Analgesic efficacy of pulsed radiofrequency in non-cyclic mastalgia: A randomized controlled trial

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Background: Non cyclic-mastalgia is a challenge among women. We aimed to study the effects of adding pulsed radiofrequency to tamoxifen 10mg daily in treatment of non-cyclic mastalgia.

Methods: We conducted a randomized prospective open blinded endpoint, level IV trial in the outpatient pain clinic of Mansoura University Oncology Center during the period from 2018 till 2019. Patients were randomly allocated into two groups. Group A (n=13) received tamoxifen 10mg tablet once daily and group B (n=13) received tamoxifen 10mg tablet once daily and pulsed radiofrequency of the 2nd, 3rd and 4th thoracic dorsal root ganglia. We monitored numerical rating scale (NRS) and quality of life (QOL) before and at intervals of 2 weeks, 1, 2 and 3 months after treatment; complications; side effects of tamoxifen; and number of patients who needed analgesia.

Results: Numerical rating scale significantly decreased in group B compared to group A at 2 weeks (P = 0.002) and 1, 2 and 3 months (P<0.001). Group B showed marked improvement in QOL at 2 weeks, 1, 2 and 3 months(P<0.001). No complications were reported in both groups. Patients who needed analgesia were more in group B than group A (P=0.018).

Conclusions : Combined usage of pulsed radiofrequency and tamoxifen 10mg daily is a safe line of treatment of non-cyclic mastalgia and markedly improves QOL.

Keywords: Pulsed radiofrequency; non-cyclic mastalgia; tamoxifen

Introduction

Mastalgia or breast pain is a common medical problem among women.[1] Its intensity is variable ranging from mild to severe and disturbs quality of life (QOL) through affecting sexual, physical, and social activities.[2]

Mastalgia is classified into three main categories: cyclic, non-cyclic and extra-mammary mastalgia. As regards non-cyclic mastalgia, most cases have unknown aetiology while a minority of cases are due to mastitis, pregnancy, trauma, macrocysts, thrombophlebitis, psychological disturbance and cancers.

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Typically, it presents in the fourth decade of life. Many women are postmenopausal at onset of symptoms. Unfortunately, the course of non-cyclic mastalgia may be long and persist for many years.[3]

Mastalgia may be bilateral or unilateral. In unilateral cases, pain may be located in only one part of the affected breast. It can be referred from the breast to the axilla and down to the medial aspect of the upper arm. The affected breast is often extremely tender and may show swellings and congestion.[4] A variety of medical therapies have been recommended for treatment of mastalgia. These traditional lines of treatment include non-steroidal anti-inflammatory drugs (NSAIDs), vitamins, progesterone, diuretics, thyroxin, bromocriptine, danazol, tamoxifen and plant extracts as evening primrose oil (EPO).[5]

For few decades, tamoxifen is routinely used in mastalgia treatment. However, several side effects have been observed in form of weight gain, nausea, hot flushing, bloating, menstrual irregularity, amenorrhoea, vaginal dryness and

thromboembolism.[6] Moreover, its value in alleviating non-cyclic mastalgia is doubtful when compared to cyclic mastalgia.[7] From this point, searching for an ideal safe line of treatment for non-cyclic mastalgia is mandatory.

Pulsed radiofrequency (PRF) has recently been developed as an alternative therapeutic technique for relief of chronic breast pain.[8] To our knowledge, it is the first trial to study the effects of adding pulsed radiofrequency of 2nd, 3rd and 4th thoracic dorsal root ganglia (DRG) in treatment of non-cyclic mastalgia through assessing both pain intensity and QOL.

Materials and methods

Study design and participants

Our research was a randomized prospective open blinded endpoint, level IV study, carried out in the outpatient pain clinics of Mansoura University Oncology Center during the period from October 2018 till February 2019. We enrolled 26 patients suffering from non-cyclic mastalgia that did not respond to traditional treatment for one month (well-fitting bra, reduction in dietary fat intake, EPO[9], oral or topical NSAIDs).[10] Patients aged from 20 to 60 years with numerical rating scale (NRS) ≥ 4 were enrolled. Written informed consents were obtained from all participants.

