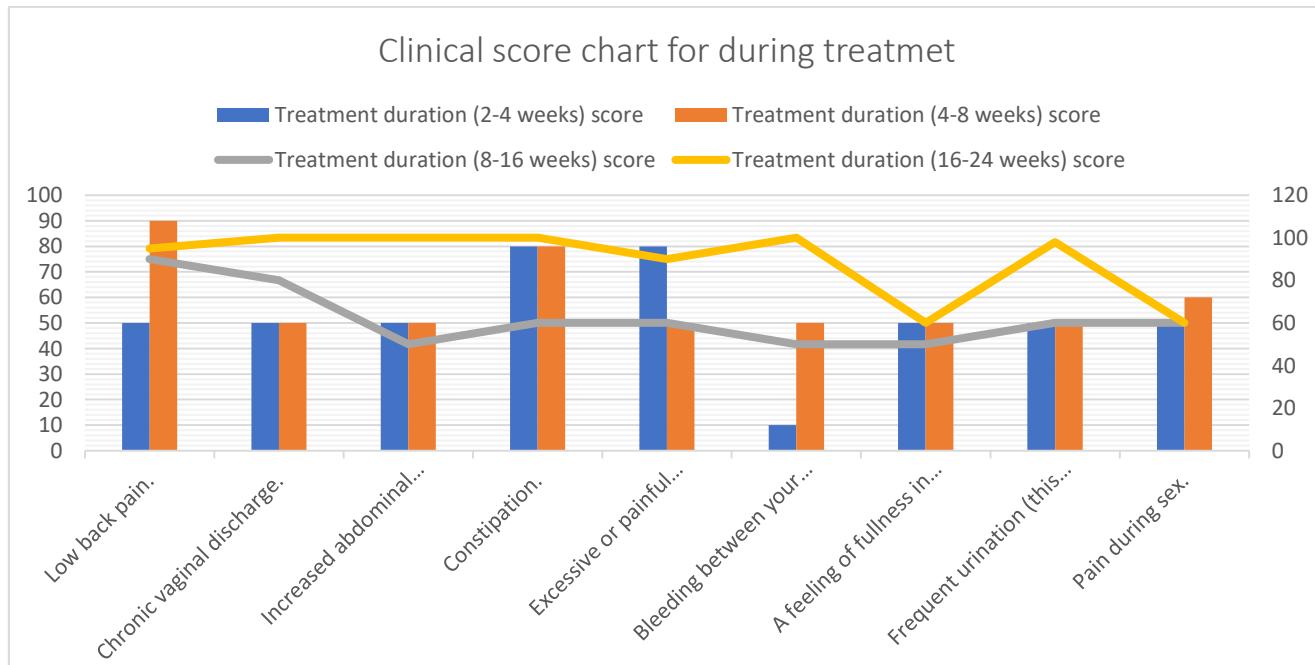


Figure: 5 Symptomatic Clinical score during the study

Effectiveness and result of the Electrohomoeopathy remedies during and after the study

Result (Study-1) as per the final scanning diagnosis on 07-Dec-2029, as per the USG pelvis report condition has been resolved patient result showed no evidence of free fluid. No mass/collection is seen in the RIF. No aperistaltic, non-compressible, blind ending structure seen in the RIF or any other ectopic/subhepatic location to appendicitis. No probe tenderness seen. No bowel dilatation is noted. Forward peristalsis is seen. Small right renal concretion. No hydronephrosis. It was also reported that compared to the previous scan dated 28-Sep-2019, the right hemorrhagic cyst has resolved and is no longer visualized.

Result (Study-2) The final diagnosis as per the patient concluded on the same day thickened endometrium with features endometrial hyperplasia. Suggest endometrial biopsy correlation. Left ovarian hemorrhagic cyst. The patient underwent in the treatment with the

Electrohomeopathy remedy stated in Oct-2020. Result as per the final scanning diagnosis on 11-Mar-2021, uterus is normal in size Endometrium cavity is normal ultrasonography of pelvis seen.

