Microcoagulation of Junctional Dorsal Root Entry Zone is Effective Treatment of Brachial Plexus Avulsion Pain: Long-term Follow-up Study

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Aim To analyze long-term clinical results of coagulation lesions of the dorsal root entry zone (DREZ) in patients with deafferentation pain due to brachial plexus avulsion and to correlate the pain relief after DREZ coagulation with pain duration before the DREZ coagulation.

Methods Twenty-six patients with intractable deafferentation pain after brachial plexus avulsion lesion were treated for pain at the Department of Neurosurgery. Junctional coagulation lesion was made with bipolar forceps along the DREZ. The patients assessed post-operative analgesic effect using a visual analog scale at 1 week, 1 year, 3 years, and 5 years after the surgery.

Results The greatest pain relief was reported immediately after the DREZ procedure. Over the 5-year follow-up period, the pain relief effect gradually and significantly decreased. There were no significant differences between the pain relief evaluated at 1 week and after 1 year and between the pain relief evaluated at 1 week and after 3 years. There was a correlation between the pain duration before the surgery and pain relief after the surgery, with best correlation found between pain duration before surgery and pain relief 5 years after DREZ procedure ($r = 0.623$, $P = 0.007$).

Conclusion The long-term follow up showed that the pain relief gradually decreased over 5 years after surgery. However, the pain relief still did not significantly decrease after 3 years.

There is experimental and clinical evidence that pain generators in brachial plexus avulsion are at least partially located in the deafferented dorsal horn (1-3). The term *deafferentation pain* has been defined as pain or dysesthesia caused by interruption of the peripheral or central afferent input in the central nervous system (4). When the large lemniscal afferents within peripheral nerves or dorsal roots are altered, the inhibitory control of the dorsal horn is reduced (5). It was suggested that dorsal horn deafferentation by cervical posterior rhizotomy in the rat provides a reliable model of chronic pain due to brachial plexus avulsion and that this deafferentation pain is successfully relieved by microsurgical dorsal root entry zone (DREZ) rhizotomy (6). Pain following brachial plexus avulsion is the most typical manifestation of the chronic deafferentation pain in humans (4). Preganglionic lesion of the dorsal horn of the cervical spinal cord due to root avulsion may lead to important pathological changes responsible for the induction of pain sensations in 90% of the patients (7). Medications, neurostimulation techniques, and various ablative surgical procedures other than DREZ surgery, including cervical anterolateral cordotomy, mesencephalic spinothalamic tractotomy, and medial thalamotomy, have not shown long-term efficacy and are not exempt from disabling side effects (8,9). On the contrary, the neurosurgical procedure of coagulation lesions in the DREZ has been shown effective in pain relief after brachial plexus avulsion (10-16). The DREZ was chosen as a possible neurosurgical target to stop abnormal firing of impulses, which most probably originate in the central portion of the dorsal nerve roots, in Lissauer's tracts and Rexed's laminas I-V of the dorsal horn. The idea of a DREZ lesion was put forward in 1972 (17,18) and 4 years later, it was accepted as a useful pain-relieving therapeutic procedure (7). The aim of DREZ lesioning is the treatment of neuropathic pain associated with dysfunction in the gating circuitry of the dorsal horn and generated by dorsal horn hyperactive neurons (1,5). The original procedure in the DREZ region, which includes series of focal radiofrequency heat lesions 2-3 mm apart along the line of the posterolateral fissure at the site of the avulsion of the rootlets (7,19), has been updated by Rawlings et al (20). A series of DREZ lesions may also be produced with microsurgical lasers (21-23). Dreval (24) reported on ultrasonic DREZ operation for the treatment of pain due to brachial plexus avulsion. Computer-assisted DREZ microcoagulation for posttraumatic spinal deafferentation pain is described by Edgar et al (25). In our previous study, we described our experience and clinical results of microsurgical junctional DREZ coagulation performed for pain relied in different deafferentation syndromes (26). Since the DREZ procedures are the most effective in the treatment of pain, particularly brachial plexus avulsion pain, and the good results have tendency to diminish with time, the studies to analyze the long-term effects of the procedure on pain after brachial plexus avulsion are needed.

The aim of the study was to determine long-term clinical results of the DREZ coagulation lesion, primarily the duration and degree of pain relief, in patients with deafferentation pain due to brachial plexus avulsion.