Sample size

It was calculated using G Power 3.0.10 program. Assuming α (type I error) = 0.05 and β (type II error) = 0.2 (power = 80 %) and effect size (δ) = 0.6 yielded a total sample size of 26.[8,11]

Randomization

Each patient was randomly allocated into one of two groups (Group A and B) using variable sized blocks (3, 3, 3 and 4). Opaque sealed envelopes technique was used for allocation concealment. Group A (n=13) received tamoxifen 10mg tablet once daily, while group B (n=13) received tamoxifen 10mg tablet once daily and PRF of the 2nd, 3rd and 4th thoracic DRG.

Exclusion criteria

Cyclical mastalgia (abnormal oestrogen, progesterone and prolactin hormones levels), extra-mammary mastalgia (cervical MRI, chest examination and ECG), patients refusal to participate, suspicion of malignancy (mammogram was done for all participants), acute inflammatory breast conditions; presence of polycystic ovarian diseases, cervical hyperplasia, pregnant patients, lactating women, coagulopathy disorder, sepsis at the site of injection, history of thromboembolic disease, mental disorder and disturbed anatomy (congenital, traumatic, and postsurgical) which increase the intervention difficulty.

Technique

We inserted an intravenous cannula. All required resuscitation drugs and equipment were available. All participants were monitored for vital signs and oxygen saturation throughout the procedure and up to one hour after performance of block.

Resuscitation equipment were available including endotracheal tubes of different sizes, self-inflating bag and mask, a ventilator, chest tubes and drugs as atropine and adrenaline.

We performed the procedures on a 64 MDCT scanner (Brilliance 64-Philips). The acquisition parameters of CT were 200mAs, 120kVp, 512 × 512 matrix, 1.172 pitches; 4mm slice thickness and 64 × 0.625mm section collimation.

Patients were positioned prone, then 2nd, 3rd and 4th thoracic disc levels were detected in the sagittal plan, then the target corresponding thoracic nerve roots were identified in the axial plan. After marking the entry points, povidone iodine was used for skin sterilization, and then the skin was anaesthetized by 2ml lidocaine 2% at each entry point. The Baileys radio frequency 22G, 10cm needles with 10mm active tip were introduced to face the 2nd, 3rd and 4th thoracic nerve roots (Figures 1a and b).

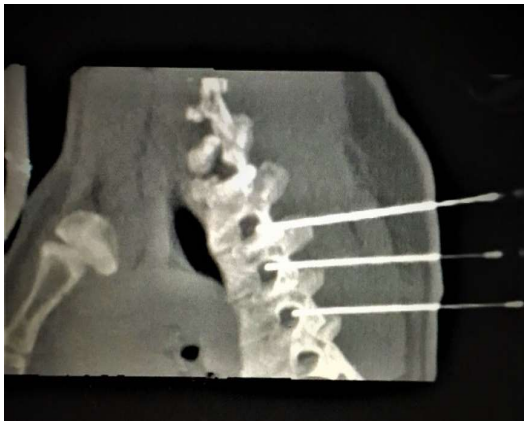

Figure 1a: Sagittal view of the needles at the 2nd, 3rd and 4th thoracic nerves roots.

Figure 1b: 3-Dimensional view of the needles at the 2nd, 3rd and 4th thoracic nerves roots.

If the pleura or the lung were within the pathway of the needle, saline injection was done to push them away from the field (Figure 1c).

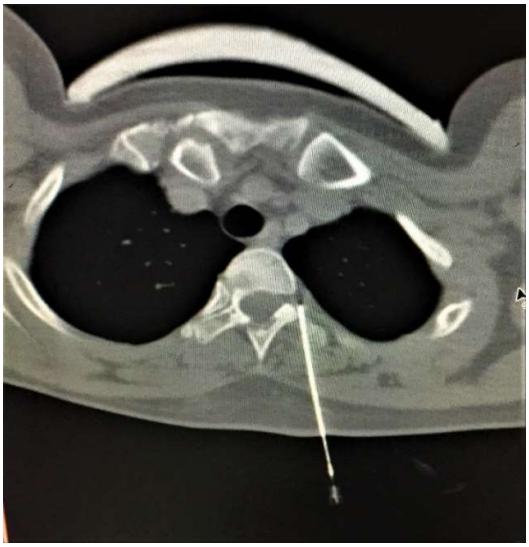

Figure 1c: Axial view of the needle at the 2nd thoracic nerve root.

Once we confirmed the place of the needles tips, the sensory and motor stimulations was done by the RF generator to get sensory paraesthesia along T2, T3 and T4 dermatomes at 0.4–0.8V (Figures 1c, d and e, respectively), and intercostal fasciculation were obtained at double the sensory amplitude.

