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Assessment of Interleukin-6 in Young Swimmers Suffering from Myofascial Pain Syndrome Using LidocainePhonophoresis: A Randomized Controlled Trial

Mohamed Abdel-Moneim Abo-EL-Roos[*1], Emam Hassan El-Negmy[2], SamahAttia El-Shemy[2], Asser Abdel-Hay Sallam[3]

[1]Master in Physical Therapy for Pediatrics, Department of Physical Therapy for pediatrics, Cairo University, Egypt
[2]Department of Physical Therapy for Pediatrics, Faculty of Physical Therapy, Cairo University, Cairo, Egypt
[3]Department of Orthopedic Surgery, Suez Canal University, Ismailia, Egypt

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ABSTRACT

To investigate interleukin-6 in athletic children suffering from myofascial pain syndrome (MPS) using lidocaine phonophoresis. Myofascial pain syndrome is considered a major health dilemma affecting both adults and children due to overuse injuries. Moreover, it is one of the most common conditions of chronic musculoskeletal pain of patient's in general medical practice. The exact cause of MPS is unidentified. However, it could be diagnosed among physicians by the presence of hypersensitive nodules referred to as myofascial trigger points (MTrPs) within a taut bands of skeletal muscle. Forty five young swimmers(boys) with MPS in the upper trapezius muscle (10 - 14 years old) participated in the study. Assessment of serum interleukine-6, functional activities and cervical range of motion were measured before and after treatment. They were randomly assigned to three groups (n=15 in each), first one kept as a control group (A) and allocated to special designed physical therapy program. Equally, study groups received similar physical therapy program assumed to the control. Treatment submission was assembled as 40 minutes, 3 times / week for three consecutive months. After treatment there was a significant enhancement within the control and study groups. Group C revealed a higher degree of response to treatment. Both lidocaine phonophoresis and special designed physical therapy program simultaneously could provide very useful and interesting treatment of neck pain in youth athletes using IL-6 as a tool of diagnosis.

*Corresponding Author

Name: Mohamed Abdel-Moneim Abo-EL-Roos
Phone: 00201206530584
Email: aboelroosemohamed@yahoo.com

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INTRODUCTION

Numerous sport injuries occur in the skeletal muscles due to insufficient rest and these injuries can involve the muscle-tendon unit, bones, bursa and the physics (Luke *et al.*, 2011). Myofascial pain syndrome is considered as a common injury which is characterized by formation of trigger point in several muscles, taut bands, characteristic radiating pain and brisk contraction of a skeletal muscle (local twitch reaction). The patients mostly undergo weakness, pain, restricted mobility and involuntary dysfunctions (Yang *et al.*, 2012; Turo *et al.*, 2012).

The etiology of MPS is unknown but many factors such as bad posture, chronic diseases, leg length discrepancy and overuse will enhance such syndrome. It may cause changes such as: diminished elasticity, thickening of the myofascial tissue and hindering muscle to relax completely. So the affected muscle will work tougher to counteract the restriction exist in the antagonistic muscle causing neuromuscular response known as "guarding" against the painful area (Wilke *et al.*, 2016).

Repetitive contractions occur during all activities especially in sports. Overhead throwing, swimming, jumping and running involve eccentric activities causing myofascial trigger points (Rivers *et al.*, 2015). Overuse injuries in swimmers are the most common and in the same time they difficult to deal because of the distance and repetition of training. Also, these injuries can develop number of MTrPs as commonly caused by overloading in swimmers and commonly present with shoulder, neck dysfunction (Richardson, 1999).

Myofacial trigger points in the neck are common complaint in swimmers because of the involvement of the upper trapezius in most cases. The neck is a weak structure and technique of swimming is important to avoid strain and repetitive stress. It seems that backstroke, freestyle and butterfly techniques would have the exact cause for neck strain as the head is always aligned with the spine and the swimmer looks straight up putting the muscles of the neck under constant tension (Mountjoy *et al.*, 2016).

Active myofascial trigger points usually associated with higher levels of intramuscular proinflammatory biomarkers and pain which considered as common signs of taut bands. In particular, plenty of mediators like tumor necrosis factors (TNF-α), interleukins (IL-6,8), bradykinin and substance P increase instantly after occurrence ofMTrPs. Likewise, patients with MTrPs have amplified levels of biomarkers in uncomplicated intramuscular spots proposing that such irritation is a systemic response not limited to a small area (Pedersen and Febbraio, 2008).

