AVAZZIA BIOFEEDBACK ELECTRO STIMULATION TECHNOLOGY (AVAZZIA BESTTM) DEVICE VERSUS CONVENTIONAL TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) FOR SHORT TERM RELIEF OF CHRONIC MUSCULOSKELETAL PAIN: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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Objective: TENS and TENS-like devices are frequently prescribed for chronic pain management. This study determines the efficacy of conventional TENS versus Avazzia BEST TM for the management of chronic musculoskeletal pain.

Method: This prospective randomized controlled study was conducted on 60 patients in University Malaya Medical Center. Measured outcomes include immediate post-treatment pain score followed by post-treatment 24 hours pain severity and pain interference score, using visual analogue scale and brief pain inventory questionnaires. Data was analyzed using SPSS with statistical significance set at $p < 0.05$

Results: Majority of the patient (71.7%) were females with mean age of 54.1. Soft tissue injury, tendinitis or bursitis consists 61.7% of chronic pain. The baseline characteristics of patients recruited in both arms were similar ($p>0.05$). Pain score at 24 hours post-treatment was significantly lower with Avazzia BESTTM (mean VAS score 22.0 vs 46.8, $p<0.001$). There were no differences found in immediate pain score post treatment, 24 hours post-treatment pain severity and pain interference score. Based on patient global assessment of treatment satisfaction, a third of patients on Avazzia BESTTM were very satisfied with the treatment compared to 13.3% on conventional TENS. All the patients recruited were willing to continue on their current treatment.

Conclusion: Avazzia BESTTM provides better pain relief at 24 hours post treatment compared to conventional TENS

1. INTRODUCTION

Transcutaneous electrical nerve stimulation (TENS) was developed and used since the 1960s and its principles is based on the gate control theory by Melzack and Wall.[1] This involves the delivery of a constant external voltage of low frequency (1-100 Hz) and low intensity pulse current across the skin via electrodes to the nerves. Stimulation of large diameter afferents by TENS inhibits nociceptive fiber evoked responses in the dorsal horn by saturating the A and B fibers[1], blocking nociceptive transmission to the central nervous system.

However, the clinical effectiveness of TENS is inconclusive in the management of acute and chronic pain of various causes[2,3,4,5]. Nevertheless, TENS has stood the test of time and is still being widely used, complimenting pharmacological treatment aiming to improve analgesia and quality of life in chronic pain patients.

Developments in electrotherapeutic technology resulted in proliferation of TENS and TENS-like devices, but most have met with limited success[6]. A recent TENS-like device, Avazzia BEST™ (Biofeedback Electro Stimulation Technology) delivers higher frequency (1-500 Hz), high intensity, and pulses of short duration . This electrotherapy process begins with application of a probe on the treatment site. The probe transmits currents and received signals from the treated area that reflects the changes in the physical properties of the affected tissues (hence biofeedback).

These devices are US FDA cleared for symptomatic relief and management of chronic, intractable pain and adjunctive treatment in the management of post surgical and post traumatic pain[7]. Similar to conventional TENS, this device is non invasive, inexpensive, safe and can be administered by patients themselves.

Till date, there is no study done to compare the effectiveness of this device compared to conventional TENS.

2. METHODOLOGY

This is a prospective randomized controlled trial comparing the efficacy of conventional TENS versus Avazzia BEST^{TM} for 24 hours control of chronic musculoskeletal pain.

Inclusion Criteria:

All patients eligible for TENS referred by the orthopaedics department to the physiotherapy unit for pain relief, deemed suitable by physiotherapists between 1 November 2012 and 31 March 2013.

1. Age > 18years old
2. Chronic musculoskeletal pain for > 3 months and has been on some form of analgesics
3. TENS naïve patients

Exclusion Criteria:

1. Those with cardiac pacemakers and arrhythmias
2. Pregnant patients
3. Patients who has epilepsy
4. If there were additional or dosage increments in their current analgesics
5. Musculoskeletal pain over head and neck region

2.1 Sample Size

We used PS sample size software to determine our required sample size of 44. First, we determine the minimal clinically important difference in the VAS score as 20 out of 100 mm as a significant change from baseline[8]. A VAS score standard deviation of 23 is based on a pilot sample of 50 current patients. We set an α of 0.05 and power 0.8. The required sample size allowing 10% dropout was calculated to be 25 for each arm.

