

Comparison of topical glyceryl trinitrate patch and local steroid injection in term of pain relief for treatment of lateral epicondylitis

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Abstract

Introduction: Lateral epicondylitis (L.E) is a common disease which effect people involved in manual job tasks. The dominant arm is generally affected the most. The annual incidence of this disease has been reported to be 1-5 percent in general population. It occurs in equal frequency in both male and females and is common in 35-40 years of age. The designation of lateral epicondylitis is a misnomer since it has been proved now that it is not an inflammatory disorder rather a degenerative disorder in the tendon of common extensor origin. It mostly affects extensor carpi radialis brevis muscle origin which is a part of common extensor origin and occur due to cumulative microtrauma exceeding the normal tissue capacity to repair.

Aim: To compare glyceryltrinitrate patch and local steroid injection in term of mean pain score reduction for treatment of lateral epicondylitis.

Study design: Randomized controlled trial

Place and Duration: In the Department of Orthopedic Surgery, District Headquarter Hospital (DHQ) Teaching Hospital, Kohat and DHQ hospital Timergara for one year duration from March 2019 to March 2020.

Material and Methods: In this study a total of 112 patients which was calculated with the help of EPI sample size calculator version 2 with following parameters. Power of study ($1-\beta$) = 90%, Confidence level = 95 %, Mean of group A = 3.15 + 1.53, Mean of group B = 2.28 + 1.28 4 Sample A = 56, Sample B = 56. Consecutive non probability technique was used for sample collection.

Results: In this study mean age in group-A 34 years with $SD \pm 18.79$ where as mean age in group-B was 35 years with $SD \pm 19.62$. In group-A 41(73%) patients were male, 15(27%) patients were female. Where as in group-B 42(75%) patients were male, 14(25%) patients were female. Difference in the mean pain score among two groups was as in Group A mean pain score was 4 ± 1.18 . Where as in group-B mean pain score was 3 ± 1.17 .

Conclusion: Our study concludes that glyceryltrinitrate patch is better than local steroid injection in terms of mean pain score reduction in the treatment of lateral epicondylitis.

Keywords: glyceryltrinitrate patch, local steroid injection. Mean pain score reduction, lateral epicondylitis

Introduction:

Lateral epicondylitis (L.E) is a common disease which effect people involved in manual job tasks. The dominant arm is generally affected the most. The annual incidence of this disease has been reported to be 1-5 percent in general population.^{1,2} It occurs in equal frequency in

both male and females and is common in 35-40 years of age.³ The designation of lateral epicondylitis is a misnomer since it has been proved now that it is not an inflammatory disorder rather a degenerative disorder in the tendon of common extensor origin. It mostly affects extensor carpi radialis brevis muscle origin which is a

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part of common extensor origin and occur due to cumulative microtrauma exceeding the normal tissue capacity to repair.³⁻⁵ The most common overuse syndrome is related to excessive wrist extension and commonly referred to as “tennis elbow,” but it is actually more common in non-tennis players. The patient complains of pain over the lateral elbow that worsens with activity and improves with rest. Pain can vary from being mild (eg, with aggravating activities like tennis or the repeated use of a hand tool), or it can be such severe pain that simple activities like picking up and holding a coffee cup (ie, “coffee cup sign”) will act as a trigger for the pain.^{6,7} Pain is increased with resisted wrist extension, with the wrist radially deviated and pronated and the elbow extended and with resisted middle finger extension.^{8,9}

Historically different treatment modalities for treatment of lateral epicondylitis have been advised such as conservative treatment with physiotherapy, oral non steroidal anti inflammatory drugs (NSAID), local steroid injections, injection of autologous blood which delivers growth factors, local botulinum toxin injection, topical glyceryl trinitrate (GTN) patches and surgery.^{10,11}

Local steroid injection is one of the commonest treatment modality prescribed in cases for which initial conservative management like activity modification and NSAID do not work. It is associated with complications like irritation, change of skin colour, skin and perilymphatic atrophy, soft tissue calcification, skin defect, hypopigmentation, sterile abscess, ecchymosis, and allergic rash. Osteomyelitis of humerus after three injections of corticosteroid has also been reported.^{12,13}

In recent years new treatment modality with transdermal GTN patch has been introduced which is a noninvasive treatment modality with limited adverse effects.

