

# Efficacy of Adcon-L gel or Healon-GV in epidural fibrosis after lumbar microdiscectomy

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## ABSTRACT

**Objective:** To evaluate the efficacy of anti-adhesion barrier agents following lumbar microdiscectomy.

**Methods:** Healon GV or Adcon-L was applied to a laminectomy defect overlying the duramater in 60 patients assigned to 3 randomized groups: Group I - Adcon-L (n=21), Group II - Healon GV (n=21), and Group III - control group, no adhesion barrier used (n=18). We conducted this study between 2004 and 2006 at Selcuk University, Konya, Turkey.

**Results:** No significant difference was found between the 3 groups either in the outcome measurements according to visual analogue score and the Oswestry Disability Index or in the radiological evaluation of epidural fibrosis by application of those anti-adhesion barrier agents. When comparing group III with groups I and II, we could not find a statistically significant difference in the clinical results and in the outcome measures ( $p>0.01$ ).

**Conclusion:** The epidural application of popular anti-adhesion barriers, after lumbar microdiscectomy was not found to be effective regarding outcome measures in human spinal surgery.

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The control of scar formation has been one of the main concerns in disc surgery and the subject of research for many years. A large variety of materials have been implanted onto the duramater in experimental and clinical studies to prevent or reduce scar formation.<sup>1-19</sup> In our study, we used 2 popular anti-adhesion materials, Adcon-L (Gliatech, Cleveland, Ohio) prepared from a mixture of dextran sulfate and gelatin, and Healon-GV

(Pharmacia & Upjohn, Kalamazoo, Michigan) a non-pyrogenic solution of a highly purified high molecular weight fraction of sodium hyaluronate extracted from animal tissue, dissolved in a physiological buffer into the epidural space. None of the barrier materials have been universally accepted for this use.<sup>20-22</sup> The aim of this study was to evaluate whether there is a priority in the fibrosis-neutralizing effect of 2 popular adhesion barriers, Healon GV or Adcon-L after lumbar microdiscectomy.

**Methods.** This retrospective clinical study was conducted between 2004 and 2006 at Selcuk University, Konya, Turkey. We randomly enrolled 60 patients into 3 groups: Group I (n = 21), Adcon-L and Group II (n = 21), Healon GV, and Group III, control group (n = 18) no adhesion barrier was used. After lumbar microdiscectomy, the patients were followed up clinically for 12 months. The protocol received ethical and scientific approval from the hospital investigational review board. Inclusion criteria included: 1) diagnosis of lumbar radiculopathy; 2) neuro radiological evidence of lumbar disc herniation, with or without foraminal stenosis; 3) not more than one previously performed lumbar microdiscectomy. Exclusion criteria included: 1) presence of spondylolisthesis, 2) a previous herniated disk operation in the same segment, 3) allergy or history of hypersensitivity to these substances, 4) history of dementia or serious cognitive impairment, 5) history of clinically relevant hepatic, renal, or cardio-pulmonary insufficiency or disease. We used the Oswestry Disability Index (ODI) version 2.0, developed by Fairbank et al.<sup>23,24</sup> The ODI scoring was defined as follows: 0-20% minimal disability - the patient can cope with most living activities, usually, no treatment is indicated apart from advice on lifting, sitting, and exercise; 21-40% moderate disability - the patient experiences more pain and difficulty with sitting, lifting, and standing, travel and social life are more difficult, and they may be disabled from work; 41-60% severe disability - pain remains the main problem in this group but activities of daily living are affected, these patients require a

