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The effect of transcutaneous electrical nerve stimulation on the level of interleukin “6” and “10” post pleurodesis

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Abstract---Objectives: Transcutaneous electrical nerve stimulation (TENS) has been used to control post-pleurodesis pain with contradiction results. We aimed to assess the efficacy of TENS on post- pleurodesis pain in relation to: (i) Interleukin 6; (ii) Interleukin 10; (iii) pain. Methods: Between September 2020 to October 2021, 68 patients underwent pleurodesis post posterolateral thoracotomy. Sixty patients were enrolled in the present study and randomized in two groups: Group A TENS group (30 patients) who received postoperatively TENS for 2 days and Group B placebo group (30 patients) without TENS. In both groups (i) serum cytokines (IL-6, IL-10) were measured by ELISA before surgery and at 1, 6, 12, 24 and 48 postoperative hours (POHs); (ii) at the same POHs, the pain score was measured using critical care pain observational tool (CPOT). Repeated measures of analysis of variance assess the difference between two

study groups. A value of $P < 0.05$ was considered statistically significant. Results: In the current study, a total of 60 patients participated and they were randomly distributed into 2 groups (30 patients/group). Statistical analysis shown that there was a significant change of pre-post treatment at groups A, ($p < 0.05$). Between-group analysis revealed no significant change in pre value of all variables as ($p > 0.05$) while post-treatment there was a significant change in all variables as ($p < 0.05$). Conclusion: TENS is useful as an adjunctive to NSAIDs and opioids for reducing the level of interleukin “6” and “10” and in turn pain relief post pleurodesis and it leads to reduction in subsequent medications requirements. TENS is a valuable strategy to alleviate pain post pleurodesis with no adverse effects and with a good hemodynamic stability.

Keywords---transcutaneous electrical nerve stimulation, pleurodesis, pain, analgesia, interleukin “6”, interleukin “10”.

Introduction

Pleurodesis are often the foremost painful types of incision that patients can experience. Pain may inhibit effective coughing, deep breathing and restrict early postoperative mobilization. As a result, lung ventilation and independence self-care won't be optimal with an inclination to lung infection. Furthermore, inadequate acute postoperative pain management may contribute to the event of a chronic post- pleurodesis pain syndrome [1]. The goal of the clinician is to develop an analgesic regimen that has an effective pain relief and to permit post pleurodesis patients the flexibility to take care of their functional residual capacity by deep breathing. Effective clearance of secretions with cough and early mobilization can result in quicker recovery and shorter length of hospital stay [2]. Systemic administration of opioids is the simplest and common method to produce analgesia for postoperative pain, but it's going to be related to several undesirable effects, like respiratory depression, sedation, nausea and vomiting [3].

Thoracic epidural analgesia is often considered the ‘gold standard’ for postoperative pain treatment after pleurodesis, but this method may fail, to be contraindicated or impossible for a range of reasons [4]. The physiotherapy management for this condition includes the pain management with TENS, inspiratory exercises, expiratory exercises, segmental breathing exercises, and thoracic expansion exercises [5]. Pain may be a common symptom felt during postoperative period at the incision site, which could interfere with pulmonary functions and healing. Respiratory complications are the most common complications which will occur in postoperative period which usually develops during the primary 48 hours after the surgery [6].

Anesthesia and tissue dissection during insertion of intercostal drainage tube contributes to changes in lung volume and gas exchange. due to anesthesia the motility of cilia reduces and causes retaining secretions, thereby causing atelectasis. Reduction in functional capacity has implication for postoperative

complications and the course of recovery. Therefore, an early pain reduction helps to stay the patient relieved from the adverse effect of analgesia, cough, and thereby helps to hurry up recovery [7].

