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CAN RADIOTHERAPY BE A NEW TREATMENT FOR POST-LAMINECTOMY LOW BACK SYNDROME?

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ABSTRACT

Introduction: Post-laminectomy peridural fibrosis and arachnoid adhesions related to lower back pain are common problems after laminectomy operations. Previous studies have shown that radiotherapy might prevent low back syndrome after laminectomy.

Methods: In this study, 23 male Wistar albino rats were used. Group I included nine rats that underwent laminectomy (L group), group II included nine rats treated with laminectomy and perioperative radiotherapy (L + R group). Group III included five rats and was used as a control group that did not undergo treatment. Laminectomy was performed in the L3 and L4 lumbar vertebral regions of group I and II rats. Rats in-group II also received perioperative radiotherapy in the laminectomy area. Radiotherapy was perioperative provided with electron radiation to a total dose of 700 cGy as a single fraction.

Results: Histopathological grade 0 epidural fibrosis and grade 1 fibroblast cell density ratios were 44.44% and 88.88% in the L + R group, 0% and 33.33% in the L group, respectively. Arachnoid adhesions were present in 88.8% of the L group, but only 44.4% of the L + R group. Grade 3 epidural fibrosis was shown in four rats (44.44%) in the L group and one rats (11.11%) in the L + R group.

Conclusion: Results indicate that perioperatively provided radiotherapy is significantly advantageous in preventing post-laminectomy adhesions and is not toxic.

Keywords: fibrosis, low-dose radiotherapy, failed back surgery syndrome, post-laminectomy

Level of Evidence: Level II, experimental study.

INTRODUCTION

Laminectomy is indicated for the surgical treatment of radicular nerve pain, spinal obstruction, pressure-related paresis, and plegia. Previous research indicates that lower back and radicular pain recurs in as many as 24% failed back surgery syndrome (FBSS) cases after laminectomy, which is a significant proportion [7,16].

Epidural scar tissue, also known as the post-laminectomy membrane, is the primary cause for these complications. Peridural fibrosis is a common cause of pain in patients after spinal surgery. Gabriel et al. indicate that a common cause of fibrosis is tissue regeneration due to the destruction of epidural fat, intraspinal hematoma, and replacement of the erector muscles of the spine into the spinal canal at the operation site [7,16].

Fibrosis may lead to pain and neurolysis because it exerts pressure [4,10], and postoperative scar formation usually inhibits the regeneration of peripheral nerves (8,9). Salvage surgery has a high complication rate because of further scarring [5,10,13]. Many different methods have been developed and various materials have been implanted on the dura for preventing or reducing scar formation. Although the results have shown only moderate efficacy in the inhibition of epidural fibrosis, numerous materials

and methods, including stimulation implants for the spinal cord, autogenous adipose grafting, mitomisin, Gelfoam, Oxiplex, non-steroidal anti-inflammatory drugs, Gore-Tex, carboxymethyl cellulose, Adcon-L, and radiotherapy, have been applied to prevent scar formation [2,4,9,11,14-15,23].

Evaluation of the literature showed that low-dose perioperative radiotherapy can inhibit peridural fibrosis in FBSS cases [2-3,8-9,22,24]. Perioperative low-dose external-beam irradiation can improve pain and clinical symptoms, and external radiotherapy or brachytherapy can enhance the outcome of laminectomy operations [24].

MATERIALS AND METHODS

This exploratory study was performed at the Animal Research Center, Faculty of Medicine, in our University, in 2014. Twenty-three 4-month-old male Wistar albino rats were used. Their weights ranged from 250 to 300 g; they were housed under standard laboratory conditions (12 h light/dark cycle) at a constant temperature (25˚C) and humidity (50 %–60 %). They were allowed free access to food and water. The rats were divided into three groups. Group I included nine rats on which laminectomy was perfomed. Group II also included nine rats on which laminectomy and perioperative radiotherapy was performed. Finally, group III included five rats that did not undergo treatment and were used as a control group. Laminectomy was performed in the L3 and L4 lumbar vertebral region; in addition, the rats in group II received perioperative radiotherapy at the laminectomy area.

Surgery

All surgical interventions were performed under sterile conditions. General anesthesia was applied using 5 mg/kg xylazine (Rompun, Bayer, Istanbul, Turkey) and 60–100 mg/kg ketamine hydrochloride (Ketalar, Eczacıbası, Istanbul, Turkey). The depth of anesthesia was assessed by administering a painful stimulus to the tail vein of the rats at 15-min intervals. Following immobilization of the subjects on the operation table, they were first numbered on the inner surface of their ears. The lumbar region was then shaved. The operation area was sterilized with a 10% polyvinylpyrrolidone–iodine mixture. The lumbar fascia was opened after making an approximately 3-cm-long midline skin incision over the spinous processes. The paravertebral muscles were subperiosteally dissected from the spinous processes and laminas. The operation was performed under a microscope, and the operation site was exposed by a small automated retractor.