Myofascial pain syndrome could be treated with nonsteroidal anti-inflammatory medications, physical restoration, stretch and spray procedures and workout (Lavelle *et al.*, 2007). Ultrasound is preferable in management of MPS. The thermogenic effect of Ultrasound increases the momentarily blood flow resulting in a transient increase in the flexibility of dense collagenous structures such as tendons, ligaments and joint capsules, consequently decreases the pain and accompanying muscle spasm (Unalan *et al.*, 2011; Ilter *et al.*, 2015).

Phonophoresis is frequently used to treat pain associated with muscular disorders, enhancing skin absorption of the topical medication's molecules to the profound soft tissue via ultrasound waves (J, 2011; Argoff *et al.*, 2004). Lidocaine is the drug of choice applied in conjunction with therapeutic ultrasound for the treatment of MPS (Byl *et al.*, 1993).

There were lack of research works concerning lidocaine phonophoresis on MTrPs, so IL-6 is a good tool for assessing the efficacy of lidocaine phonophoresis and pulsed ultrasound in the treatment of MPS.

MATERIALS AND METHODS

Study design and subjects

Design of the present study was randomized controlled and single blinded. Ethical approval was obtained by Ethical Board (No. P.T.REC/012/001708), Cairo University, Egypt. The duration of the study was situated from December 2017 to December 2018 according to the ethical research measures. The data of the current study are available at Clinical Trials. Gov. PRS (ID: NCT04185194). The study was conducted on 45 boys (athletic swimmers), 10-14 years old with MPS in upper trapezius muscle and they were recruited and treated in outpatient clinic of Ismaily Sporting Club, Egypt. Children were diagnosed according to (Hubbard and Berkoff, 1993; Ardiç *et al.*, 2002) who described the presence of an active MTrP in the upper trapezius which manifested as,

1. Localized pain and tenderness in cervical trigger points in the upper trapezius.
2. Tender spots in one or more palpable taut bands.
3. A characteristic pattern of referred pain distributed in the ipsilateral, posterolateral cervical paraspinal region, mastoid process or temporal area
4. Palpable or noticeable local twitch reaction on snapping palpation at the utmost sensitive spot in the taut band.
5. Limited range of motion in lateral bending of the cervical spine to the opposite side.

All children were randomly allocated to the study and masked using sealed envelopes.

Inclusive criteria

All children have regional neck pain and unilateral tenderness in cervical trigger points of the mid-point of the upper trapezius which was from II to IV score according to tenderness grading system. They were allowed practicing their regular sport activities. Children who suffered from neurological and dermatological disorders, fibromyalgia, drug allergy and history of findings of cervical injury whether orthopedic or soft tissue were excluded from the study.

Sample Size calculation

The sample size was primarily planned using G*power (version 3.0.10, Neu-Isenburg, Germany) to define the number of children in every group. One-way analysis of variance, α level 0.05, power preferred was 95%. Accordingly, the sample size was calculated 45 children in addition to 5 boys to account dropout proportions (Figure 1).

Materials

Materials used for evaluation of IL-6 was ELISA method (enzyme linked immunosorbent assay) (Simons *et al.*, 1999), neck disability index to evaluate functional activities (Vernon and Mior, 1991) and cervical range of motion (CROM) was measured by universal manual goniometer.

Therapeutic ultrasound (Medserve, Prosound, ULS-1000, England), infrared with luminous source, tungsten lamp (Welsh, 1992; Chen *et al.*, 2013) and lidocaine hydrochloride gel 5% for transdermal penetration by phonophoresis were the three tools used for treatment.

Procedure

Serum IL-6, NDI scores and CROM were measured before and after treatment. The optimum time for detection of serum IL-6 was 19 pm. - 5 am. according to its circadian rhythm (Tabatabaiee *et al.*, 2019; Vgontzas *et al.*, 2005). Blood samples were collectedfrom antecubital veins into chilled tubes contained ethylendiaminetetraacetic acid (EDTA). Normal reference range was 0 – 16.4 picogram/milliliter (Tan, 1992).

Neck disability index was calculated through ten items and each section is recorded on a |0 - 5 scales, so 5 measured the ultimate disability. The final percentage for children was calculated by excluding working and driving sections in the Arabic version (Shaheen *et al.*, 2013).

Goniometric measurement of the cervical range of motion was performed for three times for each movement, and the mean range was calculated (Pietrobon *et al.*, 2002). Normal values or cervical range of motion were obtained according to (Tousignant *et al.*, 2000).