Transcutaneous electrical nerve stimulation (TENS) is a popularized name for electrical stimulation produced by a transportable stimulator accustomed to treat pain. Pain control TENS unit typically produce endless train of pulsed current at frequencies starting from 1-120 Hz. The pulses are normally rectangular in shape, biphasic and the pulse duration is often 50-200 μ s [8]. Johnson et al. reported that the efficacy of transcutaneous electrical nerve stimulation in producing analgesia in cold induced pain was assessed employing a range of 5 stimulating frequencies (10Hz, 20Hz, 40Hz, 80Hz, and 160Hz) in 83 normal healthy subjects. TENS frequencies between 20 and 80Hz produced greatest analgesia, while frequencies below and above this level (10 and 160Hz) produced effects of lesser magnitude [9]. Cheung D & C et al. reported that high TENS has been used to control postoperative pain after thoracotomy and improve the pulmonary functions [10].

Material and Methods

Study design

It is a prospective randomized unicentral study including series of consecutive patients undergoing standard pleurodesis, the topics were randomly assigned to either an energetic TENS or placebo TENS group, employing a computer-generated randomization sequence. Exclusion criteria were (i) previous history of chronic chest diseases; (ii) previous history of chronic renal failure; (iii) previous history of cardiac diseases; (iv) diabetic patients; (v) patients with neurological diseases; (vi) patients with pacemaker's implantation (vii) uncooperative patients (viii) and (xi) debilitated patients with unstable hemodynamics.

In all patients, blood samples for the interleukin 6 and 10 measurement were drawn preoperatively and at the identical postoperative hours (POHs) in addition to the critical care pain observational tool measurement were also recorded. The intergroup differences of the variables were then performed to represent the effectiveness of the TENS treatment. Based on other studies, the sample size calculation assumed that the difference between TENS group and placebo group on the critical care pain observational tool (CPOT) scale would be clinically significant. Signed informed consent was obtained by all patients and the study was approved by the Ethics Committee of faculty of physical therapy, Cairo university.

Patient population

Between September 2020 to October 2021, 66 patients underwent pleurodesis post posterolateral thoracotomy. Sixty patients were enrolled in the present study and randomized in two groups of both sexes with an age range of 30 to 40 years old with moderate pain severity post pleurodesis and was selected from Intensive Care Unit, National Cancer Institute, Faculty of Medicine, Cairo University. This

study conducted one-hour after recovery from anesthesia for 48 hrs., two sessions per day. All patients will be divided randomly into two groups A and B.

Group (A): 30 patients received two sessions per day using TENS with frequency 80 Hz for 45 minutes for each session one-hour after recovery from anesthesia for 48 hrs., in addition to diclofenac sodium 75 mg as a NSAID (non-steroidal anti-inflammatory drugs) for incisional pain relief and morphine 5 mg as an opioid for central pain desensitization.

Group (B): 30 patients received the previous mentioned medications in addition to placebo effect of TENS.

Randomization occurred within the order during which patients were enrolled within the study in keeping with the computer-generated randomization schedule prepared before the beginning of the study. On the day before the operation, postoperative TENS was discussed with each patient. All patients were advised that the TENS treatment didn't prohibit the administration of analgesics; during this way, they were specifically instructed to request medication to alleviate pain. Groups were assumed comparable because they involved similar surgical procedures by the identical surgeon within the identical period. Both groups of patients received identical anesthesia. After the operation, all patients had a medication using intravenous (IV) patient control analgesia (PCA) as the following: 5 mg morphine IV bolus initially, followed by 1.2 mg/h which may be maximally delivered by any patient with a 5–10 min lockout period for the primary 48 POHs as an opioid for central pain desensitization additionally to nonsteroidal anti-inflammatory 75 mg as a NSAID (non-steroidal anti-inflammatory drugs) for incisional pain relief (administered via an intramuscular route at a dose of 15 mg every (6–8 h) was given when the patient experienced severe pain.

Device and TENS application

The TENS device delivered an asymmetric square biphasic wave form at a frequency of 80 pulse/s and a pulse width of 250 μ s. The placebo TENS device appeared similar to the treatment of TENS devices, including operating detector light and batteries, but didn't provide current. Two standard sterile disposable adhesive electrodes were placed on the skin on either dorsal side of the incision 2 cm away the suture line. the quality of the incision dressing wasn't disturbed. The TENS group adjusted the stimulus intensity until a tingling sensation was felt, whereas the placebo TENS group was told that the electrical stimulation was silent, producing no sensation. However, within the placebo group the TENS unit also displayed an active detector light, seemed to the patient that the unit was active.

