Effect of transcutaneous electrical nerve stimulation on renal tissue perfusion and hemodynamic stability for patients with hypovolemic shock: A randomized controlled trial

Asmaa Aly Mahgoub [(1)], Sanaa Saber Mohamed [(2)], Ghada Shalby Mahran [(3)], Manal Mohamed Abdel-Naeem [(4)], Mostafa Samy Abas [(5)], Alaa S. Abd-Elkader [(6)], Alaa Ali M. Elzohry [(7)], Ahmed Talaat Ahmed Ali [(8)]

(1) Assistant professor, Critical care and emergency nursing Department, Faculty of Nursing, Assiut University, Assiut, Egypt. Email: Asmaa_sara16@aun.edu.eg.
(2) Lecturer, Critical care and emergency nursing Department. Faculty of Nursing, Sohag University, Sohag, Egypt. Dr.sanaa_saber@yahoo.com
(3) Assistant professor, Critical care and emergency nursing Department, Faculty of Nursing, Assiut University, Assiut, Egypt. Email: ghada.mahran@nursing.aun.edu.eg.
(4) Assistant professor, Critical care and emergency nursing Department, Faculty of Nursing, Assiut University, Assiut, Egypt. Email: drmanalcritical@aun.edu.eg.
(5) Associate professor, Anesthesia and intensive care Department, Faculty of medicine, Assiut University, Assiut, Egypt. Email: mostafasamy@aun.edu.eg.
(6) Lecture, Clinical pathology Department, Faculty of medicine, Assiut University, Assiut, Egypt. Email: Alaa57.fox@aun.edu.eg.
(7) Consultant of Anesthesia, King Saud University (KSMC), KSA. Email:alaa.zohiry@hotmail.com
(8) Lecturer, Anesthesia and intensive care department, Faculty of medicine, Assiut University, Assiut, Egypt. Email: talaat83@aun.edu.eg.
Correspondence should be addressed to Asmaa Aly Mahgoub
Email: asmaa_sara16@aun.edu.eg
Postal address: Critical care and emergency nursing Department, Faculty of Nursing, Assiut University, Assiut, Egypt..

Abstract

Background: Transcutaneous electrical nerve stimulation (TENS) is widely practiced method to increase blood flow in clinical practice as some authors have observed that, in addition to its analgesic effects, TENS can alter skin temperature and increase blood flow. **Objective:** Was to evaluate the effect of transcutaneous electrical nerve stimulation application on the renal tissue perfusion and hemodynamic stability for patients with hypovolemic shock. **Methods:** A prospective, single-blind, randomized, controlled trial was conducted as patients were randomized into two groups (active TENS (intervention group) and sham TENS (control group). Active TENS group received resuscitation protocol and transcutaneous electrical nerve stimulation while sham TENS group received resuscitation protocol only. Data was collected from ICU. Improvement of renal tissue perfusion was considered the primary outcome and secondary outcomes was improvement of hemodynamic parameters. **Results:** TENS application had caused a highly statistical significant change in serum creatinine and NGAL test (74.43 ± 7.16 in intervention group versus 114.48 ± 13.6 2 in control group) and (7.35 ± 0.7716 in intervention group versus 20.76 ± 2.11 in control group (P = 0.007 & P= 0.000) respectively. There was highly statistical significant difference before treatment and after treatment regarding urea, creatinine and NGAL test in the control group (P= 0.002 & P= 0.006& P= 0.000) respectively and there was highly statistical significant difference before treatment and after treatment in TENS group regarding to serum creatinine (P= 0.003). **Conclusion:** Application of transcutaneous electrical nerve stimulation had significant improvement for renal tissue perfusion and hemodynamic parameters. **Recommendation:** TENS should be included as one of the ICU therapeutic modalities to improve patient's outcomes.

Keywords: Hemodynamic stability; Hypovolemic shock; Renal tissue perfusion; NGAL; Transcutaneous electric nerve stimulation.

Introduction

Transcutaneous electrical nerve stimulation (TENS) consists of a generic application of low-frequency, pulsed electrical currents transmitted by electrodes through the skin surface to stimulate the primary afferent pathways (peripheral nerves) to produce various physiological effects. **(Dubin et al., 2018)**

Stimulation (TENS) is a practical and useful therapy and mainly known for its analgesic action. It is a non-pharmacological, non-invasive, inexpensive, easy to use and widely applied therapeutic modality used in clinical practice. The common electrical pulses emitted by TENS devices are described as monophasic rectangular, balanced asymmetrical biphasic rectangular, or symmetrical biphasic rectangular;

the biphasic pulses are the most commonly used. (Cecconi et al., 2014, Ince, 2017 and AFP Machado, et al., 2012)

