

The Effectiveness of Wet Cupping Therapy and Evaluation of Changes in Lactic Acid Levels in Patients with Myofascial Pain Syndrome

Miyofasial Ağrı Sendromu Olan Hastalarda Yaş Kupa Tedavisinin Etkinliğini ve Laktik Asit Seviye Değişikliğinin Değerlendirilmesi

¹Müeyesser ARAS^a, ²Nermin DİNDAR^b, ³Turgut KÜLTÜR^c, ⁴İlkan BOYUNAĞA^b,
⁵Esra Dilek KESKİN^c, ⁶Kaleem Ullah RAJPUT^d, ⁷Gamze DURSUN^b

^aDepartment of Physical Medicine and Rehabilitation, Yıldırım Beyazıt Faculty of Medicine, Ankara, TURKEY

^bDepartment of Biochemistry, Kırıkkale University Faculty of Medicine, Kırıkkale, TURKEY

^cDepartment of Physical Medicine and Rehabilitation, Kırıkkale University Faculty of Medicine, Kırıkkale, TURKEY

^dBritish Cupping Society-London, United Kingdom

ABSTRACT Objective: Wet cupping therapy is used as a traditional and complementary therapy with a wide application all around the world for especially pain conditions. The aim of this study was to evaluate the effectiveness of wet cupping therapy (WCT) and to assess the changes in lactic acid (LA) levels in isolated leucocyte of the venous and cupping blood samples in patients with myofascial pain syndrome (MPS). **Material and Methods:** Patients aged between 18 and 65, and diagnosed with MPS were included the study. The Visual Analogue Scale (VAS) was recorded baseline, at 1st and 3rd months, Nottingham Health Profile (NHP) and Beck Depression Index (BDI) scores were recorded at baseline and 1st month follow-up in patients. The level of LA in isolated leucocyte of venous and cupping blood were also measured before and after 15 days WCT. **Results:** There was a significant decrease in VAS level from baseline to 1 and 3 months ($p<0.001$) and in BDI, NHP from baseline to 1 month ($p<0.05$). We found a significant decrease in the concentration of LA in isolated leucocyte of cupping blood 15 days after WCT ($p<0.05$). The median level of LA in isolated leucocyte of venous blood was lower than the levels before WCT but it wasn't statistically significant ($p>0.05$). **Conclusion:** In conclusion, WCT is found to be effective in clinical improvements of VAS, BDI and NHP scores in our study. This study also suggests that WCT may be beneficial for pain through reducing LA levels in cupping blood in patients with MPS.

Keywords: Cupping therapy; myofascial pain syndrome; lactic acid

ÖZET Amaç: Yaş kupa tedavisi bütün dünyada özellikle ağrılı durumlarda yaygın olarak kullanılan geleneksel ve tamamlayıcı bir tedavidir. Bu çalışmanın amacı, yaş kupa tedavisinin (YKT) miyofasial ağrı sendromu (MAS) tedavisinde etkinliğini ve venöz kan ile kupa kanından izole edilen lökositlerde laktik asit (LA) düzey değişikliklerini değerlendirmektir. **Gereç ve Yöntemler:** Miyofasial ağrı sendromu tanısı alan 18-65 yaş arası hastalar çalışmaya dahil edilmiştir. Hastaların tedavi öncesi ve sonrası 1. ve 3. ayda Vizüel Analog Skalası (VAS), tedavi öncesi ve sonrası 1. ayda Nottingham Sağlık Profili (NSP) ve Beck Depresyon Ölçeği (BDÖ) kaydedildi. Ayrıca hastaların tedavi öncesi ve sonrası 15. günde venöz ve kupa kanından izole edilen lökositlerde laktik asit düzeyleri ölçüldü. **Bulgular:** Başlangıca göre 1. ve 3. aylarda VAS ($p<0,001$), 1. ayda BDS ve NSP ($p<0,05$) düzeylerinde anlamlı düzeyde düşme vardı. On beş gün sonra kupa kanından izole edilen lökositlerdeki LA düzeylerinde anlamlı olarak düşme tespit edildi ($p<0,05$). Venöz kandan izole edilen lökositlerdeki LA düzeyinde YKT öncesine göre düşme vardı fakat istatistiksel olarak anlamlı değildi ($p>0,05$). **Sonuç:** Sonuç olarak, bizim çalışmamızda YKT VAS, BDS ve NSP skorlarının klinik olarak düzelmesinde etkili bulunmuştur. Bu çalışma ayrıca YKT'nin MAS'ı olan hastalarda kupa kanında LA düzeylerini azaltarak ağrıda faydalı olabileceğini göstermektedir.