After the surgical technique, the patient was transferred to the post anesthesia care unit and electrodes were placed. TENS immediately started one-hour after recovery from anesthesia and were performed with a duration of 30 min two sessions\ day within the first 48 POHs. Two investigators were involved in data collection during this study and were trained to standardize treatment and measurements. Investigator (1) was in charge of the patient evaluation and pain assessment in all entirely subjects. Investigator (2) applied TENS treatment in all

patients. Only investigator (2) knew if the subject has received dynamic or placebo TENS therapy. Both investigator (1) and the subject was blinded to the TENS therapy. Further, to attenuate investigator bias, the investigator who applied TENS therapy instructed patients to mention nothing about their stimulation-related perception to the investigator who was assessing pain intensity.

Assessments criteria

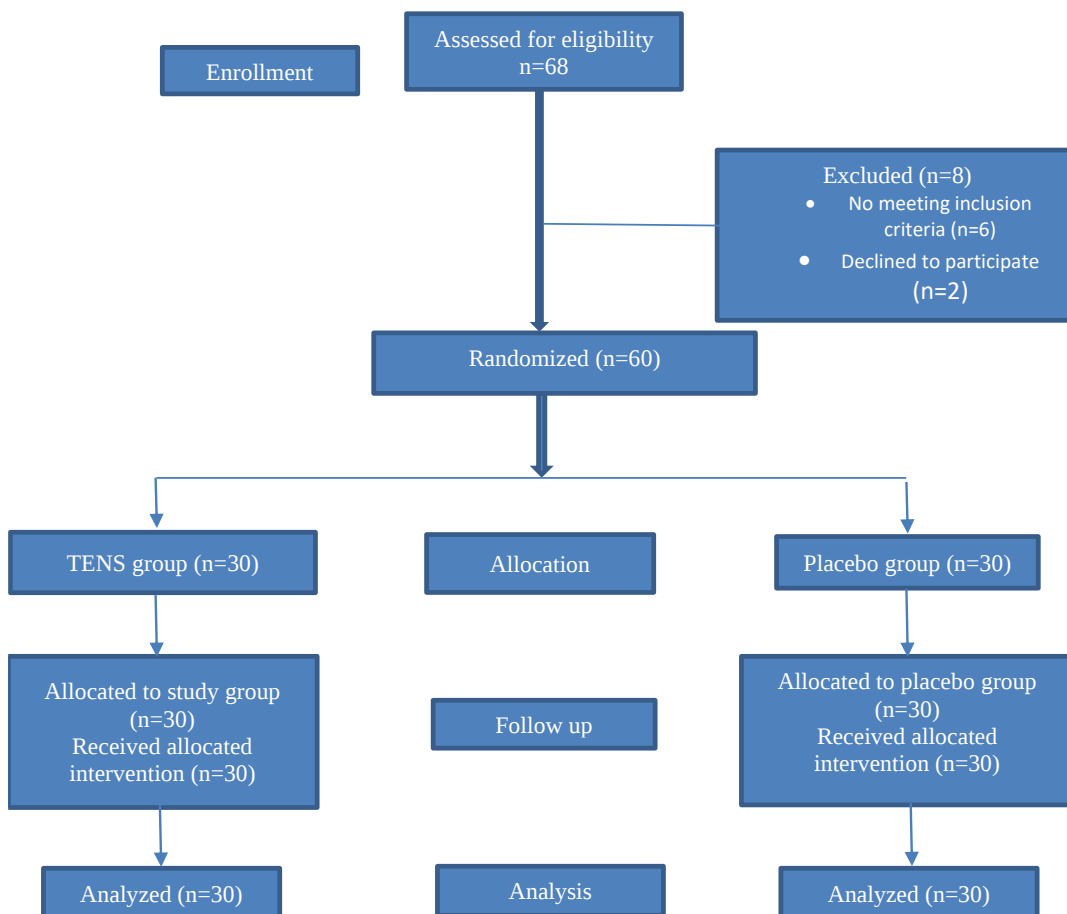
Blood samples were collected from an antecubital vein in intervals as follows: before surgery and at 6, 12, 24 and 48 postoperative hours (POHs). The sample left for 30 min for clotting of blood, followed by centrifugation at 3000 G for 5 min, and so stored in deep refrigeration at -80°C until serum cytokines measurements were performed (pg/ml). Serum cytokines consisting of IL-6 and IL-10 were measured by the identical technologist using available enzyme-linked immunosorbent assay (ELISA). The technologist was blinded of which patients were within the TENS group.