Since 1965, TENS has become known worldwide and is also considered to be one of the most common therapeutic resources used in clinical practice for the relief of chronic and acute pain. However, in recent decades, some authors have observed that, in addition to its analgesic effects, TENS can alter skin temperature and increase blood flow. (Atalay, Yilmaz, 2009& Chauhan, 1994)

This observation led many studies to focus on the effect of TENS on the peripheral vascular system, showing increases in blood flow (AFP Machado et al., 2012). It has been suggested that transcutaneous electrical nerve stimulation (TENS) could reduce the sympathetic activity by reducing pain). On the other hand, some studies have reported that TENS may affect the autonomic nervous system by reducing over-activity of the sympathetic nervous system, even in the absence of pain) (Gangui et al., 2017). Among the therapeutic applications of TENS are pain relief, temperature alteration, and blood flow increase (Machado et al., 2012). Transcutaneous electrical nerve stimulation (TENS) is widely practiced method to increase blood flow in clinical practice (Kamali et al., 2017).

It is clear that stimulation applied to an organism impacts its endocrine and autonomic nervous systems. This impact may change cardiovascular function and result in blood flow alterations. According to the best available knowledge, however, the best location of stimulation to achieve optimal blood flow has not yet been determined. We therefore decided to study the effect of TENS application on the renal tissue perfusion and hemodynamic stability in patients with hypovolemic shock. (Ishikawa et al., 2012)

The NGAL Test is a particle-enhanced turbid metric immunoassay for the quantitative determination of neutrophil gelatinase-associated lipocalin (NGAL) in human EDTA plasma for testing on automated clinical chemistry analyzer. The main Indication for Use: An NGAL test as an aid in the risk assessment for the development of stage II or III acute kidney injury (AKI) within 1 day of patient assessment in patients in the intensive care unit (ICU) who are hypotensive (MAP<70 mmHg) and/or receiving vasopressor support providing physicians the opportunity to intervene early in order to limit the extent of renal injury (Kamali et al., 2017).

The critical care nurses determine the parameters and the duration of treatment, depending on the patient's tolerance. The nurses positioning the patient comfortably, exposing the treatment area for electrode placement. Prepare the patient's skin for electrode pad placement .Explain to the patient the expectations for duration of treatment. Instruct the patient should feel a sensation or tingling during treatment, but not pain. Monitoring vital signs and hemodynamics parameters continuously to evaluate the effect of TENS. (Faghih, 2013) Therefore decided to study the effect of TENS application on the renal tissue perfusion was using The NGAL Test and hemodynamic stability using vital signs in patients with hypovolemic shock.

Subjects and methods

Research design: randomized controlled trial was conducted in this research.

Setting: Data was collected from general and obstetric intensive care units of Assiut University hospitals. The general ICU includes four rooms, each room includes 5 beds while obstetric ICU includes three rooms, one room includes7 beds and the other contains 5 beds. The research was reviewed and approved by the Ethics Committees in faculty of medicine at Assiut University (IRB no: 17300312) and has therefore been performed in accordance with the ethical standards of the Declaration of Helsinki. It was also registered in the records of protocols system ClinicalTrials.gov (NCT04069871 identifier)

Subjects: purposive sample of 60 hypovolemic shocked Patients who were eligible to the study (adult 18 years or older, GCS 15 and who were free of acute or chronic pulmonary disease) were identified and recruited by the investigator after being informed about the study .the researchers excluded from the study any patient with one or more of the following conditions: Renal insufficiency requiring dialysis, received a previous renal transplantation, moderate to severe AKI, pregnant women, progressive

cancer, skin disorder making it impossible to use TENS and presence of a pacemaker/defibrillator.

Assessment phase

After baseline assessment, they were randomized into two groups (Active TENS versus Sham TENS) .Randomization occurred through data generated by random.org online software Haahr & Haahr 1998. The sequence of numbers was generated by researchers "blind" to the study after the selection of patients for eligibility criteria and disclosed prior to the start of the intervention program **Figure (1).**

Ethical consideration: written informed consent was obtained from all patients prior to their inclusion in the study and after they had been informed of the benefits and risks of the investigation.

Research hypothesis

The renal tissue perfusion and hemodynamic parameters for patients who received active TENS would be significantly improved than patients received sham Tens.

Tools of data collection:-Three tools were used in this study after local and international review of literature (Cecconi et al., 2014 &AFP Machado et al., 2012 & Dailey , 2013& Gangui, 2017)

Tool I: Patient's assessment tool was used to assess the patient conditions to form base line data. This tool contained the assessment of patient's profile that included Patient's code, sex and age and assessment of the patient's clinical data which included medical diagnosis, acute physiological and chronic health evaluation (APACHE) Score ,body mass index (BMI) length of ICU stay, and length of hospital stay.

Tool II: - Assessment of hemodynamics and perfusion parameters .This tool consists of vital signs, spo2, capillary refill, and skin turgor, skin mottling and central venous pressure to assess patient's hemodynamics and vital signs.