Anahtar Kelimeler: Kupa tedavisi; miyofasial ağrı sendromu; laktik asit

Myofascial pain syndrome (MPS) is an important chronic musculoskeletal system problem characterized by pain, muscle spasm, tenderness, mobility

restriction, and autonomic function disorder.¹ The pain is caused by hyperirritable spots in the stretched bands of muscle described as myofascial trigger

Correspondence: Aras MÜYESSER

Department of Physical Medicine and Rehabilitation, Yıldırım Beyazıt University Faculty of Medicine, Ankara, TURKEY

E-mail: drmuyesser@hotmail.com



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points (MTrPs).² The upper part of the trapezius muscle is one of the regions where the trigger points are most often localized.³

The purpose of MTrP therapy is to relieve pain and spasm of the affected muscles. There is a wide variety of treatment approaches including injection of local anesthetic to the trigger point, spray, exercise, massage, thermotherapy, ultrasound and electrotherapy.⁴

Wet cupping therapy (WCT) that is a traditional and complementary therapy has been practised worldwide, particularly in Asia, the Middle East and Europe.^{5,6} Wet cupping therapy is performed lacerating the skin so that blood from the applied area is drawn into the cup. The mechanism of WCT is not clear but increasing evidence-based studies suggest that WCT is particularly effective in musculoskeletal problems and a large number of conditions.⁷⁻¹²

The mechanisms that induce the onset and maintenance of MTrPs are unknown.¹³ The activation of MTrPs are driven from a kind of causes including prolonged low-load repetitive work, mechanical overload and eventually sustained muscular contraction and that the stiffness of muscle on MTrPs arised from hypercontracture of the sarcomer.¹⁴ The histological examination of muscle biopsies from MTrPs reveals structural evidence of muscle hypercontracture.¹³

The local sustained contraction in MTrPs was thought to reduce blood flow; to increase hypoxia and metabolic stress on the affected area.^{13,15} These changes were resulted in the accumulation of LA and the decrease in pH.¹³

Our study is noteworthy for evaluation the effectiveness and mechanisms of WCT in patients with MPS. The purpose of our study was to assess the efficiency of WCT and to assess the changes in lactic acid (LA) levels in isolated leucocyte of the venous and cupping blood samples in patients with MPS.

MATERIAL AND METHODS

This prospective observational clinical study was carried out on patients with MPS who visited the Physical Medicine and Rehabilitation Department, Medicine Faculty of Kırıkkale University between May 2016 and December 2016. The Ethical Com-

mittee of the Faculty of Medicine, University of Medipol University approved the study with decision dated 06.08.2015 and decision number of 402. This study was carried out according to the policies of the Declaration of Helsinki and a signed consent form was obtained from each patient.

Inclusion Criteria: (1) Patients with MPS in trapezius and rhomboid muscles diagnosed based on the criteria proposed by Travell and Simons¹; (2) aged 18-65 years old; (3) those who wanted to participate in the study.

Exclusion criteria: (1) A history of surgery in the neck and shoulder; (2) progressive neurogenic disorders, progressive cervical disc herniation and spinal disorders; (3) hematologic disorders (anticoagulant or antiplatelet agents use); (4) treatment with local techniques such as physical therapy modalities and wet/dry cupping or other complementary during the previous 3 months for MPS; (6) severe diabetes and cardiovascular or renal disease, active infectious disease or malignancy.