2.2 Randomizations

The eligible patients were given information sheet detailing the electrotherapy and noting its potential benefits. After obtaining consent, they were randomized into 2 groups- Avazzia BEST™ or conventional TENS by means of sealed envelopes (block of 6)

2.3 Interventions

2.3.1. Avazzia BEST™

Affected pain area is identified and 'painted' using a Y electrode with the device switched to the deep stimulate mode with a frequency of 30-300Hz, The electrode head is glided repeatedly over the skin to identify the 'active site'. This is the site whereby a change in the

- impedance of the electrode moving over skin
- sudden change in the humming sound emitted by the device
- Sensation of the area

This process was repeated until the gliding friction decreases or the humming sound equalizes; maximum treatment time 5 minutes. This was then followed by placing 2 self adhesive pads (2"x2") over the area for treatment with repetitive strain injury (RSI) mode for 20 minutes. RSI mode utilizes frequency range of 1 Hz to 500 Hz, with current delivery adjusted to patients comfort.

2.3.2 Conventional TENS

Two self adhesive pads (2"x2") were applied to the affected areas. Models used were ELPHA II 3000, with programme set to P1 whereby currents delivered was a continuous stimulation with frequencies (1-150 Hz), with pulse width of 50–250/ second potentially achieving painless paraesthesia in the part of the body concerned. Duration of treatment was 20 minutes, with currents adjusted to patients comfort.

Adhesive pad placements and device operations were performed by trained therapists in both devices.

2.4 General study protocol and follow ups

Data for this study are collected using a standardized case report form.

The following data was obtained on the day of recruitment

1. background demographic data
2. type of musculoskeletal pain
3. brief clinical history
4. ongoing analgesic including quantity and types

Prior to the intervention, a baseline pain score via visual analogue scale (VAS) and Brief Pain Inventory Index (BPI) questionnaire were filled up by the patients. BPI records pain intensity from 0-10, at each parameter on 'pain now', and pain 'at its worst', 'least', and 'average' over the last 24 h. This tool also assesses how much pain interferes with seven aspects of life: (1) general activity, (2) walking, (3) normal work, (4) relations with other people, (5) mood, (6) sleep, and (7) enjoyment of life.

After undergoing allocated treatment, side effects during treatment and immediate pain intensity was recorded using visual analogue scale (VAS). Pain intensity was measured using a 100-mm VAS translated both in English and Bahasa Melayu, anchored at 0 mm with the words 'no pain' and at 100 mm with the words 'worst pain imaginable'. Following treatment, patients performed exercise and physical trainings before they were allowed home with continuation of their existing analgesics.

Post treatment 24 hours, telephone calls were made to record the BPI and Patient Global Assessment to Treatment score (PGAT). This administration of telephone interview was done by a research assistant who was blinded to the interventions.

This study protocol had received approval from University Malaya Medical Center Research Ethics Committee, NO 943.17. Recruitment and intervention took place at the physiotherapy unit of the hospital.

2.5 Statistical analysis

Completed data were analyzed using SPSS version 16.

Descriptive analysis was performed on data for demographics, pain severity and quality of life. Categorical data is presented as frequencies (percentages). Normally distributed (parametric) data is expressed as mean and standard deviation.

Cross-tabulation with chi square test was done for categorical data to look for statistical significance. Data showing normal Gaussian distribution will be tabulated with the parametric chi square test whereas data with skewed distribution will be tabulated with non-parametric chi square test e.g. Fischer's exact test.

Continuous data was analyzed with student t test for parametric data and Mann-Whitney U test for non parametric data.

Level of significance is set at $p<0.05$

3. RESULTS

An initial total of 67 patients were recruited. However, 3 patients identified did not consent to participate. Subsequently, 3 patients from the conventional TENS arm and 1 patient from Avazzia BEST™ arm were dropped as the telephone call follow ups were not completed. Thus, a total of 60 patients were included in the study with 30 patients in each arm.

Table 1: Patients Baseline Characteristics

	Conventional TENS n=30	**Avazzia BEST ™ n=30**	**p-value**
Demographics			
Age*	51 (17.2)	57 (9)	0.10
Ethnicity‡			
Malay	13 (43)	9 (30)	
Chinese	5 (17)	5 (17)	
Indian	12 (40)	16 (53)	0.52
Gender‡			
Male/ Female	9(30)/ 21(70)	8(27)/ 22(73)	0.70
Education level‡			
Primary/Secondary	17 (57)	20 (67)	
Tertiary	13 (43)	10 (33)	0.43

* mean (SD)
‡ no (%)

Table 1 showed that the majority of chronic musculoskeletal pain patients were females, aged above 50, encompassing the 3 main ethnic group of the local population and had at least primary or secondary education levels. The patients' baseline data in both arms were statistically similar as depicted by the p values.

