The effect of methylene blue on peridural fibrosis formation after laminectomy in rats: an experimental novel study

Majid Reza Farrokhi, MDa,b,, Mohammad Vasei, MDb,c, Saeed Fareghbal, MDa,b,, Nasrin Farrokhi, BSa,b

a Department of Neurosurgery, Shiraz Neurosciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
b Chamran Hospital, Chamran Boulevard, Shiraz, Iran
c Department of Pathology, Shiraz Neurosciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

BACKGROUND CONTEXT: Despite progress in surgical techniques, some patients still face postoperative recurrence of pain, although the rate of successful outcomes is estimated to be approximately 70% and 86% after primary decompression spinal surgery. Recently, attention has been focused on peridural fibrosis (PF), which may be responsible for recurrent pain after laminectomy or discectomy. Methylene blue (MB) has been shown to prevent fibrosis formation in various tissues.

PURPOSE: The aims of this study were to investigate the effects of MB and assess the effects of different doses on the prevention of postlaminectomy fibrosis formation in a rat model. This preclinical model is a potential platform for future clinical trials to identify an effective agent for the prevention of clinically important epidural scar formation.

STUDY DESIGN: An established bilateral L5–L6 rat laminectomy model was used to evaluate postlaminectomy PF with macroscopic and microscopic analyses.

PATIENT SAMPLE: Seventy-five male adult white Sprague-Dawley rats that underwent laminectomy at the L5–L6 levels were divided into five groups of 15 rats each.

OUTCOME MEASURES: Dissected specimens were evaluated macroscopically and microscopically by examiners who were unaware of the group assignment to record the presence or absence of PF formation.

METHODS: Groups A and B served as controls and Groups C, D, and E received treatment. Group A (sham) underwent laminectomy, and Group B was treated with normal saline at the laminectomy site. Rats in Groups C, D, and E received 0.1 mL MB at concentrations of 0.5%, 1%, and 2%, respectively, at the laminectomy site. All rats were killed 4 weeks after laminectomy. The results were compared statistically with the nonparametric Kruskal–Wallis test and Poisson regression.

RESULTS: Peridural fibrosis was found in five rats (33%) in control Groups A and B and in two rats (10%) in MB-treated laminectomy Groups C and D. The difference between control and MB groups was not statistically significant (p=0.27). The preventive effect of MB on PF was not seen at the highest dose of MB (2%) in Group E. Severity of fibrosis was lower in Groups C (MB 0.5%) and D (MB 1%) than in Group E (MB 2%) (p<0.01). Wound healing was
not affected, and there was no cerebrospinal fluid leakage. No neurological deficits were seen.

**CONCLUSION:** Low doses of MB may be an effective agent in preventing PF formation after lumbar laminectomy in rats. Clinical significance and safety in human use are currently undetermined.

**Keywords:** Methylene blue; Laminectomy; Failed back surgery syndrome; Dura; Rat