A total of 53 patients suffering from MPS were participated in this study. Ten patients (lost to follow up for a variety of reasons) were dropped out during the study and 43 patients completed the wet cupping therapy. Exercise program was offered to all patients after WCT and drug therapy was allowed if they used.

WCT APPLICATION

Patients received WCT on the 1st and 15th days. WCT was performed by the same, experienced investigator (MD). Safety was one of the most important issue and we used disposable plastic cups with a diameter of (Altinsefa, Turkey), a hand cupping pump (Altinsefa, Turkey) and disposable sterile surgical blades (Altinsefa, Turkey). The patients were treated according to the clean WCT procedure to prevent adverse events related to WCT application (Table 1). The plastic cups were placed on skin overlying 7th cervical vertebral spine and 3 to 5 taut bands of trapezius or rhomboid muscles those were mainly tender by manual palpation (Figure 1).¹⁶ The suitable size of cups were placed on the patients (diameter range of 5-7 cm). Each WCT procedure called Triple S method lasted about 30 minutes.⁵ This method was suggested

TABLE 1: Clean WCT technique.

Primary sucking	The application areas were cleaned with antiseptic solutions. The disposable cups were placed on these points and negative pressure applied by hand cupping pump for 3-5 minutes.
Scarification	Then incisions were made on the skin using sterile surgical blades for incision.
Bloodletting	The cup soaked with heparin placed back on the skin, using hand cupping pump and the cups were filled with blood.
Removal	The cups were removed and the blood in the cups was spilled into tubes which were soaked with heparine. Application sites were covered with antibiotic cream and sterile pads. Let the patients rest for 5-10 minutes.



FIGURE 1: A view of points applied for wet cupping therapy.

by the British Cupping Society and Ministry of Health in our country.¹⁶⁻¹⁷

BLOOD COLLECTION

Venous blood samples were collected from the patients 5 minutes before WCT at 1st and 15th days. Blood samples were transferred into tubes with soaked heparine. Wet cupping blood samples were taken from the cups and placed into the test tubes with soaked heparine at 1st and 15th days.

OUTCOME MEASURES

Visual Analogue Scale of pain (VAS) was used for the evaluation of pain. VAS-pain was used to evaluate the pain intensity of the patients during the last 7 days between 0 to 100 point scale, which 0 means no pain and 100 extreme pain.¹⁸ Visual Analogue Scale was measured at baseline and at 1st and 3rd months follow-up.

Nottingham Health Profile (NHP) was applied to measure the quality of life in patients with MPS. Six subsections (pain, emotional reaction, sleep, social isolation, physical activity and energy) includ-

ing 38 queries totally and answering yes or no. Each section is graded between 0 and 100. Zero means best health status and 100 means worst state of health.¹⁹ Nottingham Health Profile was measured at baseline and at 1st month follow-up.

Beck Depression Inventory (BDI) is a self-rating Likert type scale including 21 inquiries which estimate the intensity of depression. The inquiry of inventory is calculated from 0 to 3 scores. The total score shows the intensity of depression.²⁰ Beck Depression Inventory was measured at baseline and at 1st month follow-up.

MEASUREMENT OF LACTIC ACID IN THE WET CUPPING AND VENOUS BLOOD

The cups were covered with heparin sodium before the application and dried them out. The collected blood of venous and cupping were spilled into tubes (BD Vacutainer, LH 170 IU, 10.0 ml) which were soaked with heparine. Prepared leucocyte isolate samples from the collected blood by adding 4.5 ml of dextran 70 and 3 ml of ficoll were frozen at -80°C. For analysis, the samples were reached to room temperature; LA and microprotein level of 21 patients were measured with ROCHE diagnostic Cobas c501 auto-analyzer.^{21,22}

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS v.21 software (SPSS Inc., Chicago, IL, USA). The conformity of variables with normal distribution was assessed with the Shapiro-Wilk test. Descriptive statistics of mes and standard deviations were used for normally distributed data, median and minimum-maximum ranges for non-normally distributed data. Categorical

data were given as counts (n) and percentages (%). Paired samples t test, repeated measure ANOVA and Wilcoxon tests were performed to compare the outcome parameters measured before and after the treatment period. Statistical significance was taken as $\alpha=0.05$.