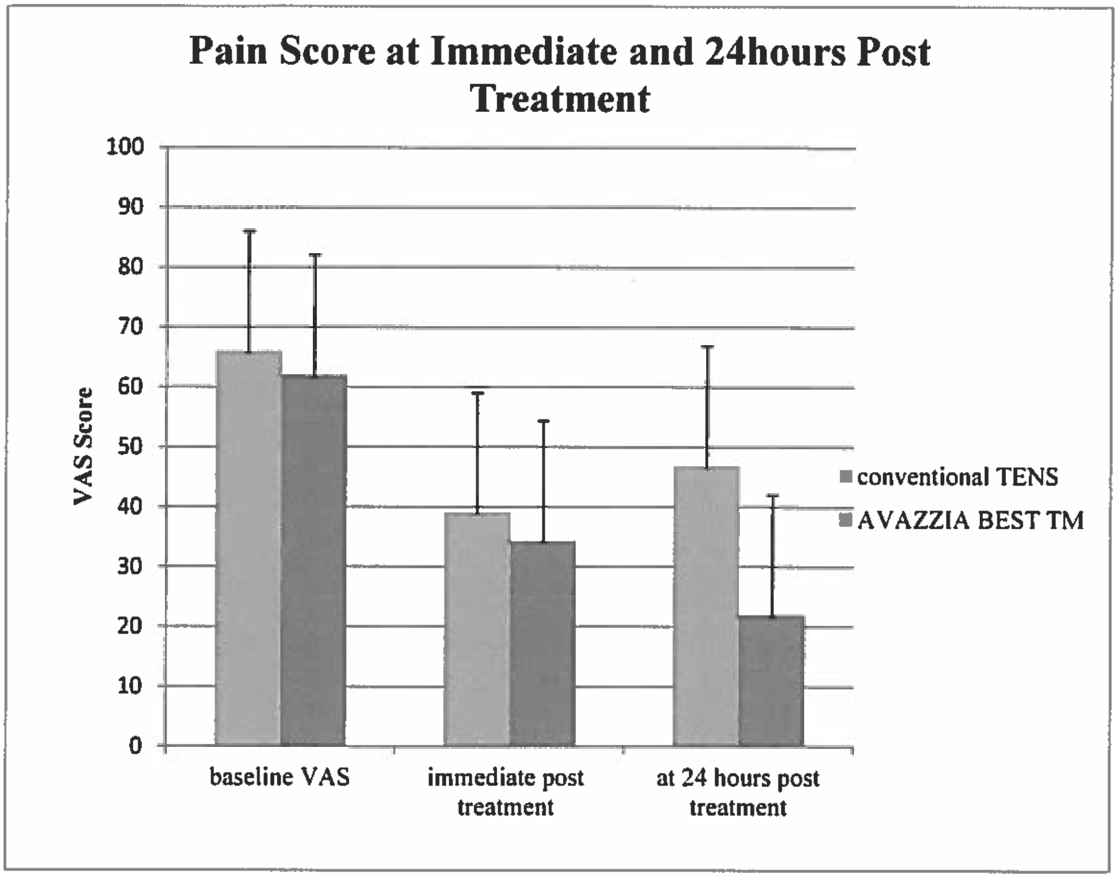
Table 2: Baseline Pain Data

	Conventional TENS n=30	Avazzia BEST™ n=30	p-value
Baseline Pain Data			
Diagnosis‡			
Back pain (Osteoarthritis of vertebral column)	3(10)	4(13)	
Frozen shoulder (Adhesive capsulitis)	7 (23)	9 (30)	
Soft tissue injury	10 (33)	6 (20)	
Tendinitis/bursitis	10 (33)	11 (37)	0.69
Duration of pain‡			
3-6months	15 (50)	17 (57)	
6-9months	4 (13)	3 (10)	
9-12months	3 (10)	0	
>12months	8 (27)	10 (33)	0.32
Number of analgesics‡			
1	20 (67)	18 (60)	
2	10 (33)	10 (33)	
3	0	2 (7)	0.35
Pretreatment VAS pain score*	66 (18)	62 (22)	0.45
Pretreatment Pain Severity Score*	5.18(1.92)	5.4 (2.06)	0.55
Pretreatment Pain Interference Score*	4.8(2.3)	4.9 (2.06)	0.81