Tool III: - patient's outcomes assessment tool included primary and secondary outcomes**.** This tool consists of renal function test as urea, creatinine and NGAL to evaluate renal perfusion

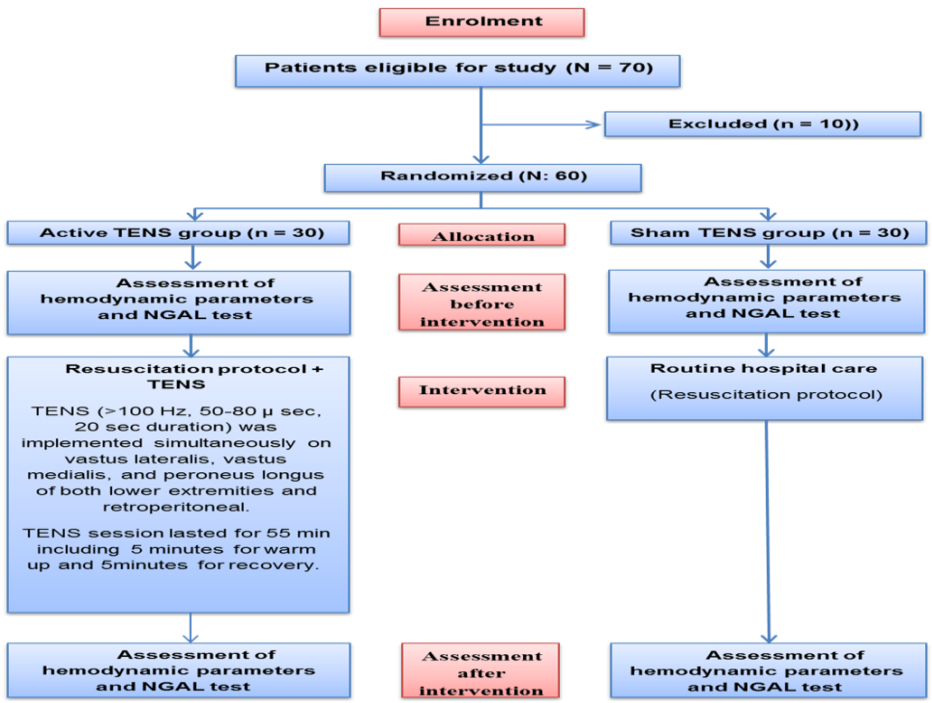

Fig. 1. CONSORT flow diagram of randomized controlled trial.

Implementation and Intervention phase

Both active TENS and sham TENS group received routine ICU care included Insertion of wide bore cannula, mostly CVP catheter, administration of oxygen therapy using different tools (simple mask up to CPAP mask) if patient is conscious and mechanical ventilation if patient was indicated, blood sample was taken for complete lab. investigations and evaluation of ABG, resuscitations firstly by fluids (crystalloid) and by backed RBCs transfusion in case of bleeding like hemorrhagic shock, correction of metabolic acidosis by NaHco3 when indicated, administration of positive inotropes like noradrenaline, adrenaline and dopamine when indicated (it is given in infusion form).

Two nurses involved in the study and trained to perform the procedures in this study. Nurse 1 was responsible for the evaluation of primary and secondary outcomes in all patients in the study and was blinded know if the patient received the active or sham TENS. Nurse 2 was responsible for administering TENS in all patients in the study. Only Nurse 2 knew if the patient received the active or sham TENS. Nurse 2 instructed patients not to report their perceptions during the TENS administration to the nurse conducting the assessments.

Application of Active TENS (intervention group)

The use of active TENS was conducted with a Neurodyn Portable TENS unit (IBRAMED) with two channels. The generator emits asymmetric, balanced, biphasic pulses. Two self-adhesive electrodes (VALUTRODE - 9 × 5 cm) were placed in parallel on retroperitoneal site in both sides with a 6-cm distance between them and on vastus lateralis, vastus medialis, and peroneus longus of both lower extremities. The TENS application was three sessions during the first 24 hour of resuscitation (one session each shift, each session take 55 minutes) at a frequency of 100 Hz and a pulse duration of 100 microseconds. The intensity (amplitude) was increased until the patient is able to feel a strong but comfortable tingling sensation. Patients were asked about the intensity of the TENS every 10 minutes. In the case of sensory habituation, the amplitude was increased until the individual again feels a strong but comfortable tingling sensation.

Application of Sham TENS (control group)

The use of the sham TENS were performed with an apparatus identical in appearance to the active TENS (Neurodyn Portable TENS, IBRAMED) that is specially designed for this study. The device remains active only during the first 30 seconds of application. After the initial 30 seconds, the current amplitude was gradually decreased over 15 seconds until it reaches the zero value, thereby interrupting the emission of electric current. The unit remained inactive for the rest of the application. The sham TENS device displays a light during the entire application, indicating to the patient that the device is active. Patients were informed that TENS may cause a slight tingling sensation or no sensation during the procedure.