L3–L4 total laminectomy was performed using a small rongeur and a high-speed drill (Aesculap Microtron GD 412, Tuttlingen, Germany). The ligamentum flavum and epidural fat tissue were excised, and the dura mater and nerve roots were exposed. After washing the site with saline, the fascia was sutured with 5/0 vicryl, and the skin was sutured with 4/0 silk. The operation site was cleaned again with 10 % polyvinylpyyrolidone–iodine mixture. The animals were kept in a room at 28˚C for approximately 30 min while recovering from anesthesia. Loss of strength in the lower extremities was not detected in postoperative early neurological examinations of the animals.

The rats were sacrificed after 6 weeks by an intraperitoneal injection of a lethal dose of sodium pentothal. The vertebral column was transversely cut approximately 0.5 cm above and below the laminectomy site with a number 20 scalpel while preserving the lumbosacral fascia. The vertebral column was then removed as a block and placed in a 10 % formalin solution.

Radiotherapy

Treatment planning was performed using a computed tomographic simulation to define the anatomy and target volume. External radiation was administered with a 6-MeV electron beam using a Varian Linear Accelerator (MNT Health Care and Trade Corporation, Turkey, Bozlu Holding). The L3-4 posterior epidural space was used as the target volume. The size of the radiation field was set at 1.5 × 2 cm, which adequately included the target volume.

Radiotherapy was applied using a total dose of 700 cGy in only a single perioperative fraction. The 85 % isodose curve was covered at a depth of 2.5 cm. The 95 % isodose curve encompassed the radiation field at a depth of 1.2 cm.

Pathology

The lumbar spines of sacrificed rats were excised en bloc, fixed in 10 % buffered formalin, and subsequently placed in decalcifying solution. The specimens were dehydrated with alcohol after decalcification and embedded in paraffin. Axial sections were obtained and stained using hematoxylin and eosin and Masson's trichrome. Each specimen was evaluated and scored for determining the rate of epidural fibrosis, cell density, and arachnoidal adhesions. Fibrosis along the dura was determined and graded according to the scale used by He et al. [11]:

Grade-0: The dura mater was free of scar tissue,

Grade-1: Only thin fibrous band(s) were observed between the scar tissue and the dura mater,

Grade-2: Continuous adherence was observed, but it affected less than two-thirds of the laminectomy defect,

Grade-3: Scar tissue adherence was large, affecting more than two-thirds of the laminectomy defect or the adherence extended to the nerve roots.

The extent of fibrosis was scored for each slice, and the distribution of grades was determined for each experimental group.

Ethical approval

This study was approved by the local Animal Ethics Committee (2014/39). The study was carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986, and associated guidelines.

RESULTS

Pathological review

Grade 0 epidural fibrosis and grade 1 fibroblast cell density rates were 44.44% and 88.88% in the L + R group, and 0% and 33.33% in the L group, respectively. Arachnoid adhesion was present in 88.8% cases in the L group, but was observed in only 44.4% cases in the L + R group (Table 1). Grade 3 epidural fibrosis was shown in four rats (44.44 %) in the L group, and in one rat in in L + R group (11.11 %) (Figure-1, 2 and 3) (Table-1).

Figure-1. Laminectomy operation under a microscope.

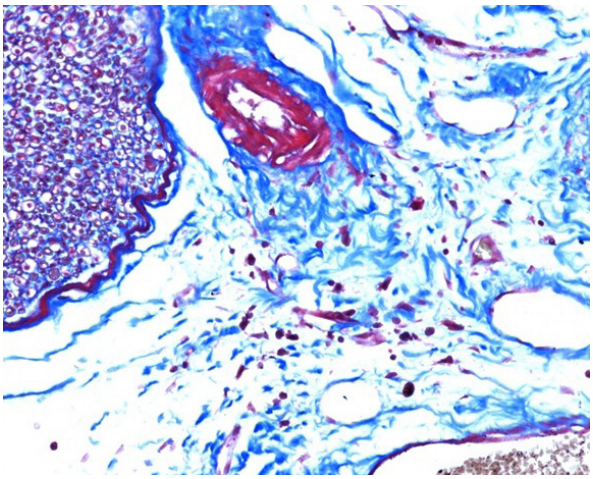

Figure-2. Grade-1 epidural fibrosis and arachnoid adhesion in a rat that received perioperative radiotherapy (Masson's trichrome staining; original magnification, 200×).