In all patients, blood samples for the IL6 and IL10 measurements were collected preoperatively and at the identical postoperative hours (POHs) as for objective inflammation and pain measurement. additionally, the critical care observational pain score at a special time of postoperative course were also recorded. The intergroup differences of the variables were then performed to represent the effectiveness of the TENS treatment

Data collection

Data were screened, for normality assumption test and homogeneity of variance. Normality test of data using Shapiro-Wilk test was used, that reflect the data was normally distributed ($P>0.05$) after removal outliers that detected by box and whiskers plots. Additionally, Levene's test for testing the homogeneity of variance revealed that there was no significant difference ($P>0.05$). So, the data are normally distributed and parametric analysis is done.

Randomization



Statistical analysis

The statistical analysis was conducted by using statistical SPSS Package program version 25 for Windows (SPSS, Inc., Chicago, IL). Quantitative data are expressed as mean and standard deviation for measurements of demographic data, IL16, IL-10, critical care observational. Qualitative data are expressed as number and percentage for gender variable and compared between both groups by Chi-square-test. Independent t-test used to compare between both groups for demographic data. Repeated measuring ANOVA-test used to compare the tested major variables of interest at different tested groups and measuring assessment points. Bonferroni correction test was used to compare between pairwise within and between groups of the tested variables which F was significant from repeated measuring ANOVA-test. All statistical analyses were significant at level of probability less than an equal 0.05 ($P \leq 0.05$).

Results

In our study, a total of 60 patients participated and they were randomly distributed into 2 groups (30patients/group). No significant differences in demographic data for age ($P=0.938$; $P>0.05$), weight ($P=0.992$; $P>0.05$), height ($P=0.159$; $P>0.05$), and gender ($P=0.095$; $P>0.05$) between group A and group B (Table 1).

Table (1): Comparison of general characteristics of subjects between both groups

Items	Groups		P-value
	Group A (n=30)	Group B (n=30)	
Age (year)	35.13 $\pm$ 3.39	35.20 $\pm$ 3.24	0.938
Weight (kg)	85.90 $\pm$ 12.70	85.87 $\pm$ 13.14	0.992
Height (cm)	170.00 $\pm$ 10.74	174.57 $\pm$ 7.54	0.159
Gender (males: females)	22 (73.30%) : 8 (26.70%)	27 (90.00%): 3 (10.00%)	0.095

Quantitative data (age, weight, height) are expressed as mean $\pm$ standard deviation and compared by t-independent test.

Qualitative data (gender) are expressed as number (percentage) and compared by chi-square test.

P-value: probability value

NS: non-significant

A total of 60 patients participated in the current study, the inflammatory proteins characteristics, critical care observational tool of this study subjects were a comparison among the baseline (pre-assessment), post-1hour, post-6 hours, post-12 hour, post-24 hour, and post-48 hour assessment (Table 2). There were significant differences ($P=0.0001$; $P<0.05$) in inflammatory proteins (IL-6 and IL-10), critical care observational tool, within group A ($P=0.0001$; $P<0.05$) and group A ($P=0.0001$; $P<0.05$) among 6-assessment points.