* mean (SD)
‡ no (%)
Number of analgesics – any/combinations of paracetamol, NSAIDS, COX2 inhibitors and tramadol

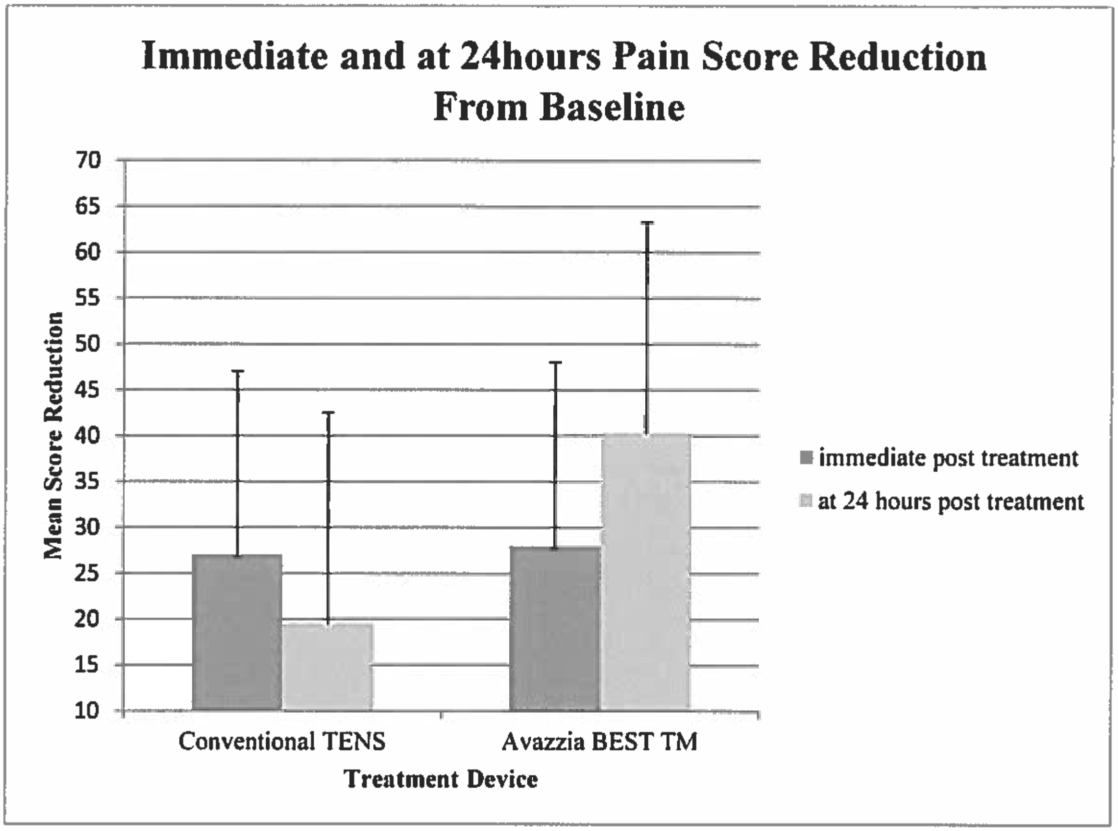
There were 4 main causes of chronic musculoskeletal pain of which majority suffered from tendinitis or bursitis. Most patients had pain for 3-6 months. Majority is taking only a single type of analgesia. The baseline pain characteristics and pain scores were also comparable between the two arms.