They were asked every 10 minutes about the intensity of TENS, reinforcing the idea that lack of sensation occurs in most cases due to habituation to the electric current. Patients were observed throughout the administration of TENS. The mode of application of the electrodes and the duration of the sham TENS was the same as described in the active TENS.

Evaluation phase

Outcomes measurement: Improvement of renal tissue perfusion was considered the primary outcome and Secondary outcomes was improvement of hemodynamic parameters.

To evaluate renal tissue perfusion, NGAL test was used which is one of the most promising and best-studied acute kidney injury (AKI) biomarkers.

Two peripheral blood samples were withdrawn (4 ml each) after good sterilization for all study participants for NGAL measurements (the first sample was taken within the first 2 hour of resuscitation and the second sample was taken after 24 hours of resuscitation). The sera were separated and stored at -20 c. Human NGALELISA kit (Bioassay Technology Laboratory Co.,Ltd) (Catalog No : E1719Hu) was used for quantitative measurement of serum human NGAL levels. The assay was performed according to the manufacturer's instructions.

The assessment of hemodynamic parameters were monitored by 24-hrcardiac monitor. The monitor was attached to the patient immediately after ICU admission to measure blood pressure, heart rate, oxygen saturation and body temperature (using a thermistor probes placed under axilla for five minutes) over the 24 hours at regular intervals according to ICU

protocol. All data were recorded on a digital recorder, with subsequent analysis being carried out by trained professionals.

2.3. Statistics

All analyses were performed using SPSS Statistical Software (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA). Continuous variables were presented as mean ± SD, and categorical variables, as frequencies. Differences between the groups at baseline were evaluated by an unpaired t test or the Mann–Whitney test for comparison of continuous variables. The Chi-square test or Fisher's exact test was employed to compare categorical variables. Analyses were performed by comparing baseline and post intervention variables in the subgroups (active TENS versus sham TENS).

Results

Personal and clinical data of the patients in the two groups were evaluated. Results showed that there were no a significant statistical difference between the two groups in relation to and clinical characteristics (P value > 0.05) **(Table 1).**

The application of TENS didn't show any significant change on heart rate (107.83 ± 3.90 in active TENS Versus 104.17 ± 4.29 in sham TENS) (P value > 0.05), whereas the resuscitation protocol resulted in a significant reduction in HR within the two groups (P value < 0.05). In addition, TENS didn't result any significant change on MAP (73.93 ± 2.62 in active TENS versus 73.80 ± 3.28 in sham TENS), whereas the resuscitation protocol resulted in a significant increase in MAP within the two groups (P value < 0.05).Moreover, TENS didn't cause any significant effect on SPO2 (98.97 ± 0.21in active TENS versus 98.53 ± 0.34in sham TENS), whereas the resuscitation protocol resulted in a significant increase in SPO2within the two groups (P value < 0.05). Also, there was not a significant effect of TENS on CVP (11.10 ± 0.64in active TENS versus 10.97 ± 0.62 in sham TENS), whereas the resuscitation protocol resulted in a significant increase in CVP within the two groups (P value < 0.05) **(Table 2).**

The application of TENS didn't show any significant change on tissue perfusion parameters (P-value > 0.05) except CO2 gap (7.40 ± 0.58 in active TENS versus 4.30 ± 0.43 in sham TENS) but within the groups there was a significant difference in CO2 gap and tissue perfusion index (P value < 0.05) **Table (3)**.

The application of TENS didn't show any significant change on skin turgor and peripheral pulse (P-value > 0.05), whereas the resuscitation protocol resulted in a significant change in skin turgor and peripheral pulse within the two groups (P value < 0.05) **Table (4).**

TENS application had caused a highly statistical significant change in serum creatinine and NGAL test (74.43 ± 7.16 in active TENS versus 114.48 ± 13.6 2 in sham TENS) and (7.35 ± 0.7716 in active TENS versus 20.76 ± 2.11 in sham TENS) (P = 0.007 & P= 0.000) respectively. There was highly statistical significant difference before treatment and after treatment regarding urea, creatinine and NGAL test in the control group (P= 0.002 & P= 0.006& P= 0.000) respectively and there was highly statistical significant difference before treatment and after treatment in TENS group regarding to serum creatinine (P= 0.003) **Table (5).**

Table (1): Distribution of personal and clinical data of the active TENS (ATENS) and sham TENS (STENS) groups, (total patients' number = 60):-

Personal and clinical data	ATENS(n= 30)	STENS(n= 30)	P-value
	mean	mean	
Height ,cm	170.52	171.34	0.40
Weight ,kg	81.6	80.1	0.52
BMI	26.55	26.33	0.60
APACHE Score (Mean ± SE)	8.53±3.51	7.60±3.81	0.33
ICU stay: (days) Mean ± SE	2.77 ± 0.30	2.73 ± 0.28	0.879