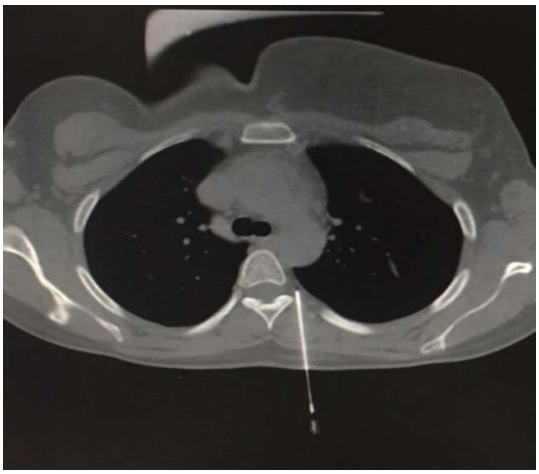

Figure 1d: Axial view of the needle at the 3rd thoracic nerve root.

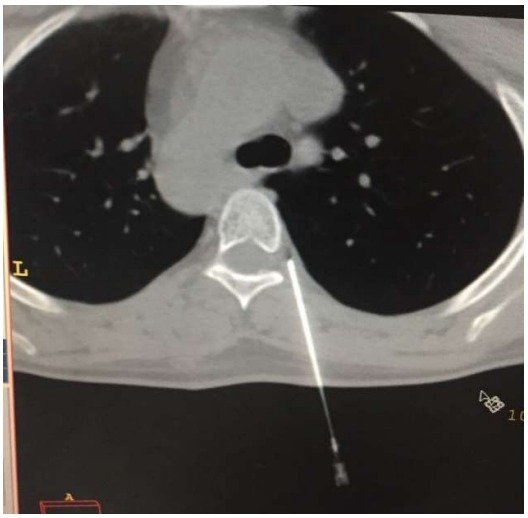

Figure 1e: Axial view of the needle at the 4th thoracic nerve root.

The PRF course was carried out at 42°C for 120s twice at each level followed by injection of 1 ml lidocaine 2% and 1 ml dexamethasone 4mg at each level.

After intervention, all patients were transferred to a recovery room for observation and followed for any complication. If NRS was ≥ 4, we gave NSAIDs in form of oral piroxicam 20mg once daily with or after food.

Primary outcome: NRS was recorded before and at intervals of 2 weeks, 1, 2 and 3 months after starting treatment.

Secondary outcomes:

1. QOL (The American Chronic Pain Association's QOL scale): It measured the daily activities of patients with chronic pain ranging from 0 = stay in bed all day and feel hopeless and helpless about life to 10= normal daily activities each day and have a social life outside of work.[12] We assessed QOL before treatment and after two weeks, 1, 2 and 3 months;
2. Complications during and after intervention as haematoma, neurological deficits, infection or respiratory insufficiency (dyspnoea or pneumothorax);
3. Number of patients who needed analgesia;
4. Side effects of tamoxifen as nausea, vomiting, hot flushes and dizziness.

Statistical analysis

SPSS (version 25) was used for statistical analysis. For continuous variables, data normality was checked by Shapiro-Wilk test. Continuous variables were presented as mean ± SD, ordinal variables shown as median and inter-quartile range while categorical data were presented as number (percentage). Independent samples t-test and Mann Whitney test were used to compare normally and abnormally distributed continuous variables with no follow-up readings respectively. A linear mixed model with unstructured co-variance was conducted using the maximum likelihood method and 95% confidence interval to compare basal and follow-up readings of the NRS score and QOL after the procedure in all patients and both study groups. P value < 0.05 was considered statistically significant.

Results

Both groups were matched as regards demographic data, duration of pain and the affected breast. However, the number of patients who needed NSAIDs after intervention was significantly higher in group B than group A (P=0.018, Table 1).

Table 1: Differences in demographic data, duration of pain, analgesia need and affected breast between the studied groups.

	Group A n=13	Group B n=13	P value
Age (years)*	30.6±5.65	30.6±5.12	0.84
Height (cm)*	162±6.65	163.9±5.6	0.43
Weight (kg)*	76.6±10.18	75±8.94	0.67
Duration of pain (months)*	8.32±1.88	8±2.04	0.77
NSAIDS needs†	4 (30.7)	10 (76.9)	0.018
Affected breast†			
Left side	7(53.8)	3(23.1)	0.39
Right side	5(38.5)	8(61.5)	
Bilateral	1(7.7)	2(15.4)	

Data are shown as *mean (SD); † numbers (percentage).

