**Ozden R, Uruc V, Dogramaci Y, and et al. Management of tennis elbow with topical glyceryl trinitrate. *Acta Orthop Traumatol Turc* 2014; 48(2):175-180.**

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**Design:** Randomized controlled trial

**Objective:** To investigate the effectiveness of topical glyceryl trinitrate (GTN) on pain relief and functional improvement for the treatment of lateral epicondylitis (LE).

**Population /sample size/setting:**

* A total of 40 participants including 12 females and 28 males, (mean age 43.2 years) with a diagnosis of lateral epicondylitis were selected based on the presence of tenderness, pain, and positive pain stimulating maneuvers between 2009 and 2011.
* The 40 patients were randomly assigned into one of 2 groups. The topical glyceryl trinitrate (GTN) group (n = 20) received GTN transdermal patches that delivered 1.25 mg of GTN every 24 hours. The control group (n=20) received placebo patches without GTN.
* Inclusion criteria included symptoms of more than 3 months, resisted wrist extension, tenderness and pain around the lateral epicondyle, positive tennis elbow pain test (Mill’s Sign), and positive chair lift test.
* Exclusion criteria included inconclusive diagnosis of LE, neurologic deficits, coexisting arthritis, medial epicondylitis, effusion of the elbow, radiculopathy from the cervical spine, previous surgery for LE, entrapment of the ulnar nerve, periarticular fracture, infection, abnormal erythrocyte sedimentation rate, and previous injections.

**Methods/Interventions/Outcome Measures:**

* Study design was a randomized, double-blind study with 6 months of follow-up. Investigators and patients were blinded to which patch was given to the patient.
* The GTN group received GTN transdermal patches that delivered 1.25 mg of GTN every 24 hours that were applied to the area of maximal tenderness once a day. The control group received placebo patches that were applied in the same manner. Patches were worn until the symptoms subsided or until the study ended at 6 months. Subjects were also instructed to avoid activities that increased their pain.
* Both groups were instructed to perform a standard tendon rehabilitation program.
* Clinical history and physical examination were performed before treatment at baseline. The primary outcome measure was the visual analogue scale (VAS), a 10 point scale assessed at baseline and at 3 weeks and 6 month follow-ups. Secondary outcomes included grip strength and treatment success. Treatment success was subjectively rated by the patient as excellent, good, fair, or poor. Treatment was considered successful when the patient had an excellent or good score.
* Sample size was based on a power calculation that showed that 20 patients per group were necessary to achieve 80% power with a significance level of P < 0.05.

**Results:**

* No significant differences or clinically meaningful differences were observed between the 2 groups at baseline for gender, mean age, dominant extremity, duration of symptoms, or VAS score.
* For within group comparisons, patients in both groups had significantly lower VAS scores and reduced elbow pain at the 3 week follow-up compared to baseline VAS scores. VAS scores in the GTN group decreased from 8.05 to 3.15 and in the control group from 8.80 to 6.45. VAS scores continued to decrease in both groups at the 6 month follow-up. The GTN group decreased further to 0.70 and the control group to 4.85.
* For between group comparisons, patients in the GTN group exhibited significantly less pain at both follow-ups compared to patients in the control group. There were statistically significant differences in mean VAS scores between the GTN group and the control group at both the 3 week follow-up (3.15 vs 6.45, P= 0.001) and the 6 month follow-up (0.70 vs 4.85, P=0.001).
* At the 3 week follow-up, no successful treatment (excellent, good) was reported in the control group. Successful treatment was reported by 18 (90%) patients in the GTN group. At the 6 month follow-up, successful treatment was reported by 3 (15%) patients in the control group, and by 19 (95%) patients in the treatment group.
* Two patients in the control group and one patient in the GTN group were affected by headache, but no one terminated treatment due to headache. No other adverse effects were reported.

**Authors’ conclusions:**

* This study showed that nitric oxide delivery via a topical patch containing glyceryl trinitrate placed directly over an area of tendinopathy is effective in improving clinical recovery and enhancing healing of LE in patients through a reduction of pain and increased strength. The treatment of tennis elbow with GTN reduces pain more rapidly.
* Both groups exhibited improvement in terms of pain reduction over the 6 months, but a statistically significant difference in mean VAS scores between groups was also found at 6 months in favor of the GTN group.
* Application of topical nitric oxide improved functional outcomes and treatment results in terms of pain relief in patients with LE.

**Comments:**

* This study supports the conclusion that a topical patch of glyceryl trinitrate placed directly over an area of tendinopathy is effective in decreasing pain in patients with lateral epicondylitis over a period of 6 months.
* Strengths of this study included subject and investigator blinding, the inclusion of a comparable control group, a mid-term follow-up time, a sample size calculation, and a clearly designated primary outcome.
* The authors failed to report the results of grip strength or any real functional outcome measure. The secondary outcome of treatment success vaguely included grip strength as a functional component of this outcome measure. This study lacked a distinct, objective functional outcome measure used to monitor progress in LE and assessed at all follow-up points.
* Limitations of this trial included failure to describe the randomization process, no mention of allocation concealment, lack of any description of the “standard tendon rehabilitation program”, no functional outcome measure, and no information on participant drop-outs, if any.
* Standard deviations and P values were reported which are not the most informative data. The authors did not provide mean differences with confidence intervals and effect sizes for between group results, because they analyzed the VAS scores using the Mann-Whitney U-test. This nonparametric test does not report those results, and so this is not a limitation of the study. A between group effect size would have been helpful in judging the magnitude of the intervention. The mean difference in the VAS scores (not reported) between the groups at 6 months was 4.15 which is clearly clinically significant. This result is corroborated by a 95% treatment success rate in the GTN group compared to only a 15% treatment success rate in the control group.
* Recommendations during the study to not provoke pain during daily activities may have led to an overall reduction of such perceived pain as seen in both groups, and this may partially explain the improvement in pain reduction observed in both groups over time.

**Assessment*:***

This adequate study provides some evidence that wearing a topical patch containing glyceryl trinitrate over an area of tendinopathy is more effective than a placebo patch in reducing pain and improving overall clinical recovery in subjects with lateral epicondylitis over a period of 6 months.