Ns: Data is represented as number (percentage) or mean ± standard deviation where appropriate

- There is no significant difference P-value >0.05 *significant difference at P-value <0.05

-Independent samples t-test for comparing two groups

-Chi-square test for qualitative variables. **APACHE**: Acute physiological and chronic health evaluation

- **BMI:** body mass index

Table (2): Distribution of the active TENS (ATENS) and sham TENS (STENS) groups in relation to hemodynamics and oxygen saturation, (total patients' number = 60):-

Hemodynamics & oxygen saturation	ATENS (n= 30)	STENS (n= 30)	P-value 1
Heart rate:			
Before treatment:			
Mean ± SE	128.50 ± 3.74	127.27 ± 3.92	0.708
After treatment:			
Mean ± SE	107.83 ± 3.90	104.17 ± 4.29	0.496
P-value[2]	0.000*	0.000*	
Temperature:			
Before treatment:			
Mean ± SE	37.01 ± 0.23	36.85 ± 0.19	0.805
After treatment:			
Mean ± SE	37.39 ± 0.15	37.27 ± 0.12	0.617
P-value[2]	0.023*	0.014*	
MAP:			
Before treatment:			
Mean ± SE	44.33 ± 2.77	50.17 ± 2.77	0.167
After treatment:			
Mean ± SE	73.93 ± 2.62	73.80 ± 3.28	0.976
P-value[2]	0.000*	0.000*	
Respiratory rate:			
Before treatment:			
Mean ± SE	20.37 ± 1.83	16.70 ± 0.80	0.373
After treatment:			
Mean ± SE	17.73 ± 1.48	16.23 ± 0.76	0.964
P-value[2]	0.002*	0.482	
SPO_2:			
Before treatment:			
Mean ± SE	97.60 ± 0.35	97.87 ± 0.49	0.244
After treatment:			
Mean ± SE	98.97 ± 0.21	98.53 ± 0.34	0.653
P-value[2]	0.000*	0.219	
CVP:			
Before treatment:			
Mean ± SE	5.37 ± 0.74	4.93 ± 0.76	0.976
After treatment:			
Mean ± SE	11.10 ± 0.64	10.97 ± 0.62	0.806
P-value2	0.000*	0.000*	

Ns: Data is represented as mean ± standard deviation.
- There is no significant difference P-value >0.05
- *significant difference at P-value <0.05
- Chi-square test
- **MAP:** mean arterial pressure
- **CVP**: central venous pressure
SPO_2: pulse oximetry oxygen saturation

Table (3): Distribution of the active TENS (ATENS) and sham TENS (STENS) groups in relation to perfusion parameters, (total patients' number = 60):-

Perfusion parameters	ATENS (n= 30)	STENS (n= 30)	P-value
GCS			
Before treatment:			0.976
Mean ± SE	13.77 ± 0.58	13.57 ± 0.64	
After treatment:			0.677
Mean ± SE	13.97 ± 0.56	13.27 ± 0.72	
P-value[2]	0.059	0.892	
CO2 gap			
Before treatment:			0.414
Mean ± SE	3.39 ± 0.53	2.87 ± 0.56	
After treatment:			0.000*
Mean ± SE	7.40 ± 0.58	4.30 ± 0.43	
P-value[2]	0.000*	0.004*	
Peripheral perfusion index			
Before treatment:			
Positive	11	36.7	9
Negative	19	63.3	21
After treatment:			
Positive	3	10.0	2
Negative	27	90.0	28

Ns: Data is represented as number (percentage) or mean ± standard deviation where appropriate.
- There is no significant difference P-value >0.05 *significant difference at P-value <0.05
-Independent samples t-test for comparing two groups -Chi-square test for qualitative variables.

Table (4): Distribution of the active TENS (ATENS) and sham TENS (STENS) groups in relation to perfusion parameters, (total patients' number = 60):

	ATENS (n= 30)		STENS (n= 30)		P-value
	No.	%	No.	%	
Capillary refill					
Before treatment:					
Positive	28	93.3	26	86.7	0.671
Negative	2	6.7	4	13.3	
After treatment:					
Positive	28	93.3	29	96.7	1.000
Negative	2	6.7	1	3.3	
P-value[2]	1.000		0.353		
Skin mottling					
Before treatment:					
Positive	2	6.7	5	16.7	0.424
Negative	28	93.3	25	83.3	
After treatment:					
Positive	2	6.7	3	10.0	1.000
Negative	28	93.3	27	90.0	
P-value[2]	1.000		0.706		
Skin turgor					
Before treatment:					
Cold	19	63.3	21	70.0	0.584
Warm	11	36.7	9	30.0	
After treatment:					
Cold	4	13.3	3	10.0	1.000
Warm	26	86.7	27	90.0	
P-value[2]	0.000*		0.000*		
Peripheral pulse					
Before treatment:					
Positive	15	50.0	17	56.7	0.605
Negative	15	50.0	13	43.3	
After treatment:					
Positive	26	86.7	28	93.3	0.671
Negative	4	13.3	2	6.7	
P-value[2]	0.002*		0.001*		