For comparing between group A and group B at pre- and post-assessment points Table (2) revealed no significant differences ($P>0.05$) in IL-6 and IL-10 between group A and group B at pre-treatment ($P=0.496$ and $P=0.480$, respectively) and post-1hour ($P=0.219$ and $P=0.380$, respectively). However, there were significant differences ($P=0.0001$; $P<0.05$) in IL-6 and IL-10 between both groups at post-6hours, post-12hour, post-24hour, and post-48hour. No significant differences ($P>0.05$) in the critical care observational tool (Table 2) between group A and group B at pre-treatment ($P=0.157$), post-6hours ($P=0.237$), and post-24hour ($P=0.724$). However, there were significant differences ($P=0.0001$, $P<0.05$) in the critical care observational tool between both groups at post-1hour, post-12hour, and post-48hour.

These significant ($P<0.05$) effects in IL-6, IL-10, critical care observational tool, from baseline assessment point to after 48-hour assessment point are favorable for group A than group B.

Table (2)
Repeated one-way ANOVA within and between groups

Variables		Assessment points						P-value
		Pre-treatment	Post-1 hour	Post-6 hours	Post-12 hour	Post-24 hour	Post-48 hour	
IL-6	Group A	499.60 ±63.69	528.97 ±63.70	247.33 ±82.62	226.27 ±91.37	232.93 ±81.72	223.63 ±82.10	0.0001*
	Group B	510.46 ±59.02	548.20 ±55.94	343.20 ±109.26	352.03 ±102.12	354.26 ±102.36	345.03 ±100.95	0.0001*
	Change	10.86	19.23	95.87	125.76	121.33	121.40	
	P-value	0.496	0.219	0.0001*	0.0001*	0.0001*	0.0001*	
IL-10	Group A	618.43 ±52.50	658.03 ±56.72	351.80 ±62.74	325.73 ±63.09	329.20 ±62.97	322.36 ±63.03	0.0001*
	Group B	607.76 ±63.24	645.06 ±56.78	539.66 ±116.81	518.70 ±112.44	499.60 ±136.19	514.56 ±112.90	0.0001*
	Change	10.67	12.97	187.86	192.97	170.40	192.20	
	P-value	0.480	0.380	0.0001*	0.0001*	0.0001*	0.0001*	
Critical care observational tool	Group A	2.63 ±1.40	3.46 ±0.68	3.63 ±0.76	4.56 ±0.50	4.26 ±0.78	5.20 ±0.82	0.0001*
	Group B	3.50 ±1.68	4.46 ±1.30	3.43 ±0.50	3.60 ±0.49	4.20 ±0.66	4.50 ±0.50	0.0001*
	Change	0.87	1.00	0.20	0.96	0.06	0.70	
	P-value	0.157	0.0001*	0.237	0.0001*	0.724	0.0001*	

Data are expressed as mean ± standard deviation (SD); P-value: probability value;
*Significant (P-value <0.05)

Post-hoc test (Bonferroni test) between pairwise of pre-assessment vs. post-assessments within each group and mean differences (Table 3) revealed there were significant differences (P=0.0001; P<0.05) in IL-6 and IL-10 within group A and group B at post-1hour, post-6hours, post-12hour, post-24hour, post-48hour compared to pre-treatment, with a higher IL-6 and IL-10 change percentages in group A at post-1hour, post-6hours, post-12hour, post-24hour, and post-48hour than group B.

There were significant differences (P<0.05) in critical care observational tool within group A (Table 3) at post-1hour (P=0.0001, post-6hours (P=0.004), post-12hour (P=0.0001), post-24hour (P=0.0001), post-48hour (P=0.0001) compared to pre-treatment. In group B, there were significant differences in critical care observational tool at post-6hours (P=0.0001), post-12hour (P=0.0001), and post-24hour (P=0.002), but no significant differences at post-1hour (P=0.073) and post-48hour (P=1.000) compared to pre-treatment with improved more critical care observational tool change percentage in group A at post-1hour, post-6hours, post-12hour, post-24hour, and post-48hour (31.56, 38.02, 73.38, 61.98, and 97.72%, respectively) than group B (27.43, 2.00, 2.86, 20.00, and 28.57%, respectively).