Result (Study-3) The patient symptoms were gradually decreased after the treatment with Electrohomoeopathy remedies patient has conceived in Nov-2020 as per the final scanning diagnosis on 09-Jan-2021, early intrauterine pregnancy noted of 1 week and 4 days.

Result (Study-4) as per the final scanning diagnosis on 17-Dec-2020, uterus is normal in size and both ovaries are normal in size no any abnormality detected.

Result (Study-5) as per the final scanning diagnosis on 18-FEB-2021, Liver no evidence of any abnormality, no abnormality noted in uterus and adnexa except Bulky hyper-reflective cervix which was also asymptomatic.

Result (Study-6) as per the final scanning diagnosis on 31-Jul-2020, Urinary bladder: Is seen in distended state. Lumen appears to be echo free. Uterus: Is anteverted and bulky, measures 97.2x39.1x47.7mm in size. It is normal in shape and contour. Normal in echo pattern. Myometrium shows no sol. Endometrial stripe is normal and measures 9.7mm. Cervix appears bulky and measures 27.4mm in AP dimension. Right ovary shows a dominant follicle measuring 17.3x15.3 mm in size. Left ovary is normal in size, outline and echo pattern. Impression included bulky uterus with Cervicitis and most of the symptoms gradually decreased.

Result (Study-7) as per the final scanning diagnosis on 09-Mar-2021, uterus is anteverted and bulky, measures 25.2x27.4 mm in size most of the symptoms resolved gradually after the follow up treatment.

Patient details mentioned in the table-3 which included patient identifier, investigator details treatment started date and status of treatment for more authentication scanning center name has been included in the study.

Conclusion

Uterine fibroid etiology is still unknown, complex, and perplexing. Traditional studies revealed that myomas rely on steroid hormones for growth and development. With cytogenetic aberrations found in roughly 40% of uterine fibroids, the genetic background appears to play a crucial role. The genesis and growth of uterine leiomyomas has been linked to abnormal ECM expression, elevated growth factors, cytokines and chemokines concentrations, and an extracellular disordered matrix. Clinical considerations. Recent research suggests that myomatosis and adenomyosis have certain pathogenetic similarities, such as excessive inflammation, increased endothelial nitric oxide generation with MMP overexpression, and inflammatory cytokines like interleukin-1 and TNF-Alfa.

Pharmacological Activity of Electrohomeopathy remedies for the treatment Uterine fibroid with the help of compatible group of Electrohomeopathy remedies present investigation is to develop safe and effective formulation which helps very effective in Uterine fibroid to improve its condition. Despite the fact that there has been a great deal of clinical experimentation on medicinal plants all over the world, Electrohomeopathy Medicine/formulations do not yet completely adhere to drug monitoring, protection, or effectiveness requirements. Despite the tremendous potential for developing conventional preparations as drugs of foreign adoption, there has been a decline in enthusiasm for researching plant preparations for their therapeutic benefit in India, due to a lack of intensive effort in this direction at the government or industry level. In this study we have used the combination medicine for the synergistic approach. Electrohomeopathy Medicine the therapeutic preparation are multifaceted blends, which initiate from natural sources, excessive efforts are essential to assure a continuous as well as satisfactory excellence. Even with lot of effort and clinical and scientific evidence showing Electrohomeopathy remedies is very much useful, cost effective and reachable for the poor population for the developing country specially India still struggling for recognition and legislation from the government side.

Ethics approval and consent to participate

Outdoor patient's data collected. This study was approved by the EHF ethics committee as per the Ministry of Health & F.W. Govt.

Of India For PDR in EH for research, promotion, and development.

List of abbreviations

S-Scrofoloso A-Angiticos C-Canceroso F-Febrifugo RE-Red Electricities WE-White Electricities

Data Availability

All the patients involved in this study the data is available with the authors for further information and details you can communicate to the corresponding author via email as mentioned in the article.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

Both the authors are equally contributed in this article through the study.