Figure 1



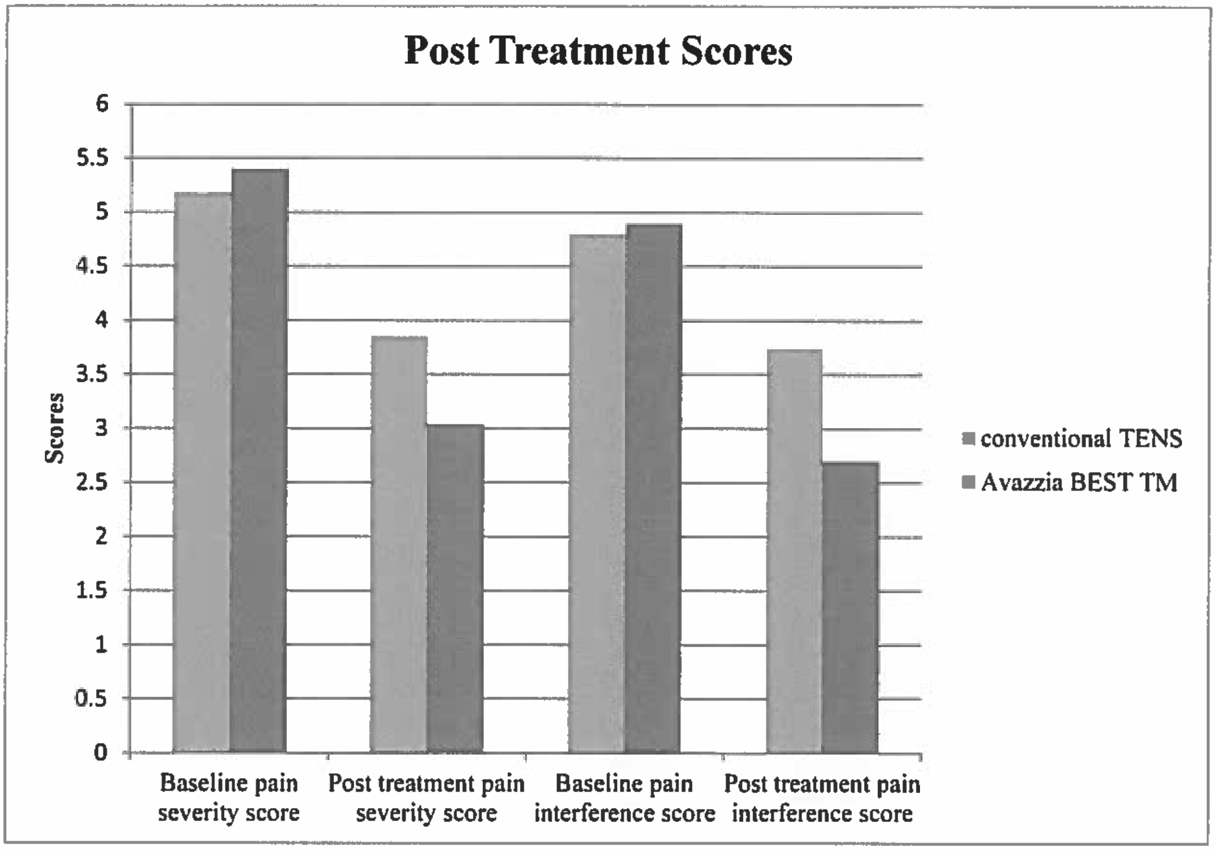
An immediate post treatment assessment of pain score showed that the mean pain score was not statistically different between patients being treated with Avazzia BEST^{TM} (mean 34.3 ± 26.60) compared to conventional TENS, (mean 39.0± 23.86, p=0.48). However mean pain score at 24 hours post treatment was noted to be significantly lower in Avazzia BEST^{TM} with an average of 22.0 ± 19.37 compared to conventional TENS with a mean of 46.0 ±20.86 (p <0.001) It was also found that in the conventional TENS arm, the 24 hours post treatment mean pain score was higher than the immediate post treatment mean (46.0 ± 20.86 vs. 39.0 ± 23.86).