detailed investigation; 61-80% crippled - back pain impinges on all aspects of the patient's life, positive intervention is required; 81-100% these patients are either bed-bound or exaggerating their symptoms. Randomization was assigned when the patient's surgical procedure was completed, and the operative site was ready to be closed. At that time, the sponsor was called for patient assignment: to receive Healon GV or Adcon-L, or not to receive any additional adhesion prevention substances (control condition). The study patients received approximately 3 ml Healon GV or Adcon-L gel to coat the nerve roots and fill the operative site. The intensity of spontaneous ongoing pain was measured by use of the visual analog scale (VAS), which ranged from 0 (absence of pain) to 10 (worst pain), on a 100 mm line, the left end of the line corresponds to no pain, and the right end corresponds to the worst pain imaginable.<sup>25-27</sup> Higher scores were indicative of more severe pain. The patients were asked to record their VAS level of low back and radicular pain while at rest as a baseline before surgery, at hospital discharge, and at the first follow-up visit 4 weeks after surgery. At the same interval, each patient underwent the ODI to evaluate patient's permanent functional disability. It consists of 10 items assessing the level of pain and interference with several physical activities, sleeping, self-care, sex life, social life, and traveling. The ODI is calculated as follows: point total / 50 X 100 = % disability. The test has been in use for 25 years and is considered the 'gold standard' of low back functional outcome tools. An MRI was performed 90 days postoperatively, (12-14 weeks) with and without gadolinium contrast. Epidural abnormality was defined as a low T1 signal of epidural material. An MRI screening of all examined patients

was impossible due to poor patient compliance. In 18 patients (6 from each group) the postoperative MRI of the lumbar spinal column was carried out randomly. Four weeks after surgery, patients were asked to return to the clinic and to record the intensity of their radicular pain on the VAS, and the ODI was also measured. Even if the outcome measures were evaluated within 4 weeks after surgery, study patients were followed up clinically for 12 months. Patients were then asked to return for follow-up visits at the end of the 1st and 12th month after surgery. During the 1st month after surgery, patients were surveyed weekly by phone for pain intensity, changes in motor and sensory function, and onset of urinary problems. The mean follow-up time in the control group was 8 (range 4-12) months, and in the study group 7.5 (range 3-12) months.

**Statistical analysis.** As age and ODI factors were distributed normally in Kolmogorov-Smirnov test, VAS-preoperative, VAS-postoperative and mean history factors were analyzed as dependent variables. Means and standard deviations (SD) were calculated, and the statistical significance of differences among each group was examined by one-way analysis of variance (ANOVA) test. Demographic characteristics known to be factors (age, gender) were analyzed as dependent variables. Nonparametric Kruskal Wallis test was performed for other variable factors, VAS-preoperative, VAS-postoperative and average preoperative pain history. Computer-assisted data analysis was performed with the help of commercially available software (SPSS 10.0,) for windows.

**Results.** All groups were similar with respect to demographic data, as summarized in Table 1. The gender

**Table 1** - Demographic and clinical data of Adcon-L gel and Healon-GV and control trial groups.

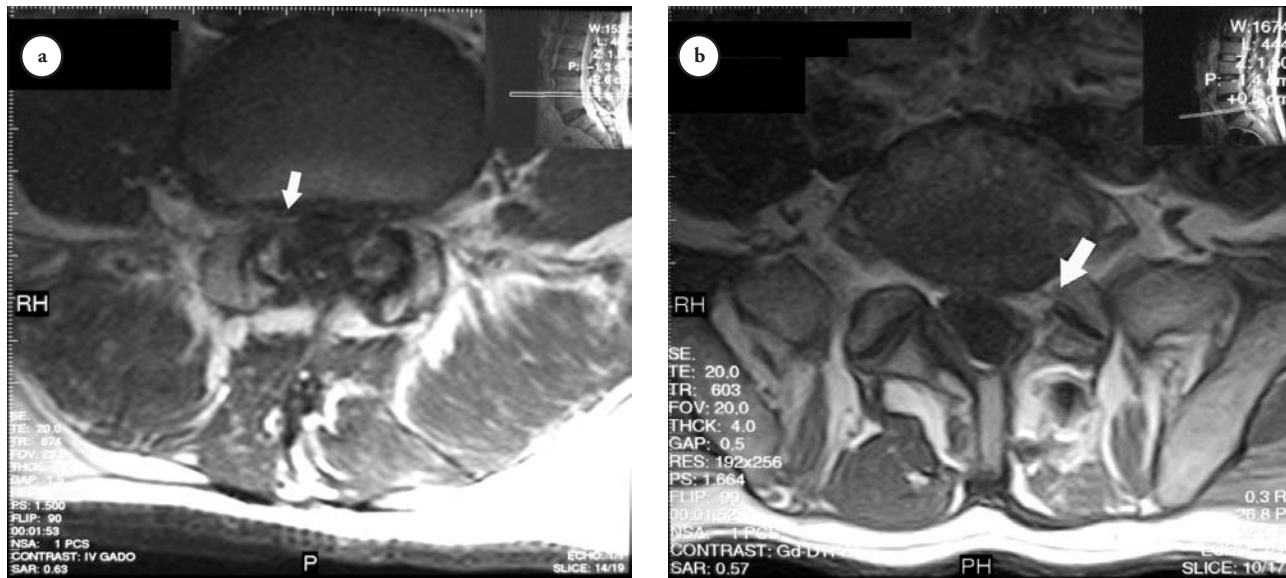
Variable	Adcon-L gel (group I) n=21	Healon-GV (group II) n=21	Control (group III) n=18
Age (yr)	47.3333±12.67	44.7619±11.57	39.7778±7.58
Gender	15 M, 6 F	14 M, 7 F	6 M, 12 F
Length of clinical history (yr)	11.1905±7.85	12.2381±8.50	13.7782±11.9
<i>Level of disc herniation</i>			
L2-L3	1	0	0
L3-L4	5	4	2
L4-L5	8	12	7
L5-S1	7	5	9
Side of disc herniation	15R, 6L	13R, 8L	9R, 9L