RESULTS

The mean age of the patients was 47.1 ± 8.8 years with female dominance ($n=31, 72.1\%$, $n=12, 27.9\%$) for females and males respectively. The mean body mass index (BMI) of the patients was 28.4 ± 4.3 kg/cm² and the mean duration of disease was 5.9 ± 4.1 years.

There was a statistically significant improvement in VAS from baseline to 1 and 3 months ($p < 0.001$). There were statistically significant improvements in BDI and NHP (except NHP social isolation subgroup) from baseline to 1 month in patients with MPS (Table 2, Table 3).

We found a statistically significant decrease in the concentration of LA in isolated leucocyte of cupping blood. It was found that WCT [$8.54 (3.76-40.49)$ mg LA/g protein versus $12.7 (3.58-100.92)$ mg LA/g

TABLE 2: The levels of Visual Analogue Scale before and after the treatment with WCT.

	Baseline	First month	Third month	p value
VAS	70.2 ± 14.5	34.7 ± 14.7	32.3 ± 15.1	< 0.001

WCT: Wet Cupping Therapy, VAS: Visual Analogue Scale, p value of between Baseline and first month $p < 0.001$, p value of between baseline and third month $p < 0.001$, p value of between first month and third month = 0.012 (analyzed by repeated measure ANOVA).

TABLE 3: The clinical parameters of patients before and after the treatment with WCT (n=43).

	Baseline	First month	p value
BDI*	13.6 ± 9.3	11.6 ± 6.1	0.001
NHP-P*	52.6 ± 35.1	22.2 ± 19.4	0.001
NHP-ER*	26.4 ± 23.7	25.0 ± 23.4	0.024
NHP-S*	25.9 ± 28.0	13.4 ± 15.9	0.001
NHP-SI*	8.1 ± 12.8	7.1 ± 11.7	0.142
NHP-PA*	25.7 ± 19.0	14.7 ± 12.5	0.001
NHP-E*	50.5 ± 37.8	27.8 ± 32.3	0.001

WCT: Wet Cupping Therapy, BDI: Beck Depression Inventory, NHP-P: Nothingham health profile-pain, NHP-ER: Nothingham Health Profile-Emotion Reaction, NHP-S: Nothingham Health Profile-Sleep, NHP-SI: Nothingham Health Profile-Social Isoaltion, NHP-PA: Nothingham Health Profile-Physical Activity, NHP-E: Nothingham Health Profile- Energy, *: analyzed by paired samples t test.

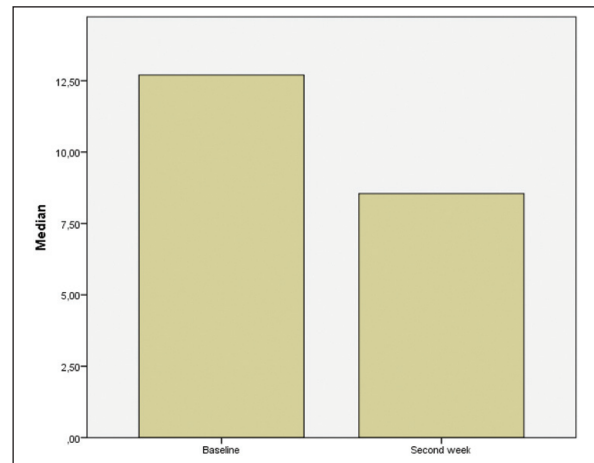


FIGURE 2: The changes in the lactic acid levels of cupping blood (analyzed by Wilcoxon test).