Patients and methods

Patients

Twenty-six patients with intractable deafferentation pain after brachial plexus avulsion lesion who had not responded to the World Health Organization (WHO) class I or II analgesics were selected for the junctional coagulation DREZ microsurgery at our Department between 1989 and 2004. The patient group consisted of 4 women and 22 men aged 25-76 years (median, 44 years). The cause of brachial plexus avulsion was either motorcycle or car accident. The complete avulsion of the nerve roots of the

brachial plexus from C5 to T1 occurred in 13 patients, upper cervical roots from C5 to C7 in 5 patients, lower brachial plexus roots C7 to T1 in 4 patients, roots C8 to T1 in 3 patients, and roots C6 to C8 in 1 patient. All 26 patients had unbearable pain in the upper limb, describing it as a combination of paroxysmal attacks of electrical shocks and continuous background pain. The pain predominated in the distal portion of the arm, ie, in the forearm, hand, and fingers, and had a radicular distribution. In the patients with upper cervical roots avulsion, the pain was felt also in the proximal portion of the arm, ie, in the lateral portion of forearm, and rarely in upper arm and shoulder. In all patients, the treatment including tricyclic antidepressants, sodium channel blocker anticonvulsants, and morphine had failed. Only a single patient with brachial plexus avulsion underwent previous operations for pain relief (dorsal rhizothomy, sympathetic ganglliotomy, and eventually the amputation of the injured upper limb) with little success.

DREZ microcoagulation procedure

The patients were anaesthetized with intermittent positive pressure ventilation with N_2O and O_2 supplemented by either Halothane or Fentanyl. For muscle relaxation, curare analogues were used. The operation on the cervical spinal cord was carried out in the patients in sitting position with the neck flexed. A hemilaminectomy of the cervical spine was performed. The extension of the hemilaminectomy depended from the spinal cord segments in which the pain was distributed. As an example, for a total plexus avulsion C5 to T1, hemilaminectomy was performed from C3 to C7. A longitudinal incision of the dura was made with an operating microscope above the posterior surface of the spinal cord. The subarachnoid space was opened to expose the spinal cord from the first normal rootlets above and below the injury or pain distribution at periphery. The radicular vessels are preserved. The segments of the affected and unaffected sides of the spinal cord and the rootlets were carefully compared under higher magnification of the microscope. For the final decision on the spinal cord level, we used also x-ray of the spine and electrical stimulation of the rootlets. The first normal upper and lower dorsal rootlet were identified and the extent of the avulsion was assessed. The dorsal roots were missing from their normal dorsolateral position on the spinal cord if complete avulsion had occurred. The scar and thickened arachnoidea-pia were excised with microscissors along the DREZ groove of the entire segments of the avulsed rootlets. The extent (length) of the surgical lesion was established on the basis of pain topography at the periphery, which corresponded with the avulsed roots of brachial plexus and corresponding dermatomes. Using a bipolar forceps, the DREZ groove was carefully opened and a junctional coagulation lesion was made extending along the entire DREZ region of the pain-producing spinal cord segments (26). The depth of penetration was marked on the tip of bipolar forceps (2-3 mm). Special care was taken to make the microcoagulation within the limits of the dorsal horn, between the cuneate fasciculus of the dorsal column medially and the corticospinal tract laterally, to avoid impairment of the sensory and motor pathways, respectively. All procedures included intraoperative neuromonitoring of the spinal cord somatosensory and motor evoked potentials with transcutaneous electrical stimulation of the tibial and median nerves and motor cortex, and recording of the potentials directly from the dorsal surface of the spinal cord above and below the junctional DREZ lesion.

Quantitative assessment of pain

The patients assessed the postoperative effect of pain relief on a visual analog scale (VAS) from 0 to 10 (0%-100%). Before the operation, every patient scored a minimum of 8 on the VAS despite very high doses of analgesics. After the pain assessment, the results of the junctional DREZ lesion surgery were evaluated by rating the pain

Table 1. Pain relief after junctional dorsal root entry zone (DREZ) microcoagulation treatment of pain caused by brachial plexus avulsion*

Degree of pain relief after junctional DREZ coagulation	Pain after junctional DREZ microcoagulation		No. (%) of patients evaluated after DREZ microcoagulation			
	residual pain (visual analog scale, %)	degree of pain relief (score)	1 week (n = 26)	1 year (n = 26)	3 year (n = 18)	5 year (n = 17)
Complete	0	4	12 (46.2)	8 (30.8)	3 (16.7)	2 (11.8)
Excellent	1-30	3	10 (38.5)	14 (53.9)	11 (61.1)	6 (35.3)
Good	31-50	2	3 (11.5)	3 (11.5)	1 (5.5)	5 (29.4)
Fair	51-99	1	1 (3.8)	1 (3.8)	3 (16.7)	4 (23.5)
Poor	100	0	0 (0)	0 (0)	0 (0)	0 (0)