yr - years, M - male, F - female, R - right, L - left

**Table 2** - Postoperative outcome data of the patients in the 3 study groups.

Variable	Adcon-L gel (group I) n=21	Healon-GV (group II) n=21	Control (group III) n=18
Intraoperative complications	None	None	1
Postoperative complications	None	None	None
Mean value of pre operative pain by VAS	9.2857±1.05	9.7143±0.95	10.0000±0.00
Mean value of postoperative pain by VAS	4.4762±0.98	4.8095±0.74	4.6667±1.23
Postoperative ODI	19.9524±9.94	19.6667±9.59	16.6667±12.50

Mean values ± standard error of the mean, VAS - Visual analog scale, ODI - Oswestry Disability Index



**Figure 1** - Axial contrast enhanced T1W MRI demonstrates a) a large amount of scarring laterally to the right L5 root at the level of L5-S1 and b) a small amount of scar tissue laterally to the left L4 root at the level of L4-L5.

distribution in the 3 groups was significantly different ( $p=0.035$ ), but there was no significant difference in age distribution ( $p=0.105$ ). The distribution of the operated segments in the total population is also shown in Table 1, with no significant differences between the study and control groups ( $p=0.237$ ). Table 2 outlines the postoperative outcome data, and shows that the line mean value of VAS pain intensity was similar in the Healon-GV and Adcon-L gel groups. Only one perioperative complication was revealed as cerebrospinal fluid leakage in group III, and no further operation was needed for that patient. Six patients were randomly selected from each group to undergo an MRI examination, as due to poor patient compliance we were unable to screen the entire population. Mean follow-up time for the MRI examination was 14 (range 12-16) months in the control group and 10 (range 8-12) months in the study groups. One patient in groups I and III and 2 patients in groups II exhibited radiological epidural fibrosis, which extended from the paravertebral muscle plane to the laminectomy defects on postoperative MRI examination. A large amount of epidural fibrosis, laterally along the right L5 root at the L5-S1 level (Figure 1a) occurred in group I. In groups II and III, a small amount of scar tissue was present lateral to the left L4 root at the L4-L5 level (Figure 1b). Group III patients, in whom no adhesion barrier was used, exhibited no difference from group I and group II patients radiologically.