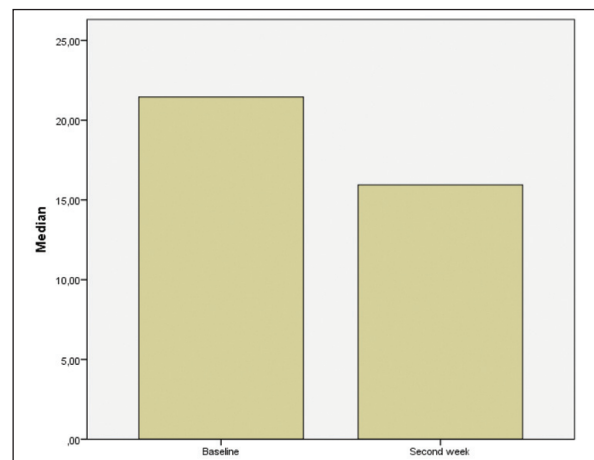


FIGURE 3: The changes in the lactic acid levels of venous blood (analyzed by Wilcoxon test).

protein] ($p=0.016$) 15 days after (Figure 2). The median level of LA in isolated leucocyte of venous blood was lower than the levels before WCT but it wasn't statistically significant [$16.24 (6.72-109.87)$ mg LA /g protein versus $22.15 (6.32-141.83)$ mg LA /g protein] ($p=0.122$) (Figure 3).

Three of patients had mild faintness and 5 of patients had itching at the cupping sites.

DISCUSSION

Cupping therapy is a complementary treatment method widely used all over the world for the treatment of different diseases.²³⁻²⁶ The results of our study evaluating the effectiveness of WCT on pain, quality

of life and psychological status of patients with MPS demonstrate that WCT resulted in significant improvements in VAS-pain following one and three months, total and subgroups of NHP and BDI scores in the first month follow-up.

The efficiency of cupping on neck pain was investigated in the study of Kim et al. and they demonstrated that there was a significant improvement in the pain of patients in accordance with our study but the wet cupping method was different from the our study.²⁷ They used double S cupping method (traditional Chinese WCT) including puncture - cupping steps and we applied triple S method including dry cupping-puncture-cupping steps.^{28,29} El Sayed et al. Suggested that triple S method was better than the double S method regarding of blood and interstitial fluid excretion and analgesic effect.²⁹

In a study of patients with carpal tunnel syndrome, Michalsen et al., found that WCT had a significant decrease in pain and quality of life similar to our study.⁶

In a study of Lauche, cupping therapy was effective in relieving VAS and quality of life (36-Item Short Form) in patients with non-specific neck pain, similar to our study.³⁰

Al Bedah et al. reported that WCT was considerably beneficial in decreasing pain and improving disability associated with persistent nonspecific low back pain at least for 2 weeks after WCT in concordance with present study. Beside the pain relief, quality of life and psychological state improvement continued following 1 and 3 months respectively.³¹

The mechanism of action of WCT is still not clear, and many theories have been proposed. Local damage to the skin in cupping application activating diffuse noxious inhibitory control may lead to stimulate the nociceptive system.³²

The analgesic mechanism in WCT was suggested to be similar to the mechanism of acupuncture that occurs with segmental, extra-segmental and central regulatory actions.⁵ We can speculate that the activation of WCT might be similar to acupuncture in our study because, the application regions of WCT was coverage area of acupoints in our study.

We hypothesized that one of the mechanisms of WCT may be through metabolic products such as LA beside the mentioned above and we measured the level of LA in isolated leucocyte in venous and cupping blood.³³

Boschmann et al. found that interstitial muscles and plasma LA increased as a consequence of intense exercise and the same result was shown by Rosendal et al. in response to repetitive arm movement.^{33,34} They suggested that change of LA levels contributed to anaerobic metabolism in the affected muscle during repetitive arm movement perhaps, because of insufficient local blood flow and nonuniform muscle contraction. Similar to the studies above mentioned, the ongoing contractions might lead to LA accumulation in the muscles of patients with MPS in the present study.¹³