Despite several treatment methods for lateral epicondylitis from local injection to complicat-

ed surgical procedures, very few methods have been significantly proven to be effective and there is lack of evidence proving one techniques superiority over another. There are very limited studies which have compared local steroid injection and topical GTN patch. This study is aimed to find out the treatment option for lateral epicondylitis which is least invasive, having limited adverse effect but better in pain relief. If glyceryl trinitrate patch is found to be better than local steroid injections in pain relief then the results of this study will be disseminated to other health professionals and suggestions will be given for rationale use of patch for L.E. This will further help us in reducing the disability associated with lateral epicondylitis.

Material and methods:

Study setting: This randomized control trial was held in the Department of Orthopedic Surgery, DHQ Teaching Hospital, Kohat and DHQ hospital Timergara for one year duration from March 2018 to March 2019.

Sample size: It has been calculated with the help of EPI sample size calculator version 2 with following parameters. Power of study $(1-\beta) = 90\%$, Confidence level = 95 %, Mean of group-A = 3.15 ± 1.53 . Mean of group-B = 2.28 ± 1.28 . Sample A = 56, Sample B = 56, Total sample = 112

Sampling technique: Consecutive non probability technique.

Inclusion criteria:

- Patients with pain and tenderness over lateral epicondyle
- 30-50 years of age
- either gender

Exclusion criteria:

- Patients with previous history of fracture around elbow
- patient with systemic rheumatoid arthritis
- patient with cervical spondylomyelopathy
- nerve entrapment on physical examination

Data collection procedure: After approval from research and ethical committee, all patients

Table 1: Age distribution (n=112)

AGE	Group A	Group B
30-40 years	40(72%)	39(70%)
41-50 years	16(28%)	17(30%)
Total	56(100%)	56(100%)
Mean and SD	34 years \pm 18.79	35 years \pm 19.62

Group A: Glyceryltrinitrate patch, Group B: Local steroid injection

T test was applied in which P value was 0.7835

Table 2: Gender Distribution (N=112)

Gender	Frequency	Percentage
Male	41(73%)	42(75%)
Female	15(27%)	14(25%)
Total	56(100%)	56(100%)

Group-A: Glyceryltrinitrate patch, Group-B: Local steroid injection

Chi square test was applied in which P value was 0.8292

who present to orthopedics out patient department, with highly suspected features of lateral epicondylitis. i.e significant lateral epicondyle pain during daily activities, tenderness over lateral epicondyle at origin of extensor muscles, increase in pain during active dorsiflexion of wrist and middle finger against resistance with elbow in extension was included in this study. The purpose of the study was explained to the patients. Informed written consent was taken from those who agree to participate in the study.

The patients were randomly allocated into two groups. Pre-treatment degree of pain was recorded on visual analogue scale for both the groups in the proforma (Appendix A). The visual analogue scale is a pain measuring instrument which is a horizontal line 100mm in length and is divided by vertical lines into 10 equal points. Each vertical line is 10mm apart as shown below. Group-A patients had received nitric oxide in form of GTN patch. This patch delivers 1.25mg of Nitric Oxide (NO) every 24 hours. For treatment purpose it was divided into four equal parts. Each part was applied over maximum area of tenderness and worn for 24 hours a day. Group-B patient had received local steroid injection, which is applied in form of 40 mg of methyl prednisolone acetate along with 1 ml of 2% lignocaine. It is administered over maximum area of tenderness on the lateral

epicondyle and content is injected into extensor group of muscles. All the included patients were advised to restrain activities involving repetitive movements of wrist and elbow during the initial 4-weeks of starting treatment.

All the patients were evaluated in OPD for the degree of pain one month after treatment. The lateral epicondyle pain was assessed on 10 points visual analogue scale by checking the degree of pain on resisted dorsiflexion. Patients were asked to rate their pain on the scale. Mean of the pain score pre and post treatment was calculated for both groups A and B.