Ns: Data is represented as number percentage. -There is no significant difference P-value >0.05
- *significant difference at P-value <0.05 - Chi-square test

Table (5): Distribution of the active TENS (ATENS) and sham TENS (STENS) groups in relation to renal function and NGAL, (total patients' number = 60):-

Renal function and NGAL	ATENS (n= 30)	STENS (n= 30)	P-value
Urea:			
Before treatment:			0.663
Mean ± SE	5.94 ± 0.76	7.66 ± 1.38	
After treatment:			0.124
Mean ± SE	5.82 ± 0.74	8.73 ± 1.42	
P-value[2]	0.280	0.002*	
Creatinine:			
Before treatment:			0.425
Mean ± SE	91.74 ± 10.31	95.09 ± 17.26	
After treatment:			0.007*
Mean ± SE	74.43 ± 7.16	114.48 ± 13.62	
P-value[2]	0.003*	0.006*	
NGAL:			
Before treatment:			0.070
Mean ± SE	7.78 ± 0.91	10.91 ± 1.30	
After treatment:			0.000*
Mean ± SE	7.35 ± 0.77	20.76 ± 2.11	
P-value2	0.484	0.000*	

Ns: Data is represented as mean ± standard deviation.
- *significant difference at P-value <0.05
-There is no significant difference P-value >0.05
-Chi-square test

Discussion

Hypovolemic shock is very critical complication that may increase the length of ICU and hospital stay or may be death .The critical care nurse should be mastering and update the care of patient in ICU to improve patient's outcomes. Validating the efficacy of TENS as an adjuvant technique for physical exercise is an important opportunity to improve the outcomes of critically ill patients. To the best of our knowledge, this is the first study to examine the effect of TENS application on patients with Hypovolemic shock.

Previous studies have found that TENS applied to ganglion region has a vasodilatation effect and leads to a reduction in peripheral systolic blood pressure (Vieira et al., 2012).Whereas application of TENS in this study didn't show any significant change on hemodynamic parameters as heart rate, MAP, SPO2 and CVP (P value > 0.05).These finding were in contrast with Silva,2015 who reported that TENS resulted in a significant reduction in SBP in the group of younger adults (TENS – pre: 111 _ 2 mm Hg; post: 105 _ 2_2 mm Hg; placebo – pre: 113 _ 1_8 mm Hg; post: 114 _ 2_5 mm Hg; GEE, P<0.01). Moreover, these results were opposite with Ozturk et al., 2016 who found no significant differences were observed in oxygen saturation and MAP during the postoperative period. This may be the hemodynamics parameters for postoperative patients improved rather than shocked or acute instability patients.

In previous studies, systolic blood pressure, which is non-invasive marker of peripheral blood pressure, was reduced by the application of TENS in the group of younger adults (Kaada et al., 1990; Indergand& Morgan, 1994; Chauhan et al., 1994; Sandberg et al., 2007). Hollman and Morgan (Hollman& Morgan, 1997) found that the application of TENS to the forearm resulted in a reduced sympathetically mediated pressure response, which is not compatible with the present findings.

The resuscitation protocol in this study resulted in a significant increase in all hemodynamic parameters within the two groups before and after treatment (P value < 0.05). This could be attributed by that hypovolemic shock causes significant organ hypo-perfusion which stimuli sympathetic response by increasing heart rate, hypotension and decrease in CVP ,which rapidly response to rapid resuscitation by decreasing heart rate, and increasing in MAP and CVP.

All of the reports relating to blood flow and TENS are based on measurements of skin temperature. Although skin temperature

measurements provide indirect estimates of skin blood flow, they do not provide information about blood flow to underlying muscle as renal tissues. Regarding to skin temperature in this study, there was a considerable difference between groups; this wasn't in line with (Indergand et al., 1994) who showed decreases in blood flow can possibly be attributed to cutaneous vasoconstriction produced by exposure to a non-thermo-neutral environment.

The application of TENS in this study didn't show any significant change on tissue perfusion parameters as peripheral perfusion index, capillary refill, skin molting, skin turgor and peripheral pulse (P-value > 0.05).These results were not in agreement with Wong and Jette1984 who reported that, in healthy people, blood flow was decreased by the application of three forms of TENS (high-frequency, low-frequency, and burst-mode). In addition, Kaada 1990 found that low-frequency and burst mode TENS may increase blood flow in patients with diabetic polyneuropathy and Raynaud phenomenon. Both of these studies attributed circulatory changes to sympathetic activity.

