

Bee propolis, Luperon depot 3.75mg treatment of uterine fibroid. A randomized, controlled clinical trialAli Farid M. Ali¹, Laila Farid,² and Samir Shaker³¹Consultant Obstetrics and Gynecology Heliopolis Hospital, Cairo, Egypt.²Consultant Obstetrics and Gynecology, Cairo Medical Centre, Cairo, Egypt.³Consultant Clinical Pathology, Heliopolis, Cairo, Egypt.elshayb1950@yahoo.com

Abstract: Introduction: Uterine fibroid is the most common benign tumors of the uterus, hysterectomy is the definitive treatment of symptomatic fibroid. Medical treatment of uterine fibroids include androgens, antiprogestogens, raloxifene and the most common used treatment GnRH agonist, we introduced for the first time in the literature Bee propolis in the treatment of uterine fibroid. **Objective:** To compare the efficacy and safety of Bee propolis vs. GnRHagonist in the treatment of uterine fibroid. **Design:** It is a randomized controlled clinical trail. **Patients and methods:** A total of 30 patients with a single fibroid measuring ≥ 8 cm were randomized into two groups group I treatment with Bee propolis and group II with GnRHa. (Luprone depot 3.75). Bee propolis was given in a tablet form 500mg three time daily for 12weeks. **Main outcome measures:** Measurement of fibroid volume, uterine volume, Hb concentration and hot flashes. **Results:** Statically significant decrease in the fibroid and uterine volume in both groups but more in the group 1 ($p < 0.01$) statistically significant increase in Hb concentration in the two groups but more in the group I ($p < 0.01$). No hot flashes recorded in group I ($P < 0.0001$), hot flashes recorded in all group II. **Conclusion:** Bee propolis is a new line treatment of uterine fibroid with more reduction in fibroid volume, uterine volume and increase in the Hb concentration more than GnRHa no reported hot flashes. [Ali Farid M. Ali, Laila Farid, and Samir Shaker. **Bee propolis, Luperon depot 3.75mg treatment of uterine fibroid. A randomized, controlled clinical trial.** *Life Sci J* 2018;15(11):94-97]. ISSN: 1097-8135 (Print) / ISSN: 2372-613X (Online). <http://www.lifesciencesite.com>. 12. doi:[10.7537/marslsj151118.12](https://doi.org/10.7537/marslsj151118.12).

Keyword: Uterine fibroid, Bee propolis, GnRHa, hot flashes Luperon depot 3.75.**1. Introduction:**

Uterine fibroids are the most common benign tumors of the uterus^{(1),(2)}. Receptors for both estrogen and progesterone have been identified in fibroid⁽³⁾, some investigator have shown that fibroids tissues are a source of Estrogen. Estrogen secreted by fibroid tissue may reach a sufficient concentration within the local compartment to support its own growth, allowing independence from ovarian estrogen^(4,5,6,7,8,9). Surgical treatment is by Myomectomy⁽⁹⁾ and Hysterectomy. Hysterectomy is the definitive line of treatment of symptomatic fibroid but the place of Medical treatment is in the following conditions: (a) contraindication of surgical treatment^(B) women who want to save their uterus. (c) Young women asking for infertility treatment.

Medical treatment^(10,11). Rank from. Androgens⁽¹²⁾ antiprogestogens⁽¹³⁾ (mifepristone),⁽¹³⁾ anti estrogen (raloxifene)⁽¹⁴⁾ and GnRHagonist (GnRHa)⁽¹⁵⁻²²⁾. The most commonly used medical treatment is GnRH agonist but due to its side effect (hypoestrogenic symptoms) which prevent long term treatment by this drug^(22, 23). The aim of this work is to compare Bee propolis^(24,25,26,27) with Luperon depot 3.75m for treatment of fibroid by a clinical randomized controlled trial.

2. Material and Methods**Study Design**

It is a prospective, randomized, -blind controlled clinical trial.

A total of 30 subjects with a single uterine fibroid measuring ≥ 8 cm were eligible to be included in the study.

Inclusion Criteria

(1) Women aged 25-45 years with a single intramural uterine fibroid 8cm with abnormal uterine bleeding, infertility, pelvic pain, dysmenorrhea, and pressure effect.

Exclusion Criteria

Excluded subjects included (1) women with Multiple fibroid (s). (2) Women with uterine fibroid who were under treatment with any type of estrogen or progesteron. and (3) women with a Previous failed medical or surgical treatment for fibroid. (4) combination of fibroid and adenomoyosis.