Special designed physical therapy programincluded myofascial trigger points pressure relief, exercise program and infrared (IRR). The program was applied on the three groups as follows,

Myofascial trigger points pressure release,

This technique was used to locate the trigger points in the upper trapezius muscle of the prone patient. Pincer compression was done to palpate trigger points and were grasped firmly between the fingers and thumb till referred pain occurred (Simons *et al.*, 2002).

Time for each pressure was for twenty seconds. The treating finger was then elevated from the trigger point for the same period of the applied pressure and the sustained pressure was applied again. The total duration of the technique for each trigger point was for five minutes or more, until relaxing of the taut band and gradual increase of the depth of penetration of the treating fingers (Chaitow and W, 2001).

Stretching was applied after release technique in the sitting position with the palm of the therapist hand over the temporo-occipital area (to bend the neck to the opposite side), with the head turned to the same side.Time was applied slowly, within limits of discomfort, and maintained for thirty seconds. Repetition was applied 3 times in each set (Lewit and Simons, 1984).

Range of motion exercises

Gentle exercises were applied from supine lying within limit of pain with neck supported by a pillow followed by relaxed breathing exercise for 3 times (nose to nose) to obtain active relaxation. After that the child was asked to tuck the chin downwards with gentle rotation to the right and left slowly without holding contraction and was performed for 10 times (Ingbar, 2000).

Strengthening exercises were done by shoulder shrugging and was performed to strengthen the upper trapezius. Isometric neck exercises was accomplished by external force. It was applied in all directions, thereby limiting pain. Contraction was held for 3 seconds and rest was maintained for the same time. The exercise was performed for 10 times (Welsh, 1992).

Infrared radiation (IRR): with luminous source (tungsten lamp) was applied on posterior neck region in prone lying after being tested for thermal sensation using test tubes containing cold and warm water respectively. The child's treated area was cleaned using methylated spirit and cotton wool

Table 1: Intervention

Criterion	Groups		
	Control A (n=15)	B (n=15)	C (n=15)
Treatment program	Special designed physical therapy program	Special designed physical therapy program + pulsed ultrasound (the area of the transducer head was 4 cm2, the treatment head was kept in a slow circular motion and was in skin contact at the palpated trigger points)	Special designed physical therapy program + lidocaine hydrochloride gel 5%phonophoresis (the painful area containing MTPs was rubbed adequately with ultracaine gel)
Duration	40 minutes	40 minutes	40 minutes

Table 2: Demographic data

Demographic data	Groups	x̄±SD	*p*
Age (years)	A	11.93 ±1.33	0.845
	B	11.87 ±1.36	
	C	11.67 ±1.23	
Weight (kg)	A	28.20 ±4.65	0.132
	B	30.93 ±4.27	
	C	31.00 ±3.76	
Height (m)	A	1.14 ±0.12	0.145
	B	1.21 ±0.08	
	C	1.22 ±0.08	
Body mass index (kg/m^2)	A	21.67 ±1.90	0.440
	B	21.33 ±1.68	
	C	20.80 ±1.96	

$\bar{x}$: Mean; SD: Standard deviation; *p*: Probability value

prior to IRR treatment. The three groups received IRR for 20 minutes, at a height of 40 - 60 cm.

Intervention

Table 1 illustrates groups, treatment program and duration.

N.B:50% duty cycle, frequency: 1 MHz and intensity: 1.5 w/cm^2 for 10 minutes were the parameters of therapeutic ultrasound applied only in both study groups according to (Goraj-Szczypiorowska *et al.*, 2007).

Statistical Analysis

Prior to statistical analysis quantitative data was checked for homogeneity of variances. Normality measures have been investigated to identify the data distribution; kolmogorov-smirnov test, Shapiro-Wilk test, histograms and Q-Q plots. For both homogeneity of variances and normality tests, p values were greater than 0.05 suggested homogeneity and normality of data. All data were represented as mean ± standard deviation. Paired t- test was done to compare between pre and post treatment results within each group.

One- way analysis of variance (ANOVA) used for the parametric data stood to determine the difference before and after treatment results among groups. Post hoc tests to determine the significant difference between groups, so least significant difference (LSD) to determine the possible changes between two independent groups. All statistical analyses were conducted at 95% confidence level and were performed using IBM SPSS statistics (version 22).

RESULTS

Demographics of all children presented in Table 2 found to be statistically non-significant difference as $p > 0.05$. Moreover, no significant difference was found at pre-intervention assessment of all measured variables between groups.