NRS was significantly lower in group B than group A at 2 weeks (P =0.002) and became much lower after 1, 2 and 3 months (P<0.001, table 2).

Table 2: Differences in numerical rating scale (NRS) between the studied groups

NRS	Group A (n=13)	Group B (n=13)	P values
Basal	8 (7.5-8.5)	8 (7-9)	0.62
Two weeks	5 (4-5)	3 (2.5-4)	0.002
One month	4 (4-5)	2 (1.5-2.5)	< 0.001
Two months	4 (3.5-4)	1 (1-2)	< 0.001
Three months	3 (3-4)	1 (1-2)	< 0.001

NRS; numerical rating scale; Data are shown as median (IQR).

Group B showed marked improvement in QOL at 2 weeks, 1, 2 and 3 months (P<0.001, Table 3).

Table 3: Differences in quality of life (QOL) between the studied groups

QOL	Group A (n=13)	Group B (n=13)	P values
Basal	2 (2-3.5)	2 (1.5-3.5)	0.85
Two weeks	7 (7-8)	9 (8-9.5)	< 0.001
One month	8 (7-8)	9 (9-10)	< 0.001
Two months	8 (7-8)	10 (10-10)	< 0.001
Three months	8 (7-8)	10 (10-10)	< 0.001

QOL: Quality of life; Data are shown as median (IQR).

No complications were reported in both groups as regards both PRF and tamoxifen.

Discussion

Mastalgia is a painful condition affecting up to 70% of women. Indeed, it is a challenge that affects QOL in a way similar to other painful conditions such as arthritis or cancer.[13]

In the current study, we clarified the value of adding interventional PRF of the 2nd, 3rd and 4th thoracic dorsal root ganglia to the routine treatment, tamoxifen 10mg tablet once daily, in management of non-cyclic mastalgia.

In our study, the improvement in NRS with radiofrequency could be explained by activation of temperature-independent pathway that leads to cessation of the current pain and promptly changes pain conduction to normal.[14] This goes hand in hand with Kim et al who used PRF of the 4th thoracic spinal root in a 52 years old female patient complaining of chronic mastalgia after breast reduction. They reported long-lasting pain reduction {Visual analogue score (VAS) 20-30/100 mm} for 9 months without any particular exacerbation of pain and without any side effects.[15]

Moreover, Fam et al found that PRF with steroid injection on the 2nd and 3rd thoracic DRG is a safe and effective method for intercostobrachial neuralgia post-mastectomy treatment. VAS decreased significantly after 1 week, 1, 3 and 6 months respectively (from 7.48±1.46 to 5.01±2.61, 3.26±2.37, 4.44±2.8 and 4.7±2.88 respectively, $p<0.05$).[8]

Interestingly, our study reported gradual improvement in NRS with time in group B to reach its full effect after one month ($P< 0.001$). This goes hand in hand with authors who proved that pain with PRF become progressively better and takes up to several weeks to show a maximum effect.[16]

An important observation was the higher need for NSAIDs within the first few days among group B. This could be due to the pain induced from needles entrance in the back. Moreover, the inflammation of the nerve roots caused by PRF and the release of interleukins, tumor necrosis factor-α, and phospholipase A2 could add a pathophysiological explanation for the initial increased need for analgesia with PFR.[17]

Another finding in our report was the dramatic improvement in QOL among group B. Of course, we could explain this finding by better pain relief in this group. Our results are in agreement with authors who used PRF in post-herpetic neuralgia patients and found dramatic pain relief with subsequent enhanced QOL. They used 36-Item Short Form Survey (SF-36) score to assess QOL.[18]

Also, our study emphasized safety and well tolerance of tamoxifen and PRF in both groups as evidenced by absence of complications. This could be explained by usage of CT that minimizes technical errors. Absence of complication with tamoxifen 10mg daily was supported by the previous report of Jain et al.[11]

In summary, combined usage of PRF and tamoxifen 10mg daily could be considered a safe line of treatment of non-cyclic mastalgia. Also, adding PRF to the traditional tamoxifen 10mg therapy markedly improves QOL. We recommend large scale multicenter studies with larger simple sizes to generalize our findings.

Limitations of study: A single center study with relatively small sample size.

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