Results of this study show that there was highly statistical significant difference between the two groups in relation to serum creatinine, NGAL test after treatment (P = 0.007 & P= 0.000) respectively. This can be explained by that electricaltherapy could increase the renal perfusion rate and its excretory function**.** One possible explanation for the increase in blood flow is the activation of sensory neurons mediated through large myelinated afferent nerve fibers which, in turn, activate local inhibitory circuits within the dorsal horn of the spinal cord. Such circuits may inhibit sympathetic transmission in the spinal cord. The arrangement of inhibitions mediated by fibers is probably segmental. Polysegmental inhibitory circuits also exist, but they tend to require higher intensity stimuli to activate them since these inhibitory mechanisms are largely mediated by A delta and C afferents.

These findings were in line with Janda et al., 1996. Who investigated the effect of electrotherapy on established ischemic renal failure in rats? In this study, electrotherapy with Rebox apparatus was performed directly on the ischemic kidney at a frequency of 1 – 10 kHz. The results showed a significant enhanced diuresis and sodium excretion. Also our results were in line with Iorio et al., 2012 who studied High-frequency external muscle stimulation in acute kidney injury. There was a significant difference in serum creatinine in electrotherapy group.

Another study by Kjartansson and Lundeberg 1990 showed that treatment with ENS (high intensity, high/frequency) increases blood flow in an ischemic surgical flap compared with placebo-ENS. The increased blood flow level correlates well with the long-term survival of the flap. The increase in blood flow generally started 10-15 min after the commencement of treatment. Repeated ENS treatments on consecutive days resulted in gradual improvement of the blood flow.

Conclusions

Application of transcutaneous electrical nerve stimulation had significant improvement for renal tissue perfusion and hemodynamic parameters.

Recommendation

- TENS should be included as one of the ICU therapeutic modalities to improve patient's outcomes.

- Using others invasive parameters to assess tissue perfusion for patient undergoing therapy.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Funding Statement

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors thank all patients who participated in the study. The authors express

their gratitude to critical care physicians and nurses caring for patients in the ICUs where the study was done.

References:

Dubin A, Henriquez E, Hernández G. Monitoring peripheral perfusion and microcirculation. Curr Opin Crit Care. (2018) 24:173–80. doi: 10. 1097 /MCC. 0000000000000495.

Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intens Care Med. (2014) 40:1795–815. doi: 10.1007/ s00134-014-3525.

Ince C. Personalized physiological medicine. Crit Care. (2017) 21 (Suppl 3): 308. doi: 10.1186/s13054-017-1907-7.

AFP Machado, EF Santana, PM Tacani, RE Liebano.: The effects of transcutaneous electrical nerve stimulation on tissue repair: A literature review. Can J Plast Surg (2012); 20 (4):237-240.

Atalay C, Yilmaz B.: The effect of transcutaneous electrical nerve stimulation on post mastectomy skin flap necrosis. Breast Cancer Res Treat (2009); 117:611-4.

Chauhan A, Mullins PA, Thuraisingham SI, Taylor G, Petch MC, Schofield PM. (1994): Effect of transcutaneous electrical nerve stimulation on coronary blood flow. Circulation; 89: 694–702.

Dailey DL, Rakel BA, Vance CG et al. Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. Pain (2013); 154, 2554–2562.

Gangui M, Behrouz Attarbashi Moghadam, Nastaran Ghotbi, Azadeh Shadmehr, , Mohammad Masoumi: Immediate effects of transcutaneous electrical nerve stimulation on six-minute walking test, Borg scale questionnaire and hemodynamic responses in patients with chronic heart failure. J. Phys. Ther. Sci (2017); 29: 2133–2137.

Gregorini C, Cipriano Junior G, Aquino LM, Branco JN, Bernardelli GF: Short-duration transcutaneous electrical nerve stimulation in the postoperative period of cardiac surgery. Arq Bras Cardiol (2010); 94: 325–331, 45–51.

Ishikawa S, Suga H, Fukushima M, Yoshida A, Yoshida Y, Sunagawa M, et al: Blood fluidity enhancement by electrical acupuncture stimulation is related to an adrenergic mechanism. J Acupunct Meridian Stud (2012); 5:21e28.

Indergand HJ, Morgan BJ. : Effects of high-frequency transcutaneous electrical nerve stimulation on limb blood flow in healthy humans. Phys Ther (1994); 74: 361–367.

Kamali F, HosseinMirkhani, AhmadrezaNematollahi, Saeed Heidari, Elahesadat Moosavi, Marzieh Mohamadi: The Effect of Transcutaneous Electrical Nerve Stimulation of Sympathetic Ganglions and Acupuncture Points on Distal Blood Flow. J Acupunct Meridian Studi (2017); 10 (2):120-124.