Statistical analysis: The data was analyzed by SPSS latest version available. Frequency and percentages was calculated for qualitative variables like gender. Mean+SD was calculated for numerical variables like age and visual analogue scores. Independent t- test was applied to compare mean pain score in both the groups A and B. p-value < 0.05 was considered significant. Visual analogue score for both groups A and B was stratified among age and gender to see effect modification. Post-stratification t-test was applied. All the results were presented in the form of tables, charts and graphs.

Results:

In this study total of 112-patients were observed to compare glyceryltrinitrate patch and local steroid injection in term of mean pain score reduction for treatment of lateral epicondylitis and the results were analyzed as.

Age distribution among two groups was as in Group A 40(72%) patients were in age range 30-40 years, 16(28%) patients were in age range 41-50 years. Mean age was 34 years with SD \pm 18.79. Where as in Group B 39(70%) patients were in age range 30-40 years, 17(30%) patients were in age range 41-50 years. Mean age was 35 years with SD \pm 19.62. (as shown in table no 1).

Gender distribution among two groups was as in group-A 41(73%) patients were male, 15(27%) patients were female. Where as in group-B

Table 3: Pre Treatment Pain Score (N=112)

Pain score	Group A	Group B
0-4 (mild)	4(7%)	3(5%)
5-7 (moderate)	43(76%)	43(77%)
7-10 (severe)	9(17%)	10(18%)
Total	56(100%)	56(100%)
Mean and SD	7 ± 3.97	7 ± 3.77

Group A:Glyceryltrinitrate patch, Group B: Local steroid injection
T test was applied in which P value was 1.0000

Table 4: Pain Score At Follow Up (N=112)

Pain score	Group A	Group B
0-4 (mild)	45(81%)	40(72%)
5-7 (moderate)	11(19%)	16(28%)
7-10 (severe)	00(00%)	00(00%)
Total	56(100%)	56(100%)
Mean and SD	4 ± 2.40	5 ± 2.47

Group A: Glyceryltrinitrate patch, Group B: Local steroid injection
T test was applied in which P value was 0.0319

Table 5: Mean reduction in pain score (N=112)

	Pre treatment pain score	Post treatment Pain score	Mean reduction of pain	P Values
Group A	7 ± 3.97	4 ± 2.40	3 ± 1.57	0.0001
Group B	7 ± 3.77	5 ± 2.47	2. ± 1.30	0.0012
P values	1.0000	0.0319	0.0004	

Group A:Glyceryltrinitrate patch, Group B: Local steroid injection

Table 6: Stratification of mean reduction in pain score with age (30-40 years) (n=112)

	Pre treatment pain score	Post treatment Pain score	Mean reduction of pain	P Values
Group A	8 ± 4.91	4 ± 3.73	4 ± 1.18	0.0001
Group B	8 ± 4.83	5. ± 3.66	3. ± 1.17	0.0003
P values	1.0000	0.1550	0.0001	

Group A: Glyceryltrinitrate patch, Group B: Local steroid injection

Table 7: Stratification of mean reduction in pain score with age (41-50 Years) (N=112)

	Pre treatment pain score	Post treatment Pain score	Mean reduction of pain	P Values
Group A	7 ± 3.80	4 ± 2.40	3 ± 1.40	0.0001
Group B	7 ± 3.97	5 ± 2.47	2. ± 1.50	0.0018
P values	1.0000	0.0319	0.0004	

Group A:Glyceryltrinitrate patch, Group B: Local steroid injection

42(75%) patients were male, 14(25%) patients were female. (as shown in table no 2)

Difference in the mean pain score among two groups was as in group-A mean pain score was 4 ± 1.18. Where as in group-B mean pain score was 3 ± 1.17. (as shown in table no 6)

Stratification of mean pain score with age, gender is given in table no 7,8,9.

Discussion:

Lateral epicondylitis (L.E) is a common disease which effect people involved in manual job tasks. The dominant arm is generally affected the most. The annual incidence of this disease has been reported to be 1-5 percent in general population.^{1,2} It occurs in equal frequency in both male and females and is common in 35-40 years of age.³ The designation of lateral epicondylitis is a misnomer since it has been proved now that it is not an inflammatory disorder rather a degenerative disorder in the tendon of common extensor origin. It mostly affects extensor carpi radialis brevis muscle origin which is a part of common extensor origin and occur due to cumulative microtrauma exceeding the normal tissue capacity to repair.^{3,4} Our study shows that mean age in group-A 34 years with SD±18.79 where as mean age in group-B was 35 years with SD ± 19.62. In group-A 41(73%) patients were male, 15(27%) patients were female. Where as in group-B 42(75%) patients were male, 14(25%) patients were female. Difference in the mean pain score among two groups was as in group-A mean pain score was 4 ± 1.18. Where as in group-B mean pain score was 3 ± 1.17.

