

**Peng B, Pang X, et al. A randomized placebo-controlled trial of intradiscal methylene blue injection for the treatment of chronic discogenic low back pain. Pain 2010;149:124-129.**

Design: Randomized clinical trial

Population/sample size/setting:

- 72 patients (41 men, 31 women, mean age 42) treated for discogenic low back pain at the General Hospital of the Armed Police Force in Beijing
- Entry criteria were low back pain without radiculopathy, but with MRI evidence of lumbar disc degeneration, with primary diagnosis of discogenic low back pain, lasting at least 6 months and not responding to physical therapy and/or opioids
- Exclusion criteria were disc herniation, spinal instability, spondylosis, lumbar canal stenosis, spondylolisthesis, disc degeneration with endplate Modic changes, neurologic disease, infection, inflammatory arthritis

Main outcome measures:

- 136 consecutive patients meeting entry criteria were given discography
- Positive discogram was one that reproduced the usual pain pattern and had posterior annular disruption, but had at least one negative adjacent disc
- 72 positive discograms were obtained; these were randomized to receive one of two injections at the time of the discogram: either methylene blue (MB, n=36) or saline placebo (n=36)
- MB was 1 ml of 1% MB with 1 ml of 2% lidocaine; placebo was 1 ml of saline with 1 ml of 2% lidocaine
- Two main outcomes were measured at 6, 12, and 24 months: pain on numeric rating scale (NRS) from 0-100, and Oswestry Disability Index (ODI) from 0-100
- Secondary analyses included patient satisfaction, complications, and medication usage
- Between baseline and 6 months, there was a large improvement for the MB group on NRS (from 72.3 to 24.9) and ODI (from 48.5 to 16.0); for placebo, there was no significant improvement on NRS (from 67.3 to 63.5) or ODI (from 49.4 to 48.4); these scores were maintained at 12 and 24 months
- At 24 months, 92% of the MB group, but only 14% of the placebo group, was satisfied or completely satisfied with the outcome of treatment
- Blinding was apparently maintained; the patients did not successfully guess whether they had received MB or placebo
- Medication usage was lower at 24 months in the MB group (8.3% taking regular medication) than in the placebo group (43% on regular medication)
- Nerve root injury, back pain aggravation, and disc space infection did not occur in either treatment group

Authors' conclusions:

- Intradiscal injection of methylene blue is effective for the relief of discogenic low back pain, probably through a neurolytic mechanism in the annulus
- Replication by other investigators is imperative

Comments:

- Randomization, allocation concealment, and blinding appear to have been done in a way that controls important sources of bias; risk of bias is low
- Follow-up is also good: there was only 1 patient lost to follow-up, and measurements were done at 6, 12, and 24 months
- There is some ambiguity in the way that the “positive” discography was done: pain was reproduced, but its intensity was not reported, and the pressure above opening pressure was not reported; the classification along ISIS guidelines is not clear (definite, probable, etc)
- Since 136 patients had discography and 72 were randomized, it is likely that the standard that was used was fairly selective
- The outcome “medication usage” is vague; the medications (NSAID, opioid) are not specified
- The effect size is very large, and replication elsewhere is imperative; if results are reproducible in other settings, methylene blue would be an inexpensive, effective, and important treatment for low back pain
- The population was a select one in a setting which had a “pristine” discogenic pain—many common conditions were exclusionary criteria (stenosis, herniation, endplate Modic changes)
- A statement is made that “blinding was satisfactory” and that patients did not know which treatment they had received, but it is not said how this was ascertained (e.g., by blinding questionnaire where they guess which group they were in)
- The proportion of patients with 30% and 50% pain relief is not reported; this would favor the MB group, but its omission does not compromise the large effect size

Assessment: High quality for good evidence that MB is likely to be beneficial for carefully selected patients with isolated discogenic pain