Moraska et al. showed that both LA and blood flow elevated in the trigger points of muscle after practising trigger point release technique.³⁵ The explanation was the production of LA by muscle, released into the interstitial fluid and then eradicated by local blood flow. It was stated that, an increased blood flow is expected to remove LA from the interstitial space and so reducing the levels of LA. And this finding was confirmed by an increased level of LA in the cupping blood sample of first application compared to the cupping blood sample of second application in our study. It might indicate the excretion hypothesis of excess fluid and toxins from the body by WCT.³⁶

Emerich et al. found that dry cupping significantly increased LA levels on the application site and they reported that increased LA level resulted from hypoxia and local acidosis.³⁷ We applied triple S method involving dry cupping-puncture-cupping steps. We can speculate that LA accumulated on the dry cupping step and the collected LA was removed by puncture-cupping steps in the present study. Hereby WCT might indicate a tendency of anaerobic glycolysis to aerobic glycolysis.³³

It is very important to evaluate possibility of adverse events and reusing medical devices could cause contamination risk by way of blood and body fluid.²³ WCT was applied on sterile conditions in our study.

None of our patients experienced severe adverse effect, only 3 patients had mild faintness and 5 patients had itching at the cupping sites. Kim et al declared that 5 patients had adverse events of skin laceration, pruritus cutaneus, pain at the cupping sites, widespread pain; and 3 patients had experienced vaso-vagal shock in another study.^{5,27}

Traditional and complementary medicine including WCT is supported by the Ministry of Health in Turkey and a regulation on this topic was also issued.¹⁷ Thus, illegal applications will be prevented and these treatment methods would be practised by doctors similar to regulation in Saudi Arabia, China and Germany.¹⁶

The following rate of patients were approximately 80% in the WCT group similar to the study of Farhadi et al.⁵ The compliance of the patients was good and it was well tolerated by the patients in the present study as well.

A major limitation of our study was lack of a control group receiving a different treatment protocol or a control group comparing the level of LA with WCT group. Another limitation was that we have measured LA levels for 21 samples out of 43 patients, due to insufficient sample collected within the cupping blood or coagulation of blood.

CONCLUSION

In conclusion, WCT is found to be effective in clinical improvement of pain, quality of life and psycho-

logical status. We can suggest that WCT is beneficial in regard to simple application, immediate effects on pain, cost effective and time saving. In conclusion, WCT is found to be effective in clinical improvement of VAS, BDI and NHP scores. This study suggests that WCT may be beneficial for pain through reducing LA levels in cupping blood in patients with MPS. Further studies with large control groups and with long follow-up periods are needed to observe the efficacy of WCT.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Müyesser ARAS, Turgut Kültür; **Design:** Müyesser Aras, Hakan Boyunağa; **Control/Supervision:** Müyesser Aras, Nermin Dindar; **Data Collection and/or Processing:** Müyesser Aras, Gamze Dursun; **Analysis and/or Interpretation:** Müyesser Aras; **Literature Review:** Kaleem Ullah Rajput, Müyesser Aras; **Writing the Article:** Müyesser Aras, Nermin Dindar; **Critical Review:** Hakan Boyunağa, Esra Dilek Keskin; **References:** Kaleem Ullah Rajput; **Materials:** Müyesser Aras, Nermin Dindar.