The tested parameters: IL-6, NDI and CROM (flexion, extension, opposite rotation and opposite lat-

Table 3: The measured variables before and after treatment within the three groups

Variables	Groups				
	A				
	$\bar{x}$ ±SD before	**$\bar{x}$ ±SD after**	**MD**	***t* value**	*p*
IL-6	268.3 ±84.4	90.6±6.5	177.7	6.26	0.021*
NDI	31.3 ± 9.2	24.17 ±4.7	7.13	5.29	0.001*
Cervical flexion	65.60± 6.69	73.60± 6.72	-8	-10	0.001*
Cervical extension	69.47± 4.3	81.13± 3.3	-11.6	-14.5	0.001*
Cervical opposite rotation	56.6± 6.9	66.8± 5.6	-10.2	-10.4	0.001*
Cervical opposite lateral flexion	36.20 ± 3	47.27 ± 4	-11.07	-10.02	0.001*
Variables			B		
IL-6	261.4 ±85.2	68.3 ± 8.8	193.1	9.22	0.001*
NDI	33.17 ± 7.8	25.50 ± 5.1	7.67	7.99	0.001*
Cervical flexion	62.8± 4.17	74.07± 2.6	-11.2	-14.3	0.001*
Cervical extension	68.53± 4.3	80.6± 3.52	-12.7	-15.2	0.001*
Cervical opposite rotation	54.9± 6.6	68.2±4.36	-13.3	-9.7	0.001*
Cervical opposite lateral flexion	35.4 ±2.38	49 ± 3.44	-13.6	-11.	0.001*
Variables			C		
IL-6	280.6 ±82.2	14.2 ± 2.01	266.4	17.01	0.001*
NDI	37.83 ± 8.6	14.50 ± 2.7	23.33	12.08	0.001*
Cervical flexion	67.27± 5	81.9± 3.01	-14.63	-15.79	0.001*
Cervical extension	69.13± 4.7	90.47± 4.8	-21.34	-16.04	0.001*
Cervical opposite rotation	53.33± 3	79.8± 5.4	-26.54	-16.37	0.001*
Cervical opposite lateral flexion	35 ± 2.75	55.5 ±5.24	-20.53	-14.1	0.001*

$\bar{x}$Mean; SD: Standard deviation; MD: Mean difference; t value paired t- test; *p*: probability value; * *p*: Significant as p < 0.05

Table 4: The mean values of the measured variables after treatment among the three groups

Measured variables	Groups			F value	*p*
	A	B	C		
IL-6		x̄± SD			
	90.59±6.5	68.29±8.75	14.2± 2.01	756.2	0.0001*
NDI	24.17 ± 4.78	25.5 ± 5.11	14.5 ± 2.71	28.79	0.0001*
Cervical flexion	73.60±6.72	74.07±2.63	81.9± 3.01	16.15	0.0001*
Cervical extension	81.13±3.33	80.60±3.52	90.47±4.87	29.34	0.0001*
Cervical opposite rotation	66.80 ±5.63	68.20±4.36	79.87±5.48	28.63	0.0001*
Cervical opposite lateral flexion	47.27 ±4.06	49.0 ±3.44	55.53±5.24	15.29	0.0001*

$\bar{x}$Mean; SD: Standard deviationF value: Analysis of variance; *p*: Probability value; * *p*: significant as p< 0.05

Table 5: Multiple pairwise comparison of the measured variables after treatment among the three groups

Measured variables	Pairwise comparison(post- hoc tests), *LSD*					
	B and A		B and C		C and A	
	MD	*p*	MD	*p*	MD	*p*
IL-6	22.3	0.001*	54.1	0.0001*	76.4	0.0001*
NDI	1.33	0.404	11	0.0001*	9.67	0.0001*
Cervical flexion	0.47	0.778	7.83	0.0001*	8.3	0.0001*
Cervical extension	0.53	0.715	9.87	0.0001*	9.34	0.0001*
Cervical opposite rotation	1.4	0.464	11.87	0.0001*	13.7	0.0001*
Cervical opposite lateral flexion	1.73	0.278	6.53	0.0001*	19.33	0.0001*

MD: Mean difference; **p*: Significant as $p< 0.05$; *p* value: Probability value; LSD: least significant difference

eral flexion) revealed significant improvement after treatment within each group on paired t-test ($p < 0.05$) as in Table 3.

Concerning another method of assessment of the above mentioned parameters, there were a significant difference between all groups ($p < 0.05$) (Table 4). To illustrate this difference among the three groups through post hoc tests using LSD found that it was in favor of group C (Table 5).