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Limitations

The researchers involved in the study agree that there is limitation to the study because of several reasons like insufficient funding support from organizations involved in extensive research protocols, supported animal study and multicenter study for more authentication.

References

- [1] W. Bowden, J. Skorupski, E. Kovanci, and A. Rajkovic, "Detection of novel copy number variants in uterine leiomyomas using high-resolution SNP arrays," *Molecular Human Reproduction*, vol. 15, no. 9, pp. 563–568, 2009.
- [2] S. K. Laughlin, J. C. Schroeder, and D. D. Baird, "New directions in the epidemiology of uterine fibroids," *Seminars in Reproductive Medicine*, vol. 28, no. 3, pp. 204–217, 2010.
- [3] S. F. Cramer and A. Patel, "The frequency of uterine leiomyomas," *American Journal of Clinical Pathology*, vol. 94, no. 4, pp. 435–438, 1990.
- [4] M. Payson, P. Leppert, and J. Segars, "Epidemiology of myomas," *Obstetrics and Gynecology Clinics of North America*, vol. 33, no. 1, pp. 1–11, 2006.
- [5] Lauren A. Wise*† and Shannon K. Laughlin-Tommaso Epidemiology of Uterine Fibroids From Menarche to Menopause *Clin Obstet Gynecol*. 2016 Mar; 59(1): 2–24.