**Discussion.** The relevance of epidural fibrosis to failed back surgical outcome remains controversial.

Previous studies on the correlation between epidural fibrosis and clinical outcome after laminectomy are inconclusive, and clinical approaches applied to reduce postlaminectomy spinal canal scarring have produced mixed outcomes. Although numerous antifibrotic agents have been proposed for postlaminectomy application,<sup>1-19</sup> since LaRocca and MacNab first described the laminectomy membrane in 1974,<sup>2</sup> they have been under debate.<sup>28-32</sup> These studies, however, have not yet identified a material suitable for clinical use in laminectomies as a membrane barrier between muscles and the epidural space, as they theoretically reduce cellular trafficking and decrease vascular invasion into the epidural space from the overlying muscle and bone. Previous studies supported the hypothesis that postlaminectomy scar formation can be attenuated by application of 2 popular topical (Adcon-L gel, or Healon GV) barrier sheets tenting over the laminectomy space, so as to create a space between it and the underlying duramater.<sup>33,34</sup> Adcon-L is a semi-synthetic product that forms a bio-tolerated, degradable, pure mechanical barrier around the nerve root and dura mater, in order to prevent formation of peridural fibrosis and adhesions after surgical operations on the lumbar spine.<sup>28-34</sup> Degradation within the body is completed within weeks by macrophages.<sup>31</sup> In Europe and the United States, Adcon-L and Healon GV were frequently applied to the epidural space at the conclusion of spinal procedures to lessen scar formation.<sup>35,36</sup>

Previous studies<sup>35,36</sup> suggested that, patients with extensive epidural scar on the enhanced MR images of the operative site postoperatively, have been shown to be 3.2

times more likely to experience recurrent radicular pain than those patients with less extensive epidural scarring. As confirmed by the previous studies, the application of epidural morphine-Adcon-L or Oxiplex-morphine compound after lumbar microdiscectomy was found to be safe, regarding postoperative pain control.<sup>37,38</sup> In a clinical study with 100 patients, a reduced incidence of heavy scarring through the application of Adcon-L gel was described.<sup>39</sup> In this respect, a direct correlation of postoperative fibrosis and clinical symptoms could be proven, although opposite suggestions have been proposed.<sup>40-42</sup> In other previous reports, it is suggested that the local application of Adcon-L gel inhibits the natural healing of small tears of duramater, and consequently results in leakage of cerebrospinal fluid,<sup>40-43</sup> and adverse hemodynamic reactions were experienced in some patients intraoperatively.<sup>44</sup> In the prospective study of Nygaard et al,<sup>40</sup> involving 54 patients, the 12-month postoperative MRI could not prove any connection between peridural scarring and the clinical results. In an other report,<sup>45</sup> the authors found no positive effect on prevention of epidural fibrosis with Adcon-L gel in patients in whom one-level lumbar microdiscectomy was performed. Therefore, to evaluate if there is superiority in the fibrosis-neutralizing effect, we present a retrospective study of the intraoperative application of 2 different anti-adhesion barrier agents, Adcon-L and Healon-GV after lumbar microdiscectomy. To evaluate postoperative epidural fibrosis clinically, we used VAS and ODI outcome measures.

In our study, opposite to Ross et al's study,<sup>40</sup> on postoperative MRI evaluation, a significant difference in scarring could not be established between the study and control groups. However, their VAS and ODI scores ranged in the low scores suggesting good recovery. A large amount of epidural fibrosis, laterally along the right L5 root at the L5-S1 level (**Figure 1a**) occurred in group I, but in groups II and III, a small amount of scar tissue was present lateral to the left L4 root, at the L4-L5 level (**Figure 1b**) in an unexpected manner. The results in respect of epidural scar formation were the same in groups II and III, although we did not use any anti-adhesion material in group III.

In conclusion, the application of these 2 popular agents did not reveal any advantage in outcome or length of hospital stay. Postoperative outcome measurements with the application of Adcon-L or Healon GV, intraoperatively does not solve the problems of epidural fibrosis after lumbar microdiscectomy. Furthermore, in groups II and III, patients whom exhibited epidural fibrosis radiologically were symptom free. Therefore, no significant difference between the groups could

be established either in the outcome measurements according to VAS and ODI, or in the radiological evaluation of epidural fibrosis. Thus, a significant clinical influence could not be proven between Healon GV and Adcon-L by the present study.

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