Figure 2



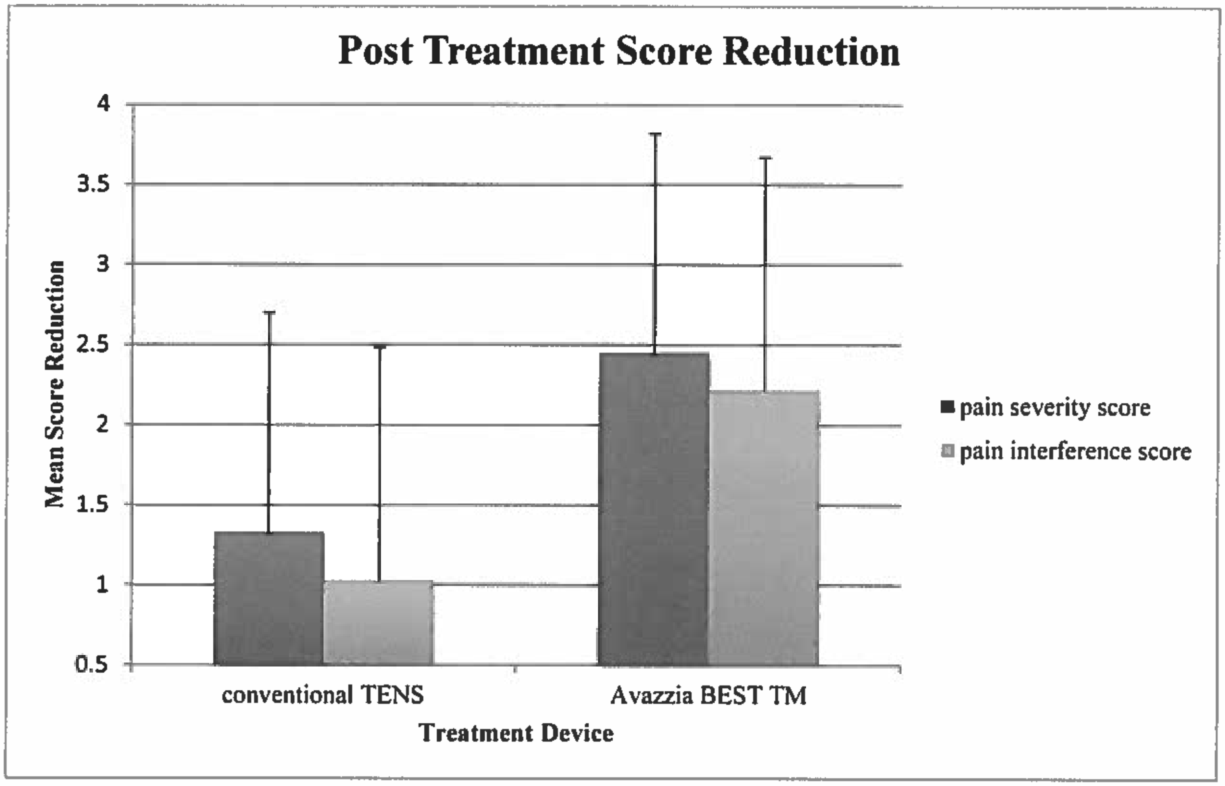
Immediate post treatment pain score reduction showed that conventional TENS achieved a mean score reduction of 27.0 ± 20.00 and Avazzia BEST™ had a score reduction of 28.0 ± 22.30 which was not statistically significant ($p = 0.90$). However, the mean score reduction at 24 hours post treatment was significant, recorded at 19.5 ± 21.39 for conventional TENS and 40.3 ± 24.88 for Avazzia TENS ($p < 0.001$).

Figure 3



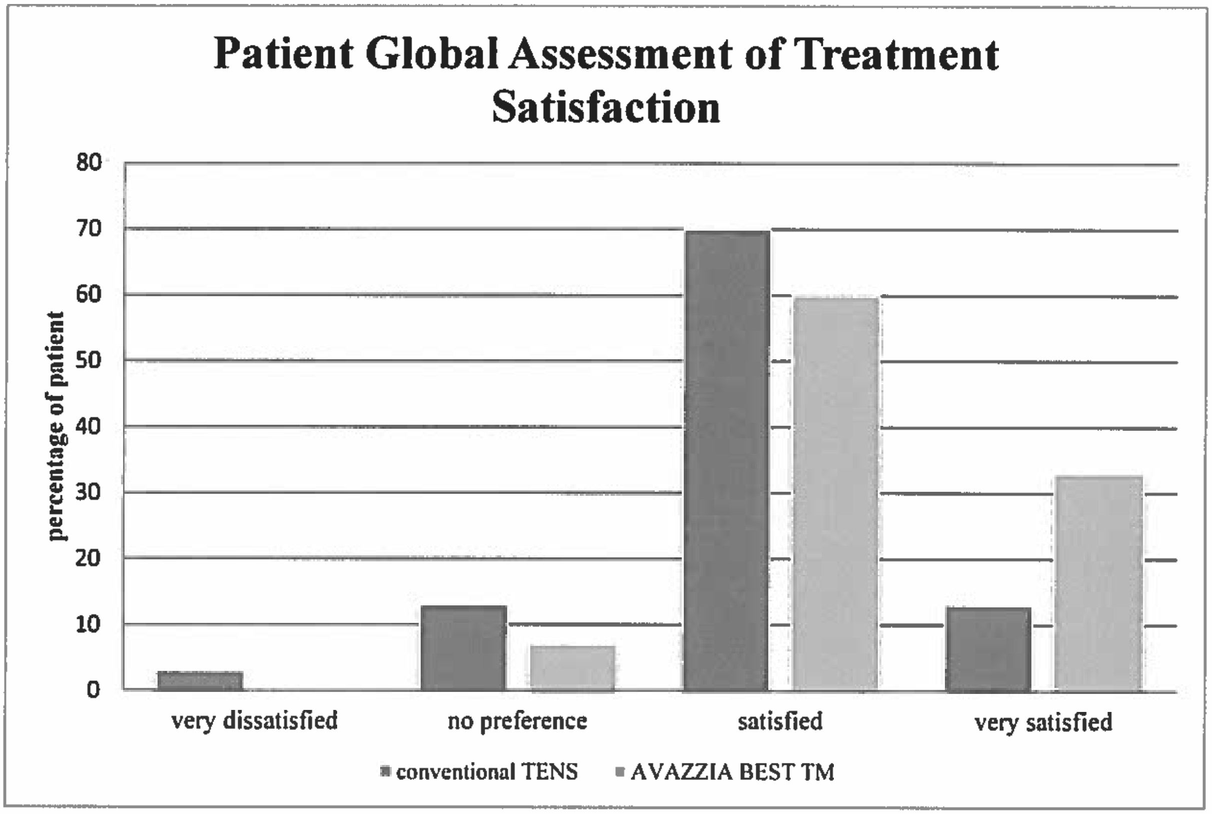
The recorded post treatment mean pain severity score was 3.9 ± 1.85 in the conventional TENS group and 3.0 ± 1.88 in the Avazzia BEST™ group (p = 0.01). Average pain interference score for conventional TENS and Avazzia BEST™ were 3.7 ± 2.89 and 2.7 ± 1.86 respectively with a p = 0.06. The scores post treatment were not statistically different between the two groups

