

Efficacy of bee venom phonophoresis in treatment of chronic pelvic inflammatory diseases

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Abstract : Background: Pelvic inflammatory disease (PID) is an infectious and inflammatory disorder of the upper female genital tract affects more than one million women each year. Women with PID are more likely to have infertility and chronic pelvic pain. Purpose of the study: This study investigated the effect of bee venom phonophoresis in treating women having chronic pelvic inflammatory disease .**Methodology:** A clinical controlled trial on thirty women diagnosed as PID from Out Patient Clinic of Gynecology Department, SidiSalm Hospital, between March 2015 and April 2016 participated in this study. They were equally divided into two groups, group (A) treated by Doxycycline100 mg/day and group (B) treated by bee venom phonophoresis (Bee venom concentration 20microgarm / one gram gel) on suprapubic region for 20 minutes, 3 times per week for 12 sessions, in addition to medical drug given in group (A). Assessment of patients in both groups (A&B) was carried out before and after 12 sessions of the treatment through blood samples to measure the level of C - reactive protein (CRP) and present pain intensity (PPi) scale for assessment of pain. **Results:** Showed a statistically significant reduction $P<0.0001$ in inflammation assessed by CRP in both groups post treatment when compared with pre treatment with high percentage of improvement, in group B was 82.39%. Also, there was noticeable reduction in pain assessed by PPi scale in both group post treatment favoring group B as 26.7% of females in group B were completely free from pain. **Conclusion:** Bee venom phonophoresis can be considering an additive method in improving curing of pelvic inflammatory disease.

Keywords: Pelvic inflammatory disease, Ultrasound phonophoresis, Bee venom.

Introduction

Pelvic inflammatory disease (PID) is an infection of females upper genital tracts that implicated a higher rate of ectopic pregnancy, pelvic adhesion, pelvic abscess, tubal obstruction, infertility and chronic pelvic pain. PID is a common and morbid condition that affects about 8-11% of women in their reproductive period **Wiesenfield et al.,**¹. The most common cause of PID are Chlamydia trachomatis or neisseria gonorrhea infection in lower genital tract and bacterial vaginosis. The most common symptoms of PID are bilateral lower abdominal pain and tenderness with walking and coitus, abnormal vaginal discharge and rarely associated with irregular vaginal bleeding **Wiesenfield et al.,**¹,**Bartlett et al.,**². Clinical examination of PID assessed by, measuring of body temperature and determining of serum leukocyte concentration or C - reactive protein **Abbhiet al.,**³. Therapeutic ultrasound (US) has been widely used in the treatment of musculoskeletal disorders such as tendinitis, tenosynovitis, epicondylitis, bursitis and osteoarthritis. US convert electrical energy into an acoustic waveform, which is then converted into heat as it passes through tissues of varying resistance

Merino⁴. There are two different techniques for administration of US therapy; Continuous US, which is typically responsible for the heat effect, uses an un modulated continuous-wave US beam with intensities limited to 0.5–2.5 W/cm². The second approach emphasizes ultrasound's non- thermal properties. This type of beam is modulated to deliver brief pulses of high intensity US separated by longer pauses of no power. Pulsed US has been recommended for acute pain and inflammation, and continuous US for the treatment of restricted movement **Merino**⁴.

Phonophoresis (PH) is a technique that briefly increases permeability of the skin. Ultrasonic waves can noninvasively delivered different medications without pain by ultrasonic waves, it used to facilitate transdermal drug delivery **Dominkus et al.**,⁵ **Klaiman et al.**,⁶ US is used to activate transdermal medication conveyance in addition to deep heating. PH was first used to treat poly- arthritis of the hand by driving hydrocortisone ointment into inflamed areas. Since 1954 it utilized as a part of different dermatological and musculoskeletal issue **Klaiman et al.**,⁶. Ultrasound PH used in the treatment of pain and inflammation in conditions as epicondylitis, tendinitis, tenosynovitis, bursitis and osteoarthritis. The technique is non-invasive, well tolerated and involves minimal risk of hepatic and renal injury **Sharma et al.**,⁷.

Bee venom (BV) ointment was used as topical application for treatment of inflammation, be venom can be used in different forms as cream, liniment, ointment or injection **Ali**⁸. Bee venom is secreted from venom gland in the late area of the worker bee. The main components of be venom are: peptides as mellitin, apamin, mast cell degranulation peptide-401(MCD-peptide), enzymes as hyaluronidase, and non-peptide components: as glucose, and fructose. Bee propolis is a brownish resinous substance collected by bees and used to seal their hives. The main components of propolis are: flavinoids (that include quercetin, apigenin, galangin), phenolics (caffeic acid phenyl ester), biologically active amines (i.e., histamine and epinephrine), and nonpeptide components which have a variety of pharmaceutical properties and terpens **Vanks and Shipolini**⁹. BV therapeutic application, has been used in treatment of certain diseases, as arthritis, rheumatism, pain, cancerous tumors, and skin malesis **Hegazi et al.**,¹⁰. Acupuncture by using BV can be explained by multiple mechanisms, such as activation of the central and spinal opioid receptor, and α 2-adrenergic activity, as well as activation of the descending serotonergic pathway have been suggested. Also, BV api puncture inhibit c-Fos expression in the spinal cord by several nociceptive models is also reported to be a possible mechanism. **Hegazi et al.**,¹¹.