Table (3): Post-hoc test (Bonferroni test) between pairwise of pre-assessment vs. post-assessments within each group

Variables	Assessment points					
	Pre-treatment	Pre-treatment	Pre-treatment	Pre-treatment	Pre-treatment	Pre-treatment
	vs.	vs.	vs.	vs.	vs.	vs.
	Post-1 hour	Post-6 hours	Post-12 hour	Post-24 hour	Post-48 hour	
IL-6	MD (change)	29.37	252.27	273.33	266.67	275.97
	Group A Change %	5.88%	50.49%	54.71%	53.38%	55.24%
	P-value	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*

IL-10	MD (change)	37.73	167.26	158.43	156.2	165.43
	Group B Change %	7.39%	32.77%	31.04%	30.60%	32.41%
	P-value	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*
	MD (change)	39.60	266.63	292.70	289.23	296.06
	Group A Change %	6.40%	43.11%	47.33%	46.77%	47.87%
	P-value	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*
	MD (change)	37.30	68.10	89.06	108.16	93.20
	Group B Change %	6.14%	11.21%	14.65%	17.80%	15.34%
	P-value	0.0001*	0.0001*	0.0001*	0.0001*	0.0001*
	MD (change)	0.83	1.00	1.93	1.63	2.57
	Group A Change %	31.56%	38.02%	73.38%	61.98%	97.72%
	P-value	0.0001*	0.004*	0.0001*	0.0001*	0.0001*
Critical care observational tool	MD (change)	0.96	0.07	0.10	0.70	1.00
	Group B Change %	27.43%	2.00%	2.86%	20.00%	28.57%
	P-value	0.073	0.0001*	0.0001*	0.002*	1.000

MD: mean difference

P-value: probability value

* Significant (P<0.05)

Discussion

The goal of many treatment programs is to reduce pain and, in this way, to increase functional ability. TENS was introduced into clinical practice in 1970 as an adjunct to other pain therapies. The mechanism of action of TENS is still not completely understood. The theory behind the technique of TENS is the gate-control theory of pain as postulated by Melzack and Wall [11]. It was thought that pain was largely transmitted by small unmyelinated C fibres which could be inhibited by the activity of myelinated A fibres. Stimulation of these larger A fibres could close the spinal gating mechanism in the substantia gelatinosa of rolandi and in turn can prevent painful peripheral stimuli from gaining access to higher cortical centres. The release of opiate like substances (endorphins and enkephalins) and activation of inhibitory reflex areas in the brain stem have been proposed as alternative mechanisms for the effect of transcutaneous stimulation [12].

Despite TENS having been used successfully for postoperative pain relief in a variety of surgical procedures, its role in controlling post thoracotomy pain remains controversial. Amanzio, et al. [13] in a study including 324 patients undergoing thoracic surgical procedure of different types reported that TENS was not effective in the posterolateral thoracotomy group, which produced severe pain, but was useful as an adjunct to other medications in other thoracic procedures such as muscle-sparing thoracotomy, sternotomy, pleurodesis and video thoracoscopy associated with mild to moderate pain. Frank, et al. [14] established TENS as efficacious treatment in the release of post thoracotomy pain with significant reduction of pain score and of recovery room stays, and improvement of spirometric respiratory functions in patients treated with TENS with respect to the placebo group.

Turna, et al. [15] in a study included 40 patients in TENS group and 38 patients placebo underwent surgical technique post mesothelioma reported that TENS provided is better for pain relief and comfort compared to IV PCA (Intravenous

patient-controlled analgesia) from the fourth postoperative day and forward, and this pain-reducing effect continued for at least two months postoperatively. Stratton and Smith [16] reported that TENS performed post pleurodesis provided a significant improvement of pain sensation and perception by visual analogue scale and diminishing in the levels of cytokines compared to the control group in a study covered 33 patients TENS group and 31 patients control group, and these results are in line with data of Liao, et al. [17]

Jain et al. [18] found that the TENS diminished the use of narcotics post pleurodesis with significant difference in respect to the control group in the first 48 POHs in research conducted all over 88 (45 patients TENS group and 43 patients control group). In contrast, Jellicoe and Stubbing [19] found no benefits in terms of pain relief after pleurodesis. The application of TENS neither decreased the frequency of pain nor did it significantly modify the requirements for analgesia.