REFERENCES

1. Simons DG, Travell JG, Simons LS. Travell and Simons' Myofascial Pain and Dysfunction: The Trigger Point Manual. 2nd ed. Baltimore: Williams & Wilkins; 1999. p.1038.
2. Li LT, Ge HY, Yue SW, Arendt-Nielsen L. Nociceptive and non-nociceptive hypersensitivity at latent myofascial trigger points. Clin J Pain. 2009;25(2):132-7.[Crossref] [PubMed]
3. Ganesh GS, Singh H, Mushtaq S, Mohanty P, Pattnaik M. Effect of cervical mobilization and ischemic compression therapy on contralateral cervical side flexion and pressure pain threshold in latent upper trapezius trigger points. J Bodyw Mov Ther. 2016;20(3):477-83.[Crossref] [PubMed]
4. Esenyel M, Caglar N, Aldemir T. Treatment of myofascial pain. Am J Phys Med Rehabil. 2000;79(1):48-52.[Crossref] [PubMed]
5. Farhadi K, Schwebel DC, Saeb M, Choubsaz M, Mohammadi R, Ahmadi A. The effectiveness of wet-cupping for nonspecific low back pain in Iran: a randomized controlled trial. Complement Ther Med. 2009;17(1):9-15.[Crossref] [PubMed]
6. Michalsen A, Bock S, Lütke R, Rapp T, Baecker M, Bachmann J, et al. Effects of traditional cupping therapy in patients with carpal tunnel syndrome: a randomized controlled trial. J Pain. 2009;10(6):601-8.[Crossref] [PubMed]
7. Cao H, Li X, Liu J. An updated review of the efficacy of cupping therapy. PLoS One. 2012;7(2):e31793.[Crossref] [PubMed] [PMC]
8. AlBedah A, Khalil M, Elolemy A, Elsubai I, Khalil A. Hijama (cupping): a review of the evidence. Focus Altern Complement Ther. 2011;16(1):12-6.[Crossref]
9. Kwon YD, Cho HJ. Systematic review of cupping including bloodletting therapy for musculoskeletal diseases in Korea. Korean J Orient Phys Pathol. 2007;21(3):789-93.
10. Kim JI, Lee MS, Lee DH, Boddy K, Ernst E. Cupping for treating pain: a systematic review. Evid Based Complement Alternat Med. 2011;2011:467014.[Crossref] [PubMed] [PMC]