Faghih1 M, Farshad M, Ghafari A and Sharifi s. An Investigation into the Effect of Transcutaneous Electrical Nerve Stimulation on Postoperative Pain Intensity in Patients with Bone Fracture: A Clinical Trial . Medical - Surgical Nursing Journal: Vol.8, issue 4;available at DOI: 10.5812/msnj.100391

Machado A, Santana EF, Tacani PM, Liebano RE: The effects of transcutaneous electrical nerve stimulation on tissue repair: a literature review. Can J Plast Surg (2012); 20: 237e 240.

Sandberg ML, Sandberg MK, Dahl J: Blood flow changes in the trapezius muscle and overlying skin following transcutaneous electrical nerve stimulation. Phys Ther (2007); 87: 1047–1055.

Silva M, Gaspar R. Chiappa, Vinicius M. da Silva, Laura M. T. Neves, Alexandra C. G. B. de Lima, Fernanda P. Tomasi1, Luiz T. G. Junior, Jos_e F. Vilela-Martin, Martim Bottaro and Gerson C. Junior: Clin Physiol Funct Imaging (2015): 14: 188–196.

Ozturk N, DoganBaki E, Kavakli A, Sahin A, UmutAyoglu R, Karaveli A, Emmiler M, Inanoglu K, Karsli B: "Comparison of Trans

cutaneous Electrical Nerve Stimulation and Parasternal Block for Postoperative Pain Management after Cardiac Surgery", Pain Research and Management (2016), Article ID 4261949.

Vieira PJ, Ribeiro JP, Cipriano G Jr, Umpierre D, Cahalin LP, Moraes RS: Effect of transcutaneous electrical nerve stimulation on muscle metaboreflex in healthy young and older subjects. Eur J Appl Physiol (2012); 112: 1327–1334.

Hollman JE, Morgan BJ: Effect of transcutaneous electrical nerve stimulation on the pressor response to static handgrip exercise. Phys Ther (1997); 77: 28–36.

Santos FV, Chiappa GR, Vieira PJ, Umpierre D, Ribeiro JP, Cipriano G Jr: Interferential electrical stimulation improves peripheral vasodilatation in healthy individuals. Braz J Phys Ther (2013); 17: 281–288.

Walsh DM, Howe TE, Johnson MI, Sluka KA: Transcutaneous electrical nerve stimulation for acute pain. Cochrane Database Syst Rev (2009); (2): CD006142.

Wong RA, Jette DU: Changes in sympathetic tone associated with different forms of transcutaneous electrical nerve stimulation in healthy subjects. Phys Ther (1984); 64: 478 e 482.

Kaada B, Vik-mo H, Rosland G, Woie L, OpstadPK: Transcutaneous nerve stimulation in patients with coronary arterial disease: haemodynamic and biochemical effects. Eur Heart J (1990); 11: 447–453.

Zadeh R, Daniel Lasserson, Samuel Fatoba, Carl Heneghan, Christopher P. Price, Ann Van den Bruel, Annette Plüddemann.: Point-of-care neutrophil gelatinase-associated lipocalin (NGAL) tests© National Institute for Health Research (2020).

Sato KL, Sanada LS, Rakel BA, Sluka KA. Increasing intensity of TENS prevents analgesic tolerance in rats. J. Pain (2012) 13, 884–890.

Sluka KA, Bjordal JM, Marchand S, Rakel BA. What makes transcutaneous electrical nerve stimulation work? Making sense of the mixed results in the clinical literature. Phys. Ther (2013). 93(10), 1397–1402.

Gardner SE, Blodgett NP, Hillis SL et al. HI-TENS reduces moderate-to-severe pain associated with most wound care procedures: a pilot study. Biol. Res. Nurs (2013). doi:10.1177/1099800413498639.

Nardo M, Ficarella A, Ricci Z et al. Impact of severe sepsis on serum and urinary biomarkers of acute kidney injury in critically ill children: an observational study. Blood Purification (2013); 35: 172–6.

Seo Y, Lee W, Hun Kwon O. Performance evaluation of BioPorto diagnostics' neutrophil gelatinase-associated lipocalin assay on automated clinical chemistry analyzer Hitachi 7600. Journal of Laboratory Medicine and Quality Assurance (2013); 35: 23–8.

Janda J, Cervenka L, Spatenka J, Heller J, Slovák P: The effect of electro stimulation with the Rebox apparatus on ischemic renal injury in rats. CasLek Cesk (1996); 135: 252-254.

Kjartansson and Lundeberg T: Effects of electrical nerve stimulation (ENS) in ischemic tissue. Scand J Plast Reconstr Hand Surg (1990); 24: 129-134, 1990.

Iorio B, Serena Torraca, Pasquale Gustaferro, GholamrezaFazeliand August Heidland. High-frequency external muscle stimulation in acute kidney injury (potential shortening of its clinical course. Clinical Nephrology (2012), Vol. 78 – No. Suppl (S37-S45).