Similar research supporting the present study was conducted by Erbil, et al. [20] on post pleurodesis pain and pulmonary functions, it included 60 patients in first group with TENS and 56 patients in other group without TENS. They assessed the pain with Visual analog scale and the pulmonary functions of the patients and thus concluded that TENS is advantageous for pain relief and improves the pulmonary functions, in addition there is no side effects for those patients underwent pleurodesis post thoracotomy.

Our study is intended to clarify whether TENS is an efficacious strategy in controlling inflammatory cytokines (IL 6 and IL10) post pleurodesis with the results of reducing postoperative pain intensity and analgesic drug intake, and of obtaining faster recovery function. additionally, to the above-mentioned criterion measurements as critical care observational tool and narcotic intake which can be plagued by patient's subjective reports, within the present study We also investigate the blood cytokine levels (IL 6 and IL10). The goal is to own an objective measure of the TENS considering that cytokine plays a pivotal role within the acute-phase inflammatory and reaction to surgical trauma.

Our study's data suggest that in comparison with the placebo group, the TENS group is associated with a lesser release of IL 6 and IL 10; the mean values of IL 6 and IL 10 at any time point of postoperative course are significantly lower in the TENS group than in the placebo group. The correlation between pain and cytokines has been recently studied. IL 6 and IL 10 are released from a variety of immune cells and can induce powerful hyperalgesia. Although, so far, there is no evidence that cytokines affect the excitability of sensory fibres, but it is through messages that can be relayed to the brain through activation of vagal afferents, and cutaneous nerves can be activated by cytokines. [21]

The levels of IL 6 and IL 10 are well-known to reflect the degree for surgical trauma because they're markers of inflammatory response. In our study, all groups underwent the identical surgical approach (pleurodesis through posterolateral thoracotomy) and was performed by the identical surgeon, and no differences are found in terms of resection. Thus, the sole factor that will explain the attenuated inflammatory cytokine response between the 2 groups is that the

use of TENS. However, it remains unclear on how TENS may reduce the amount of cytokine.

Bernardelli et al. [22] observed in their study all over 72 subjects (37 patients TENS group and 35 patients placebo group) that in patients submitted to different thoracic surgeries, TENS presented with advantageous effects not only on postoperative pain, but also in selected pulmonary-mechanical properties, hospital stay, drug intake and electrical activity of thoracic and girdle muscles. In theory, the positive effects of TENS on local muscle electrical activity may elicit a reduced inflammatory response with subsequent reduction of IL 6 and IL 10 as observed in our study. So far, TENS may interfere with catecholamine release via a series of changes in the endocrine properties of the muscle itself, which may lead to reduce the reuptake of some circulatory regulators including catecholamine themselves. Thus, TENS may inhibit sympathetic system via the blockade of both afferent and efferent neural pathways, and this could partly have affected our results considering that cytokine levels are also regulated by sympathetic system activity. Clinically, we observed that the patients of TENS group had significantly lower CPOT score with respect to the placebo group in any time of the postoperative course.

If the biological effect of TENS is characterized by the significant reduction of cytokine levels, postoperatively, the very powerful outcomes of TENS therapy is the improvement of pain on CPOT measurement and the reduction of analgesic consumption. Significant incisional pain can prevent condensed physiotherapy and patient's cooperation for achieving optimum respiratory care. the Depression of respiratory function represents an inability to breathe deeply, and cough effectively. This ends up in significant alveolar collapse, severe hypoxemia and big postoperative pulmonary complications. On the opposite hand, pain control obtained with TENS would allow the identical patients to tolerate more vigorous physiotherapy and spontaneously to come up with simpler cough during the postoperative period.