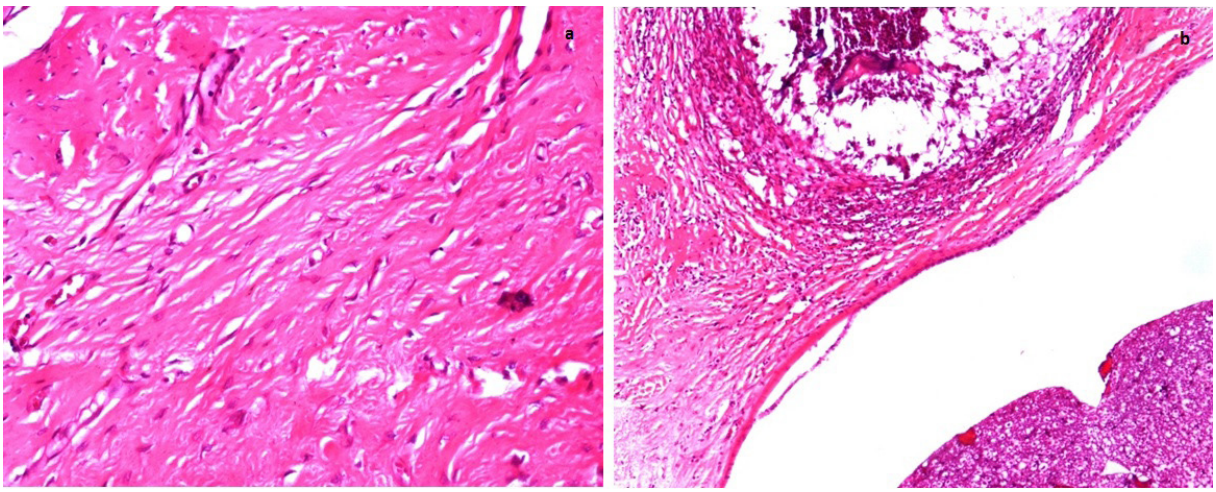

Figure-3. Grade-3 fibroblast density within the epidural fibrotic tissue in a rabbit from the laminectomy group (hematoxylin and eosin staining; original magnification, 200×).

Table 1. Rat groups and pathological results for epidural fibrosis, fibroblast cell density, and arachnoid adhesion in rats that did or did not undergo perioperative radiotherapy

Pathological evidence	L	L + R	%
Epidural fibrosis			
Grade 0	0	4	44.44
Grade 1	2	4	44.44
Grade 2	3	0	0
Grade 3	4	1	11.11
Fibroblast cell density			
Grade 1	3	8	88.88
Grade 2	3	0	0
Grade 3	3	1	11.11
Arachnoid adhesion			
Present	8	4	44.44
Absent	1	5	55.55

L: Laminectomy group; L + R: laminectomy and radiotherapy group.

DISCUSSION

Laminectomy-related salvage operations are reported to induce neurological symptoms in 8.2 % – 60 % patients because of scar-related root compression [19,21]. Therefore, many different methods are developed and various materials have been used on the dura for preventing or reducing scar formation [2,9,11,14-15]. A significant reduction in the degree of peridural fibrosis was observed in animals treated with Oxiplex or Gore-Tex. Oxiplex and Gore-Tex can prevent peridural fibrosis in the post-laminectomy areas [15].

Low-dose irradiation significantly decreases the degree of arachnoidal and peridural fibrosis and post-laminectomy syndrome; in addition, it was reported to cause no adverse neuropathic complications [6,8-9,12,24-25]. External radiation can inhibit postsurgical epidural fibrosis as effectively as the spinal membrane method [2]. In some studies, 700–900 cGy external irradiation and a 6–9-MeV electron beam energy were used and radiation was completed within 24 h postoperatively. Surgery was usually performed in the L3–L5 vertebral regions as hemi- or total laminectomy. Gross dissection and histologic sections were used for evaluating the degree of perineural fibrosis in these studies [2,24-25]. No statistically significant differences were observed in complete success rates, which ranged from 82 % to 90 % when doses were ≥900 cGy (8,9).

Therefore, we used a radiation dose of 700 cGy in this study. This study showed significant differences in rates of epidural fibrosis, fibroblast cell density, and arachnoid adhesion between rats in the L and L + R groups. Grade 3 epidural fibrosis was observed to a significantly less extent in the L + R group than in the L group according to the pathological reviews. Grade 0 epidural fibrosis and grade 1 fibroblast cell density rates were higher in the L + R group than in the L group. Arachnoid adhesion, one of the important pathological indications for a laminectomy operation, was present at a higher rate in the L group than in the L + R group. These results are consistent with those of other studies on perioperative radiotherapy for patients who have undergone laminectomy [2,8-9,21,24].

Some authors claim that low-dose radiotherapy may be carcinogenetic [1,6,12,17-19,25]. However, many authors have concluded that low-dose radiation therapy's risk of carcinogenesis is very low [20]. Further studies should be performed for evaluating brachytherapy and the use of different dose radiation schedules for preventing low back syndrome.

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