*Post hoc analysis: pain relief at 1 week vs 5 years after surgery, $P = 0.001$; 1 week vs 1 year and 1 week vs 3 years, not statistically significant.

relief from 0 (poor pain relief) to 4 (complete pain relief) according to the findings on the visual analog scale (Table 1). In cases of ≥70% overall pain relief, residual pain never exceeded 3 on the VAS, whereas in cases of 50%-70% overall pain relief, the residual pain never exceeded 5 on the VAS. Residual background pain with occasional paroxysms was scored above 5. Most of these patients permanently took WHO class I analgesics and, occasionally, opioids. The patients with >50% pain relief did not use analgesic therapy in the postoperative period.

Statistical analysis

The surgery results were scored from 0 (poor pain relief) to 4 (complete pain relief) (Table 1). The values of pain relief used were measured 4 times as follows: 1 week, 1 year, 3 years, and 5 years after the DREZ lesion. Friedman test was used to test the progressive change in pain relief after DREZ lesion during the 5 years of follow-up. For the post hoc analysis between the 4 measurements, Wilcoxon signed ranks test was performed, with correction for multiple testing. Spearman's correlations were calculated between the pain duration before the operation and the degree of pain relief after the operation. The duration of the unchanged pain relief after DREZ microcoagulation procedure was assessed by Kaplan-Meier method. With respect to the pain duration before surgery, the patients were divided into two groups, one with pain duration ≤5 years and the other with pain duration >5 years. Log-rank test was then used to test the difference in duration of the unchanged pain relief effect between these two groups. All values were expressed as the median value and range, unless otherwise indicated. $P<0.05$ was considered statistically significant. The statistical analysis was performed with Statistical Package for Social Sciences for Windows, version 9, (SPSS Inc., Chicago, IL, USA).

Results

The pain before DREZ coagulation was felt as deep pain in the area of complete anesthesia. Median pain duration before the DREZ coagulation was 7 years (range, 0.5-27 years). The area of anesthesia in patients with complete brachial plexus avulsion from C5 to T1 corresponded to C6, C7, and C8 dermatomes. Most often, the pain involved the tips of the fingers and the palm, less often the wrist and forearm. Five patients with the avulsion of the upper cervical roots C5 to C7 reported pain in the shoulder or upper arm. The dermatomal distribution of deafferentation pain corresponded to the avulsed roots of brachial plexus, as well as to the dermatomes of anesthesia. The extent of sensory deficits also corresponded to the level and extent of dorsal root lesions. The best pain relief after the junctional DREZ lesion for intractable deafferentation pain due to brachial avulsion was recorded in the first week after the DREZ procedure (Table 1). However, this effect gradually and significantly decreased over time ($P<0.001$). Of 17 patients followed-up for 5 years, 13 had a long-term pain relief of >50% (complete, excellent, or good result). One year after the surgery, 25 of 26 pa-

Table 2. Cumulative proportion of patients with no changes in pain relief effect after the junctional dorsal root entry zone microcoagulation treatment of pain caused by brachial plexus avulsion (Kaplan-Meier table)*

Interval between the surgery and the pain relief evaluation (years)	No. of patients			Cumulative proportion of patients with	
	with no changes in pain reliefeffect	with increased pain	excluded from follow-up	unchanged pain relief (%)	standard error of cumulative proportion (%)
Total (n = 26)					
0	26	4	0	100	0
1	22	4	6	84.6	7.1
3	12	5	1	66.8	9.7
5	6	0	6	37.8	11.2
Pain duration before operation ≤5 y:					
0	13	4	0	100	0
1	9	2	4	69.2	12.8
3	3	3	0	49.4	14.9
5	0				
Pain duration before operation >5 y:†					
0	13	0	0	100	0
1	13	2	2	100	0
3	9	2	1	83.3	10.8
5	6	0	6	63.7	14.7