As an effect of the clinical effects of TENS therapy, we observed that a big difference of opioid intake in patients who received TENS treatment with relevance the placebo group within the first 6 POHs. Then, TENS treatment is related to significant reduction of non-opioid intake during the subsequent postoperative course (within 48 hs). These results are in line with other reports, Sluka and Chandran [23] revealed in their animal studies that TENS during a combination with analgesic medications enhances the analgesic effect requiring a lower analgesic dose to supply the identical analgesic effect. Thus, the clinical implication of my data suggest that TENS could also be useful to scale back the opioid and non-opioid intake reducing the chance of their side effects like respiratory depression, platelet dysfunction and gastric mucosa ulceration especially in high-risk patients.

In our study group we observed that there's no detected complication after TENS treatment. However, it's reported that some patients may experience irritation at the electrode site due to the adhesive or gel used. In theory, TENS may inhibit the output of some cardiac pacemakers and therefore the use of opiates preoperatively is thought to affect the response to TENS post-operatively. [24].

Patients free from opioids have better results with TENS compared with patients who have previously received opioid analgesia. Thus, criteria of exclusion from my study were the presence of cardiac pacemakers and/or history of opioid use. Despite these side effects, if we consider the risk-benefit ratio, the chance is extremely low for selected patients.

Our data was confirmed the previous reports regarding the efficacy of TENS in controlling post pleurodesis pain, the use of TENS over short time intervals as assumed in our study, rather than continually, may be privileged by minimizing accommodation or habituation to TENS. Significant effects of TENS after abdominal and thoracic surgeries have been demonstrated in studies in which conventional TENS was applied for short periods (from 10 to 180 min of treatment time) Köke, et al. [25] Thus, lack of correspondence to TENS sensation may help to explain the different results of our study with respect to Stubbing et al. [26] who applied TENS continuously. A second factor that may explain the conflicting results is the intensity of TENS treatment. In theory, the frequency of TENS may be the predictor factor to reach the full effectiveness of the above-mentioned gating mechanism. High-frequency and low-intensity TENS are assumed to work through segmental pain inhibition process (gate control theory). In contrast, low-frequency and high-intensity TENS are assumed to be effective by the release of endogenous opiate like substances (suprasegmental effect). Thus, the pulse duration and stimulus intensity may be a predictor factor for efficacy. Animal and human studies have shown higher analgesic effect by increasing the stimulus intensity or longer pulse duration Köke, et al. [25] Combining high frequency (80 Hz) with high stimulus intensity (250 μ s for 30 min), as occurred in our study, might act both on segmental as well as on supra-spinal levels of pain inhibition systems and therefore can prohibit larger hypo analgesic effects.

Study limitations

Our study faced several limitations as follows:

First, in our study's population, TENS were used as an additional analgesic solution. Therefore, my study was unable to reveal whether the application of TENS used as the only pain solution is efficacious to control severe post pleurodesis pain or not.

Second, our study was showed that TENS had a greater effect than placebo. However, I am not able to determinate the extent of the placebo effect in this study as I did not have a 'no TENS' control group.

Third, pain rating index was assessed by means of CPOT scale only at rest. Evaluation of pain intensity during functional respiratory tasks as cough was not performed in the current study but it will be included in future investigations.

Fourth, considering the small number of my patients, larger studies are wanted to authenticate my study results.

Conclusion

Our preliminary data showed that the efficacy of the TENS in control the post pleurodesis pain when used together with patient controlled analgesia as adjunctive therapy and supports its use in patients underwent pleurodesis through posterolateral thoracotomy, we found greater reduction of the post pleurodesis pain intensity, faster functional recovery and decreases analgesic drug intake. Furthermore, the application of TENS is safe, inexpensive and easy to use. We did not observe any side effects; thus, TENS may be particularly useful for patients that have liver or kidney diseases considering that analgesic drug are extensively metabolized mainly in the liver and predominantly excreted through the kidney. However, a comprehensive team approach to pain management, involving the surgeon, anesthesiologist, physical therapist and nurse are vital for minimizing postoperative pain, morbidity and improving patient's satisfaction.

Author Contributions

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