Figure 4



This graph depicts the difference in pain severity score and pain interference score taken before and after treatment. The above figure showed the mean score reduction for pain severity and pain interference score. The average pain severity score reduction was significantly higher in Avazzia BEST™, 2.5 ± 1.58 vs. conventional TENS, 1.3 ± 1.43, ($p = 0.01$). In terms of drop in pain interference score, Avazzia BEST™ recorded a more significant drop with mean of 2.2 ± 1.30 compared to conventional TENS (mean 1.0 ± 1.31, $p < 0.001$)

Figure 5



Patient global assessment of treatment satisfaction results found that 33% of Avazzia BEST™ patients rated 'very satisfied' with the overall treatment compared to only 13% in the conventional TENS group. There was 1 patient in the TENS group who was 'very dissatisfied'. In general, a total of 93% of patients on Avazzia BEST™ and 83% from conventional TENS were beyond "satisfied".

There were no reported adverse effects in both treatment arms. All patients were willing to continue with their respective treatment.

4. DISCUSSION

Avazzia BEST™ is a novel device under the umbrella of TENS-like devices with no preexisting data on its effectiveness. We chose conventional TENS as a comparator as the currents emitted is in the high frequency range typically above 100 Hz with pulse width of 50-80 ms to match with the high frequency of Avazzia BEST™[8].

This study aimed to assess the efficacy of Avazzia BEST™ technology in alleviating pain and functional status improvement in chronic musculoskeletal pain patients after 24 hours following a single dose treatment. Our study of device efficacy is in accordance to Sluka et al, where a change in baseline VAS of 20 mm was considered clinically significant[8].

Firstly, immediate mean pain score reduction after treatment was comparable between the 2 groups. The current frequency of Avazzia BEST™ device which is high in frequency and high intensity pulses is as effective as conventional TENS in achieving immediate analgesic effects. The immediate pain relief achieved can be explained by the decrease in nociceptive input to the dorsal horn by means of selectively stimulating large Aα and Aβ fibers resulting in activation of inhibitory interneurones in lamina II[1]. A combination of exercise and functional training is incorporated into the management of chronic pain. Hence, Avazzia BEST™ can be utilized as an adjunct to modulate and reduce pain prior to the commencement of active exercise to optimize gain during their therapy.

However, the mean pain score at 24hours post treatment was noted to be significantly lower in Avazzia BEST™ with average of 22.0 ±19.37 as compared to conventional TENS 46.0 ±20.86 with $p < 0.001$. In terms of pain score reduction at 24 hours from baseline VAS, patients on Avazzia BEST™ recorded a significant drop of 40.3 ± 24.88, p value compared to conventional TENS with a reduction of only 19.5 ± 21.39, p value < 0.001 This observation can possibly be explained by the delivery of high frequency currents from TENS devices modulates the release of nitric oxide, endorphins and neuropeptides from the central neural circuitry into the blood stream[8]. A few animal model studies has shown that excitatory neurotransmitters, glutamate and substance P are decreased in the spinal dorsal horn, with blockade of δ-opioid receptors in the spinal cord reversing the antihyperalgesia produced by high frequency TENS[9,10].Despite achieving a reduction in pain score by conventional TENS, application of Avazzia BEST™ technology fare better in the magnitude of pain reduction and a more sustained antihyperalgesia effect following treatment.