*Twenty-six patients assessed up to 1 year, 18 up to 3 years, and 17 up to 5 years. In case when a pain relief effect (time dependent variable) decreased (the pain increased), such a patient was excluded from the analysis in the next time interval because the pain relief effect was lost. The patients were also divided in two groups according to the pain duration before the DREZ lesion (pain duration ≤5 years and >5 years).
†Log-rank test revealed that the unchanged pain relief lasted significantly longer after the DREZ lesion in the group of patients with preoperative pain duration of >5 years ($P = 0.011$).

tients had >50% pain relief, whereas 3 years after the DREZ coagulaton surgery, the same level of pain relief was still present in 15 of 18 followed-up patients. The post hoc analysis between the four measurements showed a significant difference between the pain relief 1 week and 5 years after surgery ($P = 0.001$). However, the differences between the pain relief after 1 week and after 1 year and between pain relief after 1 week and 3 years were not statistically significant. The persistence of pain relief effect over time was analyzed by Kaplan-Meier method (Table 2), showing the cumulative percentage of patients in whom the pain-relieving effect of surgery remained unchanged over the follow-up period. Twenty-six patients were assessed up to 1 year, 18 up to 3 years, and 17 up to 5 years. In case that a pain-relief effect (censored, time dependent variable) decreased (ir, the pain increased) in a patient, such a patient was excluded from the further analysis because the postoperative pain relief effect was lost after that time point. The postoperative results remained the same after 1 year in 22 patients. The patients were also divided in two groups according to the pain duration before the DREZ lesion (pain duration ≤5 years and >5 years). Log-rank test revealed that the unchanged pain relief lasted significantly longer after the DREZ lesion in the group of patients with preoperative pain duration of >5 years ($P = 0.011$). In the group of patients with preoperative pain duration of ≤5 years, pain relief remained unchanged for a shorter period of time. In this group of patients, 49.4% of patients had the same degree of pain relief after 3 years as after 1 week after the surgery. However, in the same period, 83.3% patients with pain duration of >5 years reported that pain relief remained the same.

A similar quality of pain was reported by patients who had experienced pain for a few months and those with a history of pain for several years. All patients described two types of pain as follows: permanent intensive pain and frequent attacks of severe intractable pain. No correlation was found between the pain duration before the DREZ microcoagulation and the degree of pain relief 1 week after operation ($r = 0.289$, $P = 0.149$). However, a positive correlation was found between pain duration before surgery and pain relief evaluation one year after surgery ($r = 0.539$, $P = 0.005$) and 3 years after surgery ($r = 0.581$, $P = 0.011$). The best correlation was

detected between pain duration before surgery and long-term pain relief 5 years after the procedure ($r = 0.623$, $P = 0.007$).

Postoperative complications

Postoperatively transient sensory neurological disturbances on the side of DREZ lesion were present in 4 patients lasted approximately 8 weeks. Neurological examination revealed signs of damage to the dorsal columns with impaired vibration and joint position sense. In 2 patients, the heel-to-knee test showed coordination disturbances of the foot on the side of DREZ surgery. Clumsiness of the foot on the side of the DREZ lesion when walking reported 2 patients. There were no signs of a pyramidal lesion. Permanent superficial and deep sensory disturbance with signs of a pyramidal tract lesion (hyperreflexia, Babinski sign, and paresis of the leg) on the side of DREZ lesion were observed in one patient. In this case, previous operations for pain relief (dorsal rhizothomy, sympathetic ganglliotomy and subsequent amputation of the injured upper limb) were not successful. The result of DREZ lesion in this patient was not good either, with only 10% pain relief in the early postoperative period. Neurological side effects were recorded in 7 patients. Three patients reported mild transient dysesthesias in the ipsilateral upper limb and 4 patients described hypoesthesia in the ipsilateral upper portion of the thorax, which was mild in 3 and moderate in one patient. These side effects were not functionally disabling.

Discussion

In this study, the best pain relief was recorded in the first week after the DREZ procedure, but it gradually decreased over time. However, after 3 years of follow-up the pain relief did not significantly decrease. Correlation was found between pain duration before surgery and long-term pain relief.