2. Material and methods

Thirty women diagnosed as having chronic pelvic inflammatory disease. They are selected from Outpatient Clinic of Gynecology Department at SidiSalm Hospital. This study was approved by ethical committee of Faculty of Physical Therapy Cairo University No: P.T. REC/012/001120.

Inclusion criteria: their age ranged from (20-38) years and their body mass index (BMI) not exceeds 30 kg/m². They complained from lower abdominal pain radiating to back with abnormal vaginal discharge as well as they were not responded to previous medical treatment and were not taken any medication for pain and inflammation all through the study period.

Exclusion criteria: All participants were free from diabetes, tubooverianabcess, hemorrhage, pelvic tumor as well as sacroiliac joint pain, Also, none of the patients was pregnant or using intra uterine contraceptive device.

All patients in both groups assigned an informal consent form before starting the study. Patients were randomly assigned into 2 equal groups, systematic random sampling technique was used in which every female with odd numbers were assigned to group A and every female with even numbers was assigned to group B. Group (A) 15 women treated by oral antibiotic (doxycycline 100 mg) twice daily for 7 days **Workowski and Berman**¹² and group (B) 15 women, treated by doxycycline 100 mg in addition to BV gel topical application with phonophoresis, Bee venom gel at a concentration 20microgarm BV/gram gel, The patient was asked to evacuate her bladder before starting the treatment session, to make sure that she was relaxed. She lied in crook lying position with small pillow under her head and lumber region to accommodate her body curves, Therapeutic ultrasound device (ENRAF model) with frequency 1 MHz, intensity 0.5 was used for phonophoresis application by bee venom gel on suprapubic region in fine circular manner for 20 minutes 3 times per week for 12 sessions. Assessment of both groups (A& B) was carried out before and after the treatment program throughout two blood samples were drawn from each patient in both groups (A and B) to

measure the level of C - reactive protein (CRP) and Present Pain Intensity (PPI) scale was used for assessment of pain Hartricket al.,¹³ before and after end of 12 sessions.

Statistical analysis

Statistical analysis was conducted using SPSS for windows, version 18 (SPSS, Inc., Chicago, IL). The current test involved two independent variables. The first one was the tested group that had two levels (group A and group B). The second one was the treatment periods, which had two levels (pre and post). The dependent variable (C-reactive protein) is numerical variable. Normality test of data using Shapiro-Wilk test was used, that reflect the data was normally distributed for C-reactive protein, so parametric statistical tests in the form of (paired t test) was used to compare between "pre" and "post" treatment for each group and "unpaired t test" was conducted to compare C-reactive protein between both groups in the "pre" and "post" treatment. While, The dependent variable (present pain intensity) is ordinal variable. Normality test of data using Shapiro-Wilk test was used, that reflect the data was not normally distributed for present pain intensity, so non parametric statistical tests in the form of (Wilcoxon Signed Rank tests) was used to compare between "pre" and "post" treatment for each group and "Mann-Whitney tests" was conducted to compare present pain intensity between both groups in the "pre" and "post" treatment. The alpha level was set at 0.05.

Results

There were no significant differences between the groups with respect to age and BMI (p>0.05), as shown in Table 1.

Table 1: Demographic characteristic of females in both groups A&B

	Group (A)	Group (B)	p-value
Age (years)	32.53±3.48	32.133±2.99	0.362
BMI (kg/m ²)	25.3±3	24.26±2.64	0.61

As shown in Table (2) regarding changes in level of c- reactive when comparing pre and post treatment there were significant improvement p<0.0001 in both group with percentage of improvement 30.46% in group A while in group B were 82.39%.

Table (2): Mean ±SD, t and P values of C-reactive protein pre and post treatment at both groups.

C-reactive protein	Means ± SD	Means ± SD	Mean difference	% of improvement	t-value	P- value
	Pre test	Post test				
Group A	51.2±17.83	35.6±18.76	15.6	30.46	3.853	0.002*
Group B	56.8±13.19	10±4.89	46.8	82.39	17.359	0.0001*
Mean difference	-5.6	25.6				
t-value	-0.977	5.112				
P- value	0.337	0.0001*				

Regarding to changes in pain sensation when comparing pre and post present pain intensity scale there were significant improvement p<0.0001 in both group, when comparing between both groups there were significant reduction p<0.0001 and this significant reduction in favor of group B, table (3) represent the frequency distribution of the present pain intensity scale in pre and post treatment at both groups.