DISCUSSION

Myofascial pain syndrome has a very high incidence specially among athletic children so it causes pain, tenderness, muscle tightness, fascial restrictions, neck pain, headache and muscle stiffness mainly in the upper trapezius muscle including hyperirritable spots (MTrPs) located within a taut band of skeletal muscle fibers (Chen *et al.*, 2013; Hou *et al.*, 2002). Myofascial trigger points are provoking pain to any stimuli weather direct or indirect trauma resulting in referred pain, tenderness and involuntary dysfunction in most cases. Trigger points lies superficially in the affected muscles and varying in size from 2 to 10 mm (Saxen, 1998; Cummings and White, 2001).

The chosen athletic swimmers (10-14 years old) in this study was in agreement with previous research works (Tanaka, 2009; Hamman, 2014) who stated that children practicing swimming usually have a high frequency of MPS as repetitive bad postural alignment and prolonged training duration represent a risk to their musculoskeletal maturity and may develop overuse injuries specially shoulder and cervical MTrPs.

Although the lack of research works on IL-6 assessment accompanied MPS: (Kumbhare *et al.*, 2009; Shah *et al.*, 2008a; Barrack *et al.*, 2014) found that IL-6, IL-8, IL-ß, TNF-α, substance P and keriatine kinase elevated are common proinflammatory mediators released in ages above 30 years suffering from MPS, the present study was designed to throw light on IL-6 in athletic swimmers (10-14 years). So assessment of serum IL-6 in this study was used as a good diagnostic tool for evaluation of the different methods of treatment like special designed physical therapy program, pulsed ultrasound and lidocaine phonophoresis.

Results of the present study showed a significant improvement in measured variables when compared between pre and post treatment of the three groups. Comparison between groups found that there was a significant difference in measurement parameters in favor of study group C could be attributed to the combined effect of pulsed ultrasound and lidocaine gel, as ultrasound enhanced percutaneous absorption of lidocaine to subcutaneous and deep tissues. This comes in agreement with previous studies (Shah *et al.*, 2008b; Mense, 2008) who found that pulsed ultrasound has mechanical properties such as cavitation, micromassage and microstreaming and can help in drug penetration specially the cavitation property. Cavitation also enhance drug penetration by modifying the structure of stratum corneum, interrupt the lipid bilayer which acts as a barrier to drug and enhancing the transportation via the duct of sweat glands and their follicles in the skin (Ogura *et al.*, 2008; Haar, 2007).

Special designed physical therapy program improved the results of all measured variables in group A which is in agreement with (Simons, 2008; Ruohuan and Zhangren, 1997) who reported that using of this program tends to lengthen sarcom-