Different authors described achieving ≥50% pain relief in 58-90% of their patients after DREZ lesion treatment of brachial plexus avulsion pain (7,9,12,14,27). Rare reports in the literature described fair results in pain relief, whereby Tomas and Haninec (28) reported only 25-75% of pain after brachial plexus avulsion in 38% of patients. However, none of them analyzed changes in pain reduction over longer period of time. In the present study, significant decrease in the analgesic effect appeared after 5 years. At the same time, 76.5% of treated patients had a long-term (5 years) pain relief of >50% (complete, excellent, or good result) and did not need additional analgesic therapy. These findings suggested the long-term efficacy of the junctional DREZ procedure, although pain relief gradually decreased. Better results were obtained in the patients with deafferentation pain history of >5 years. In such patients, pain reduction after surgery remained unchanged for a longer time. This is in agreement with other study in which patients treated after suffering pain for >6 years had with better long-term pain relief than those who had undergone treatment within the first 3 years after pain onset (29). Samii et al (30) also studied long-term pain relief in patients after DREZ lesion as a treatment of refractory pain after brachial plexus avulsion. However, in their study the degree of pain relief was not evaluated in particular time intervals. They did not find correlation between the duration of pain before surgery and pain relief after surgery. In the present study, the correlation between the pain duration before the surgery and its outcome was not detected one week after the DREZ procedure. However, this correlation was significant and confirmed in 1, 3, and 5 years after DREZ lesion surgery.

Dorsal horn and DREZ are an important integration center for facilitation and inhibition of the sensory impulses to the spinal cord (31). The normal uninjured DREZ maintains its neurophysiologic balance between afferent and efferent impulses under the control of excitatory and

inhibitory mechanisms. With both complete and partial deafferentation, this delicate balance is impaired. The similarities between our results and those from other clinical series strongly support the important role of the DREZ and deafferented dorsal horn as surgical target in brachial plexus avulsion pain patients (29,30). Our experience in one patient showed that previous neurosurgical procedures other than DREZ lesion caused changes in the dorsal horn and subsequent development of abnormal pain mechanisms in the higher levels of the central nervous system. This is in accordance with the report that second DREZ procedures have shown a mixed and unpredictable relief of recurrent pain and should be avoided (32).

Postoperative complications in patients included in the present study were rare and transient. These signs were indicative of slight impairment of the dorsal spinocerebellar tract. Permanent deficit after the DREZ lesion was found in only 1 patient and rate of other complications was well within the range of those reported in the literature (10,29,30,33,). The only other study reporting such a low percent of postoperative sensory and motor disturbances was the study by Sindou et al (29), where motor weakness and sensory ataxia reported in a few patients were attributed to the bad targeting of the dorsolateral sulcus. Other authors reported higher complication and morbidity rates after treatment of pain due to brachial plexus avulsion (30,33).

In brachial plexus avulsion, dissection of the spinal cord is sometimes difficult to achieve safely because of scar tissue adhering to the cord in the subarachnoid space. Atrophy and gliotic changes in the level of the avulsed roots can make the correct identification of the dorsolateral sulcus hazardous. It is thus important in such cases to start the dissection from the remaining roots, proximal and distal to the injured area. Also electrophysiological technique of DREZ localization with direct spinal cord stimulation could improve the safeness of the DREZ microcoagulation (28).

Spot-like radiofrequency lesions were reportedto produce the best results and that amount of pain relief thus produced was proportional to the density of tightly placed lesions (32). It is likely that the spot-like radiofrequency heat lesions do not include all major portions of the dorsal horn and all the structures in the DREZ region, which are important for the generation of the deafferentation pain. Failure to relieve pain and pain relapse after the technique of dotted microcoagulations is the result of insufficient lesioning within the dorsal horn (29). Therefore, the method of junctional DREZ microcoagulation with the help of fine bipolar forceps presented in this study could well include the tract of Lissauer, the substantia gelatinosa, and the dorsal horn neurons of the Rexed layers I-V, and is deep enough to exclude the abnormal mechanisms that fire pain impulses. This technique allowed for surgery without special equipment for temperature-controlled radiofrequency lesions (19). Also, there was no need for laser or ultrasound technology (21-24). Instead of the spot-like heat lesions (7,10,19,20), the junctional coagulation lesion in the DREZ area 2-3 mm deep continuously along the dorsolateral fissure was made, which increased the probability that all the pain-producing structures in the affected dorsal horn spinal cord segments would be included.

In conclusion, this study showed that analgesic effect of DREZ microcoagulation surgery gradually decreased over the longer period of time. However, this technique is still effective treatment of brachial plexus avulsion pain, as msot patients had >50% pain reduction even after 5 years fo surgery without the need for additional analgesic therapy. However, the results of the present study should be confirmed in a larger, randomized clinical trials comparing different surgical techniques against the microsurgical junctional DREZ coagulation.

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