11. Lütke R, Albrecht U, Stange R, Uehleke B. Brachialgia paraesthetica nocturna can be relieved by "wet cupping"--results of a randomised pilot study. *Complement Ther Med.* 2006;14(4):247-53.[Crossref] [PubMed]
12. Ahmadi A, Schwebel DC, Rezaei M. The efficacy of wet-cupping in the treatment of tension and migraine headache. *Am J Chin Med.* 2008;36(1):37-44.[Crossref] [PubMed]
13. Jafri MS. Mechanisms of myofascial pain. *Int Sch Res Notices.* 2014;2014:523924.[Crossref] [PubMed] [PMC]
14. de-Las-Pe-as CF. Interaction between trigger points and joint hypomobility: a clinical perspective. *J Man Manip Ther.* 2009;17(2):74-7.[Crossref] [PubMed] [PMC]
15. Gerwin RD, Dommerholt J, Shah JP. An expansion of Simons' integrated hypothesis of trigger point formation. *Curr Pain Headache Rep.* 2004;8(6):468-75.[Crossref] [PubMed]
16. Mahmoud HS, Abou EI Naga M, Omar NAA, El-Ghazzawy HA, Fathy YM, Nabo MMH, et al. Anatomical sites for practicing Wet Cupping Therapy (Al-Hijamah): in light of modern medicine and prophetic medicine. *Altern Integ Med.* 2013;2(8):138.[Crossref]
17. Resmî Gazete. (27.10.2014, Sayı: 29158) sayılı Geleneksel ve Tamamlayıcı Tıp Uygulamaları Yönetmeliği; 2014. p.3.
18. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain.* 1997;72(1-2):95-7.[Crossref] [PubMed]
19. Küçükdeveci AA, McKenna SP, Kutlay S, Gürsel Y, Whalley D, Arasil T. The development and psychometric assessment of the Turkish version of the Nottingham Health Profile. *Int J Rehabil Res.* 2000;23(1):31-8.[Crossref] [PubMed]
20. Hisli N. The reliability and validity study of the Beck Depression Inventory in university student Turkish Journal of Psychology. 1989;7(23):3-13.
21. Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. *Analyst.* 1972;97(151):142-5.[Crossref] [PubMed]
22. Sroka J, Kordecka A, Wlosiak P, Madeja Z, Korohoda W. Separation methods for isolation of human polymorphonuclear leukocytes affect their motile activity. *Eur J Cell Biol.* 2009;88(9):531-9.[PubMed]
23. Kim JI, Kim TH, Lee MS, Kang JW, Kim KH, Choi JY, et al. Evaluation of wet-cupping therapy for persistent non-specific low back pain: a randomised, waiting-list controlled, open-label, parallel-group pilot trial. *Trials.* 2011;12:146.[Crossref] [PubMed] [PMC]
24. Lee MS, Choi TY, Shin BC, Kim JI, Nam SS. Cupping for hypertension: a systematic review. *Clin Exp Hypertens.* 2010;32(7):423-5.[Crossref] [PubMed]
25. Lee MS, Choi TY, Shin BC, Han CH, Ernst E. Cupping for stroke rehabilitation: a systematic review. *J Neurol Sci.* 2010;294(1-2):70-3.[Crossref] [PubMed]
26. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. *Eur Spine J.* 2003;12(2):149-65.[Crossref] [PubMed] [PMC]
27. Kim TH, Kang JW, Kim KH, Lee MH, Kim JE, Kim JH, et al. Cupping for treating neck pain in video display terminal (VDT) users: a randomized controlled pilot trial. *J Occup Health.* 2012;54(6):416-26.[Crossref] [PubMed]
28. Cao H, Han M, Li X, Dong S, Shang Y, Wang Q, et al. Clinical research evidence of cupping therapy in China: a systematic literature review. *BMC Complement Altern Med.* 2010;10:70.[Crossref] [PubMed] [PMC]
29. El Sayed SM, Mahmoud HS, Nabo MMH. Methods of wet cupping therapy (Al-Hijamah): in light of modern medicine and prophetic medicine. *Altern Integ Med.* 2013;2(3):1-16.[Crossref]
30. Lauche R, Cramer H, Choi KE, Rapp T, Saha FJ, Dobos GJ, et al. The influence of a series of five dry cupping treatments on pain and mechanical thresholds in patients with chronic non-specific neck pain-a randomised controlled pilot study. *BMC Complement Altern Med.* 2011;11:63.[Crossref] [PubMed] [PMC]
31. AlBedah A, Khalil M, Elolemy A, Hussein AA, AlQaed M, Al Mudaiheem A, et al. The use of wet cupping for persistent nonspecific low back pain: randomized controlled clinical trial. *J Altern Complement Med.* 2015;21(8):504-8.[Crossref] [PubMed] [PMC]
32. Calvino B, Grilo RM. Central pain control. *Joint Bone Spine.* 2006;73(1):10-6.[Crossref] [PubMed]
33. Rosendal L, Blangsted AK, Kristiansen J, Søgaard K, Langberg H, Sjøgaard G, et al. Interstitial muscle lactate, pyruvate and potassium dynamics in the trapezius muscle during repetitive low-force arm movements, measured with microdialysis. *Acta Physiol Scand.* 2004;182(4):379-88.[Crossref] [PubMed]
34. Boschmann M, Rosenbaum M, Leibel RL, Segal KR. Metabolic and hemodynamic responses to exercise in subcutaneous adipose tissue and skeletal muscle. *Int J Sports Med.* 2002;23(8):537-43.[Crossref] [PubMed]
35. Moraska AF, Hickner RC, Kohrt WM, Brewer A. Changes in blood flow and cellular metabolism at a myofascial trigger point with trigger point release (ischemic compression): a proof-of-principle pilot study. *Arch Phys Med Rehabil.* 2013;94(1):196-200.[Crossref] [PubMed] [PMC]
36. Lee MS, Kim JI, Ernst E. Is cupping an effective treatment? An overview of systematic reviews. *J Acupunct Meridian Stud.* 2011;4(1):1-4.[PubMed]
37. Emerich M, Braeunig M, Clement HW, Lütke R, Huber R. Mode of action of cupping--local metabolism and pain thresholds in neck pain patients and healthy subjects. *Complement Ther Med.* 2014;22(1):148-58.[Crossref] [PubMed]