Table (3): The frequency distribution of the present pain intensity scale in pre and post treatment at both groups.

Present pain intensity scale	Group A		Group B	
	Pre treatment	Post treatment	Pre treatment	Post treatment
Frequency distribution				
No pain	0 (0%)	0 (0%)	0 (0%)	4 (26.7%)
Mild	0 (0%)	1 (6.7%)	0 (0%)	7 (46.7%)
Moderate	2 (13.3%)	2 (13.3%)	1 (6.7%)	4 (26.7%)
Sever	7 (46.7%)	11 (73.3%)	8 (53.3%)	0 (0%)
Intolerable pain	6 (40%)	1 (6.7%)	6 (40%)	0 (0%)

Discussion

Pelvic inflammatory disease, or PID, is infection that affect a woman's upper genital organs, the infection spreads up from the vagina and cervix into the fallopian tubes, uterus and ovaries. It is usually caused by untreated chlamydia or gonorrhea, and may be caused by other infections. Untreated PID increase incidence of infertility, ectopic pregnancy, and chronic pain **Workowski and Berman**¹².

The results of the study demonstrated that bee venom phonophoresis can treat PID which appear in reduction of CRP as well as pain level which usually associated with inflammation. on an attempt to explain this effect, it could be attributed to the influence of bee venom PH on PID which appear in bee venom may exert its action through the effect of its components. Melittin one of important component of bee venom has the ability to block the expression of inflammatory genes. So, it has inflammatory effect by inhibiting the critical DNA binding activity of NF-kB (Nuclear Factor Kappa B), which directly controls controls a number of genes involved in immune reactions **Park et al.**,¹⁴.

The pharmacological effect of bee venom on the inflammation could be explained through inhibition of Cox-2 expression that is involved in the production of prostaglandins (PG) which supports the inflammatory process **Park et al.**,¹⁴, **Jeonget al.**,¹⁵. Moreover, bee venom may act through reduction of IL-6 that increases in inflammatory conditions) and induction of IL-10, which used as a new line of psoriasis therapy **Asafova et al.**,¹⁶. Also, the current study suggested that phonophoresis of venom and its Adolapin (Biologically active peptide) and Protease(Inhibitors Biologically active peptides) may play its effect in reduce inflammation through different mechanisms. It was shown that different Adolapin biologically active peptide has an important role on human immune cell functions through inhibits the activity of different proteases like trypsin, chymotrypsin, plasmin, thrombin, thus reduce inflammation. These data might indicate that adolapin has a direct regulatory effect on basic functional properties of immune cells **Asafova et al.**,¹⁶.

In addition, quercetin, another component of propolis has a significant anti-inflammatory activity due to direct inhibition of several processes of inflammation via interaction with calcium channels and/or calmodulin, as well as through other mechanisms such as by inhibiting mast cell and basophil degranulation, neutrophil and monocyte lysosomal secretion, prostaglandins (PG), leukotrene formation and lipid peroxidation (4,6) resulting in inhibition of release and manufacture of histamine and inflammatory mediators **Mirzoeva and Calde**¹⁷.

It was reported that bee venom phonophoresis could decrease pain level in subjects with pelvic inflammatory disease as appear in visual analogue scale which may due to effect of transdermal delivery of bee venom using ultrasound (PH). These results agree with **Singh et al.**,¹⁸ who compared the efficacy of iontophoresis and phonophoresis with diclofenac sodium (1%) in the treatment of shin splints. Both iontophoresis and phonophoresis are effective methods in introducing the medication deep into the periosteum and adjacent musculo-tendinous structures. Beside the effects of bee venom as anti-inflammatory effects it also decrease surface tension of membranes, increases capillary permeability improve blood circulation and decrease the blood pressure, decrease blood coagulation, immunostimulatory and immunosuppressive, radiation protective, influences the central nervous system, anticancer, antibacterial, antifungal, antiviral effects. **Mirzoeva and Calde**¹⁷, **Park et al.**,¹⁹. Also, the results of study is agree with **Lee et al.**,²⁰ who concluded that Bee venom with its excellent nociceptive and anti-inflammatory property has been found to be effective in reducing pain associated with post-herpetic neuralgia.

Conclusion

From the study, we conclude that phonophoresis of bee venom has significant results in CRP reduction as well as pain result from pelvic inflammatory disease treatment due to bee venom components and potential effects of phonophoresis.

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