- [6] S. D. Peddada, S. K. Laughlin, K. Miner et al., "Growth of uterine leiomyomata among premenopausal black and white women," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 105, no. 50, pp. 19887–19892, 2008. (6)
- [7] T. Wang, X. Zhang, L. Obijuru et al., "A micro-RNA signature associated with race, tumor size, and target gene activity in human uterine leiomyomas," *Genes Chromosomes and Cancer*, vol. 46, no. 4, pp. 336–347, 2007. (7)
- [8] K. H. Kjerulff, P. Langenberg, J. D. Seidman, P. D. Stolley, and G. M. Guzinski, "Uterine leiomyomas: racial differences in severity, symptoms and age at diagnosis," *Journal of Reproductive Medicine for the Obstetrician and Gynecologist*, vol. 41, no. 7, pp. 483–490, 1996. (8)
- [9] G. P. Flake, J. Andersen, and D. Dixon, "Etiology and pathogenesis of uterine leiomyomas: a review," *Environmental Health Perspectives*, vol. 111, no. 8, pp. 1037–1054, 2003. (9)
- [10] M. Sabry, S. K. Halder, A. S. Allah, E. Roshdy, V. Rajaratnam, and A. Al-Hendy, "Serum vitamin D3 level inversely correlates with uterine fibroid volume in different ethnic groups: a cross-sectional observational study," *International Journal of Women's Health*, vol. 5, pp. 93–100, 2013. (10)
- [11] M. Sabry, S. K. Halder, A. S. Allah, E. Roshdy, V. Rajaratnam, and A. Al-Hendy, "Serum vitamin D3 level inversely correlates with uterine fibroid volume in different ethnic groups: a cross-sectional observational study," *International Journal of Women's Health*, vol. 5, pp. 93–100, 2013. (11)
- [12] E. M. Vikhlyaeva, "Familial predisposition to uterine leiomyomas," *International Journal of Gynecology and Obstetrics*, vol. 51, no. 2, pp. 127–131, 1995. (12)
- [13] T. M. Saldana, M. Moshesh, and D. D. Baird, "Self-reported family history of leiomyoma: not a reliable marker of high risk," *Annals of Epidemiology*, vol. 23, no. 5, pp. 286–290, 2013. (13)
- [14] G. P. Flake, J. Andersen, and D. Dixon, "Etiology and pathogenesis of uterine leiomyomas: a review," *Environmental Health Perspectives*, vol. 111, no. 8, pp. 1037–1054, 2003. (14)
- [15] G. P. Flake, J. Andersen, and D. Dixon, "Etiology and pathogenesis of uterine leiomyomas: a review," *Environmental Health Perspectives*, vol. 111, no. 8, pp. 1037–1054, 2003. (15)
- [16] S. A. Shikora, J. M. Niloff, B. R. Bistrian, R. A. Forse, and G. L. Blackburn, "Relationship between obesity and uterine leiomyomata," *Nutrition*, vol. 7, no. 4, pp. 251–255, 1991. (16)
- [17] S. Nair and A. Al-Hendy, "Adipocytes enhance the proliferation of human leiomyoma cells via TNF- α proinflammatory cytokine," *Reproductive Sciences*, vol. 18, no. 12, pp. 1186–1192, 2011. (17)
- [18] G. Wyshak, R. E. Frisch, and N. L. Albright, "Lower prevalence of benign diseases of the breast and benign tumours of the reproductive system among former college athletes compared to non-athletes," *British Journal of Cancer*, vol. 54, no. 5, pp. 841–845, 1986. (18)
- [19] M. Daniel, A. D. Martin, and D. T. Drinkwater, "Cigarette smoking, steroid hormones, and bone mineral density in young women," *Calcified Tissue International*, vol. 50, no. 4, pp. 300–305, 1992. (19)
- [20] A. J. Tiltman, "The effect of progestins on the mitotic activity of uterine fibromyomas," *International Journal of Gynecological Pathology*, vol. 4, no. 2, pp. 89–96, 1985. (20)
- [21] D. D. Baird and D. B. Dunson, "Why is parity protective for uterine fibroids?" *Epidemiology*, vol. 14, no. 2, pp. 247–250, 2003. (21)
- [22] S. Palomba, T. Sena, M. Morelli, R. Noia, F. Zullo, and P. Mastrantonio, "Effect of different doses of progestin on uterine leiomyomas in postmenopausal women," *European Journal of Obstetrics Gynecology and Reproductive Biology*, vol. 102, no. 2, pp. 199–201, 2002. (22)
- [23] D. W. Cramer, "Epidemiology of myomas," *Seminars in Reproductive Endocrinology*, vol. 10, no. 4, pp. 320–324, 1992. (23)
- [24] P. A. Richards and A. J. Tiltman, "Anatomical variation of the oestrogen receptor in the non-neoplastic myometrium of fibromomatous uteri," *Virchows Archiv*, vol. 428, no. 6, pp. 347–351, 1996. (24)
- [25] K. L. Gross and C. C. Morton, "Genetics and the development of fibroids," *Clinical Obstetrics and Gynecology*, vol. 44, pp. 335–349, 2001. (25)
- [26] E. A. Kogan, V. E. Ignatova, T. N. Rukhadze, E. A. Kudrina, and A. I. Ischenko, "A role of growth factors in development of various histological types of uterine leiomyoma," *Arkhiv Patologii*, vol. 67, no. 3, pp. 34–38, 2005. (26)
- [27] J. M. Norian, M. Malik, C. Y. Parker et al., "Transforming Growth Factor β 3 regulates the versican variants in the extracellular matrix-rich uterine leiomyomas," *Reproductive Sciences*, vol. 16, no. 12, pp. 1153–1164, 2009. (27)
- [28] M. Malik, J. Webb, and W. H. Catherino, "Retinoic acid treatment of human leiomyoma cells transformed the cell phenotype to one strongly resembling myometrial cells," *Clinical Endocrinology*, vol. 69, no. 3, pp. 462–470, 2008. (28)
- [29] K. A. Kovács, A. Oszter, P. M. Göcze, J. L. Környei, and I. Szabó, "Comparative analysis of cyclin D1 and oestrogen receptor (α and β) levels in human leiomyoma and adjacent myometrium," *Molecular Human Reproduction*, vol. 7, no. 11, pp. 1085–1091, 2001.



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