Bee Propolis was given orally each tablet 500 ml gm one tablet after meal three times daily.^(26, 27)

GnRHagonist (luperon depot) IM in a dose of 3.75mg.

All subjects underwent baseline measurement, performed in the early follicular phase. Measurements were performed at baseline and after treatment at week 12.

Statistical analysis:

Base line data analysis for patients was performed with the grouped student's t – test to assess the effective method of randomization between protocol difference were assessed by two-tailed grouped student's testing of volume changes. Significance was defined as $P < 0.05$.

Ethics:

The study was performed in accordance with the guide lines in the declaration of Helsinki and has been formally approved by the local ethical committee of Heliopolis hospital. Informed consent was obtained from all patients.

3. Results:

30 women randomized into two groups, group I (n.= 15) receiving Bee propolis tablets 500mg/3 times

daily for 12 weeks and the group II (n= 15) receiving GnRHa luperon depot (3.75).

The inclusion criteria: single fibroid $8\text{cm} \geq$ age between 25-40years, mean 35.5 years complaining of symptomatic fibroid, abnormal uterine bleeding, dysmenorrhea, pelvic pain.

Exclusion criteria: Multiple fibroid, previous failed medical, hormonal, and surgical treatment of fibroid.

Table I represents the result of treatments we found statistically significant decrease in the fibroid volume, uterine volume $p \leq 0.01$ and statistically significant increase in the Hb concentration $P < 0.01$. No reported hot flashes in group I. but reported in all patients in group II. ($P < 0.0001$).

Table 1: fibroid volume, uterine volume, Hb concentration in both groups I, II after 12 weeks of treatment.

Patient Characteristics	Group I n= 15	Group II n= 15	P. value
Fibroid volume	Before treatment 170.6±10.6 After treatment 15.8±2.1	Before treatment 165.7±8.6 After treatment 18.4±1.7	<.001
Uterine volume	Before treatment 335±10.3 After treatment 158±12.5	Before treatment 350±15.3 After treatment 144±6.7	<.001
Hb concentration	Before treatment 7.5±1.3 After treatment 13.2±1.8	Before treatment 7.75±1.5 After treatment 12±1.9	<.001
Hot flashes	Negative in all cases	15	< 0.0001

4. Discussion

We introduced for the first time in the literature Bee propolis as a novel treatment of fibroid. To test the efficacy and safety of this treatment; we conducted a randomized clinical controlled trail with the most commonly used drug, GnRH agonist Luperon depot. (3.75mg), which reduced estrogen⁽²²⁾ level by two mechanisms (a) reduced ovarian estrogen to a menopausal level (b) reduced local estrogen which produced in the fibroid by estrogen synthetase aromatase^(7,8,9,25) P 450 enzymes.

It was demonstrated that Bee Propolis is a potent inhibitors of cytochrom P450 and so reducing the level of estrogen^{(30), (31), (32)}. For the first time in literature, we used Bee propolis in treatment of fibroid.^{(27), (29), (30), (31)}.

In the present study we demonstrated reduction of fibroid volume and uterine volume, Both in Bee propolis and GNRH agonist group. $P < 0.01$ regarding Hb concentration it increases in Bee propolis group more than GnRH group. $P < 0.01$ We do not encounter symptoms of Menopause (Hot flashes) in Bee propolis

group. But we found it in all GnRH a group. ($P < 0.0001$)

The reduction of fibroid volume and uterine volume in Bee propolis group can be explained by its direct effect on local production of estrogen in the fibroid through autocrine-paracline^(4,5,7,8) and blocking⁽²⁷⁾ aromatase P450.

So GnRH agonist have a dual action of reducing estrogen locally in fibroid, and ovarian from the ovary opposite to Bee propolis which reduced estrogen only from fibroid in addition Bee propolis stimulate apoptosis, Pro apoptosis, suppresses proliferation, reduce growth factors and blood supply^(27,28,29,30,31, 32).

Regarding the recurrence rate of fibroid after treatment we do not encounter any recurrence during period of follow up. (6 Month) in Bee propolis group but we encountered 12 cases in GnRHa. agonists (luperon depot 3.75m).

So we can say that Bee propolis may be the first line of medical treatment of fibroid. The limitation of our study that our cases are not sufficient and lack more randomization.

5. Conclusion:

So, in conclusion we find that Bee propolis is effective for treatment of uterine fibroid than GnRHa, more reduction in fibroid volume and uterine volume, more increase in Hb. Concentration and no reported hot flashes and recurrence. In addition to this Bee propolis has a positive impact of women health (anti-inflammatory, anti viral, anti-bacterial and anti-fungal, and antioxidant.

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