In human subjects following administration on high frequency TENS, it was found that there was a time dependent increase in concentrations of β-endorphins in the circulation and cerebrospinal fluids, also rise in methionine enkephalin in cerebrospinal fluids[11,12]. A longer duration of treatment for Avazzia BEST™ which included application of a probe prior to adhesive pad may confer additional treatment effect. The reduction in skin impedance achieved by moving electrode over skin can theoretically results in deeper current penetration into tissues.[13]A constantly changing waveform emitted by Avazzia BEST™ high speed microprocessor during contact with skin could improve the analgesic effect. It is usually recommended that current amplitude and pulse duration of TENS devices should be constantly adjusted when the sensation decreases[14].

Taking analgesics into consideration, there is pharmacological evidence that patients and animal models tolerant to opiods achieved a poorer pain control with TENS[15,16]. In our study there were no subjects on morphine, however we do not account oral tramadol, a weak μ opiod receptors antagonist to be influencing the results in the conventional TENS group. Oral tramadol is not the first line or a frequently prescribed analgesic for musculoskeletal pain in our settings.

The extended analgesic effect is further supported in this study by a statistically significant drop in pain severity score in patients whom received Avazzia BEST™ with a mean reduction of 2.5 ± 1.58 compared to conventional TENS 1.3 ± 1.43, p value= 0.005. In terms of drop in pain interference score, Avazzia BEST™ recorded a significantly larger drop with mean 2.2 ± 1.30 compared to conventional TENS 1.03 ± 1.31, $p < 0.001$. The reduction in pain interference score is reflected in improvement in quality of life over 24 hours, achieved even after 1 dose of treatment.

In a number of studies done on arthritic patients, higher frequency TENS has shown to increase joint function.[17,18,19] Once the pain is controlled, patients are able to perform active exercise regimes, activities of daily living and return to work. This is particularly important in our clinical settings where TENS devices are not provided for the patient for home usage.

Each subsequent visit to the physiotherapy unit utilising Avazzia BEST™ treatment can potentially provide them with a more optimum pain control, at least for the next 24 hours as shown in this study.

Scoring of global assessment in treatment satisfaction scale can aid in determining treatment options which they perceived as personally meaningful[20]. Majority of the patients in both arms were generally "satisfied and very satisfied" and up to 93% of patients on Avazzia BEST™ scored beyond satisfied. This is in keeping with patients' response to treatment in terms of improvement in pain and physical functioning can be deduced by measures of treatment satisfaction[20].

4.1 Limitations and Recommendations

Firstly we recognized that the management of chronic pain patients is a complex process and any treatment is likely to have limited benefits. Moreover, this study provides a single dose treatment with followed up only for 24 hours in a group of chronic pain patients. According to meta analyses, most of the TENS study done previously spans over treatment duration of at least 10 days to 6 weeks, with a few underpowered single use study[21]. Although there is a promising effect from Avazzia BEST™, the long term pain relief is yet to be elucidated. Thus a future study on this device with a longer treatment regime will definitely add value to this current study.

Secondly, patient selection for TENS treatment is according to physiotherapists' assessment. Although not involved as a researcher, this has confined patients' recruitment. Future studies should include musculoskeletal pain of other origins such as osteoarthritis, rheumatoid arthritis and fractures.

Thirdly, we selected Brief Pain Inventory (BPI) questionnaires in attempt to measure outcome in pain and functional improvement in this study. This is because our patients' demographics encompassed the 3 main ethnicity in Malaysia, therefore we require a questionnaire which is validated in Bahasa Melayu[22] and English, simple to understand and has an easy telephone administration for this study. The BPI assessment tool, although good in capturing pain interference in mood, sleep, and enjoyment of life, but is incomplete in areas of emotional functioning. The Beck depression index or the 5 questions from SF36 is recommended to complete the IMMPACT recommendation for pain assessment in future study[23].

5. CONCLUSION

Avazzia BEST^{TM} demonstrated a marked improvement in VAS score with a significant reduction in pain severity and pain interference score 24 hours post-treatment. Although the effect of a single dose treatment with this device is promising, the long term efficacy is yet to be elucidated.

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