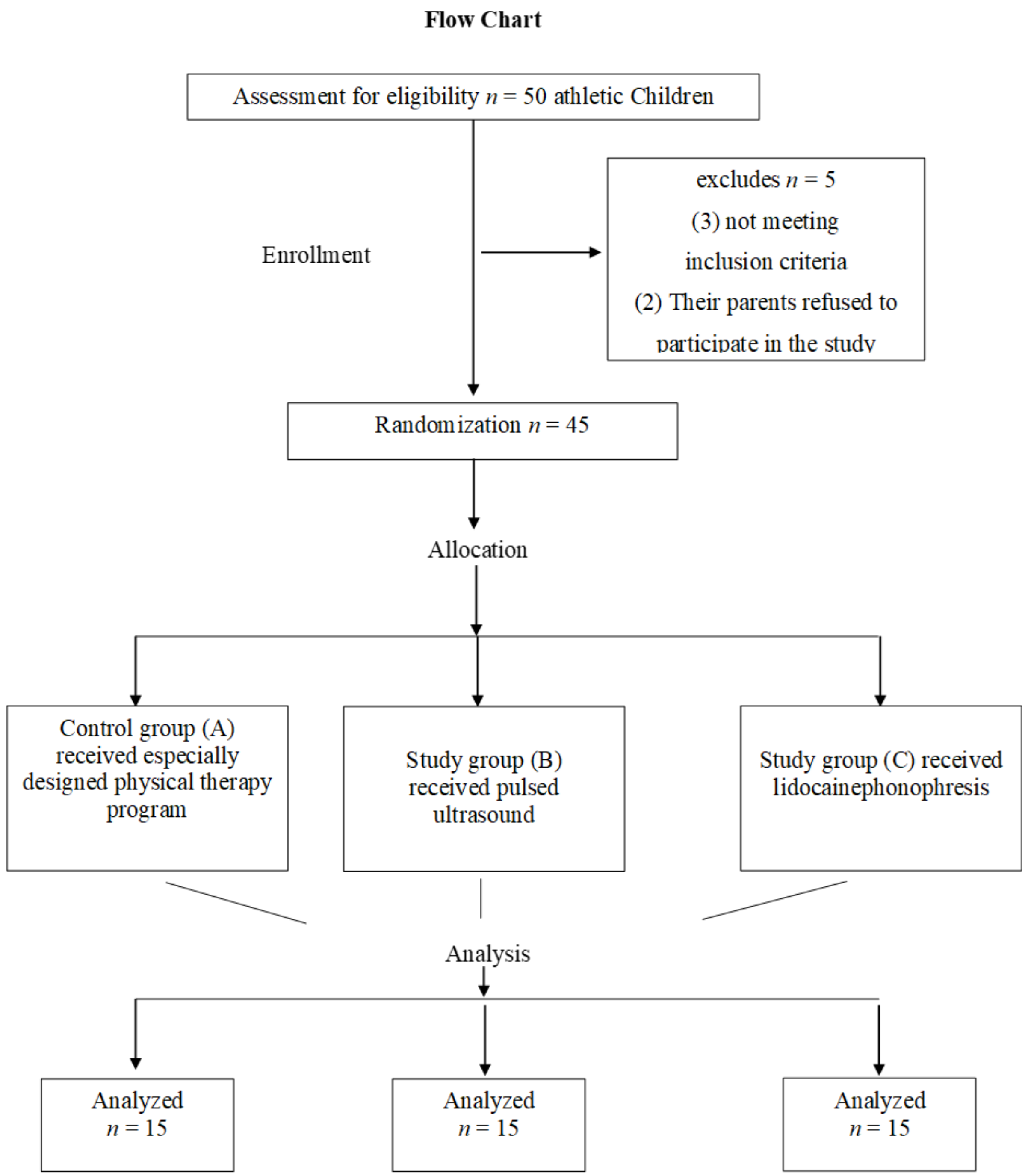

Figure 1: Flow chart of the participants in the study

eres, increase ROM, decrease energy consumption, reduce the release of noxious substances and help in pain reduction following a progressive pressure relief due to counter irritant effect that may produce relaxation of the involved muscle.

Significant improvement in group B was due to the positive effect of pulsed ultrasound and special physical therapy program comes in agreement with (Watson, 2000) who reported that pulsed ultrasound was effective on pain reduction in MTPs of upper trapezius which is attributed to the thermal effect of pulsed ultrasound can increase blood circulation leading to enhance of the elimination of pain. Also. He added that therapeutic ultrasound can increase nerve conduction and cell membrane permeability diminishing inflammation in a form of hyperemic muscle tissue, enhancement of cell energy consumption and improve angiogenesis of ischemic tissue. All these effects increase the rate of tissue healing and decrease of muscle spasm.

Using lidocainephonophoresis and special designed physical therapy program revealed a significant improvement in all measured parameters in group C which is in agreement with (Lin *et al.*, 2012; Dalpiaz *et al.*, 2004) who reported the ability of lidocaine to decrease sensory input from MTrPs and releasing local tenderness by lowering degree of reflex mechanism responsible for referred pain.

Also, lidocainephonophoresis has a good therapeutic effect which related to its blocking action on voltage gated sodium channels in nerve endings in the myofascial trigger points. The lidocaine has the ability to decrease sensory input from the myofascial trigger point, releasing local tenderness and indirectly decrease symptoms in the painful area by lowering degree of reflex mechanism responsible for the referred phenomenon (Dalpiaz *et al.*, 2004).

CONCLUSIONS

The results of this study provided the proof that the combination of lidocaine (PH) and special designed physical therapy program simultaneously could provide very useful and interesting treatment of neck pain in youth athletes using IL-6 as a tool of diagnosis especially at the upper trapezius muscle. These effective modalities found significant decreased in serum IL-6 concentration of blood plasma, enhanced functional activities of the neck and increased cervical range of motion in flexion, extension, opposite rotation and opposite lateral flexion.

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Recommendations

Lidocainephonophoresis is recommended to be included as an effective physical therapy modality for the treatment of myofascial pain syndrome in athletic swimmer. Future studies should be conducted to investigate the effect of lidocainephonphoresis using other inflammatory mediators.

Conflict of Interest

None

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