A study conducted by Raif et al to find out the efficacy of GTN patch in terms of pain relief in the treatment of L.E found that there was significant improvement in pain relief in lateral epicondylitis, they concluded that the mean visual analogue score (VAS) decreased from 8.05+ 1.53 to 3.15 + 1.53 at 3 weeks follow up.¹ In another study conducted by Nipun et al on local steroid injection in treatment of lateral epicondylitis found that the VAS in preinjection phase

Table 8: Stratification of mean reduction in pain score with gender (Male) (n=112)

	Pre treatment pain score	Post treatment Pain score	Mean reduction of pain	P Values
Group A	7 ± 4.91	4 ± 2.40	3 ± 1.57	0.0001
Group B	7 ± 3.80	4 ± 2.40	3 ± 1.40	0.0001
P values	1.0000	1.0000	1.0000	

Group A: Glyceryltrinitrate patch, Group B: Local steroid injection

Table 9: Stratification of mean reduction in pain score with gender (female) (n=112)

	Pre treatment pain score	Post treatment Pain score	Mean reduction of pain	P Values
Group A	7 ± 3.77	5 ± 2.47	2. ± 1.30	0.0012
Group B	7 ± 3.97	5 ± 2.47	2. ± 1.50	0.0018
P values	1.000	1.000	1.000	

Group A: Glyceryltrinitrate patch, Group B: Local steroid injection

was 6.20+ 1.61 and at 6 weeks follow up the pain decreased to 2.28 + 1.28SD.⁴

Similar results were observed in another study conducted by Chartier Bet al.¹⁴ in which Pain was decreased most at week 2 of the study (p=0.002), tenderness was measured at week 6 and 12, each with improvement and (p=0.02), and peak force at weak 24 was increased (p=0.03). According to the journal, "at 6 months, 81% of treated patients was asymptomatic during activities of daily living, compared with 60% of patients who had tendon rehabilitation alone."

This gives us the Control event rate (CER) of 60%, for the patients with the placebo patch, and an Experimental event rate (EER) of 81%. Relative risk reduction (RRR) was calculated at 35%, absolute risk reduction at 21%, and numbers needed to treat (NNT) was.

The NNT shows that a practitioner needs to treat 5-patients who have tennis elbow with GTN in order to have 1-patient show benefit.

Similar results were observed in another study conducted by Ozden Ret al.¹⁵ which shows that there were no significant differences in any of the baseline clinical parameters between groups. At the 3rd week follow-up, there were statistically significant differences in the pain measured us-

ing VAS between groups (mean VAS score of the control and treatment groups were 6.45 and 3.15, respectively) (p=0.001). Patients in the GTN group and control group had lower VAS pain scores and reduced elbow pain at 3-weeks (3.15 vs 8.05 in the GTN and 6.45 vs 8.80 in the control group). In the control group, no patient had excellent or good results while 18(90%) patients in treatment group reported successful treatment. There was statistically significant difference in the VAS measured at 6 months between groups (mean VAS score of the control and treatment groups were 4.85 and 0.70, respectively) (p=0.001).

Conclusion:

Our study concludes that glyceryltrinitrate patch is better than local steroid injection in terms of mean pain score reduction in the treatment of lateral epicondylitis.

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Role and contribution of authors:

Dr Basit Hussain, collected the data, references and did the initial writeup

Dr Imtiaz Ahmad, collected the data, and helped in introduction writing.

Dr Zeeshan Faisal, helped in collecting the data, introduction and discussion writing.

Dr Abdus Samad Khan, collected the references and helped in discussion writing.

Dr Raziq Shah, collected the references and helped in conclusion writing.

Dr Muhammad Imran Javed, collected the references and helped in interpretation the data, went through the article did critical analysis and did final changes.

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