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## Epidural Fibrin Glue Injection Stops Persistent Postdural Puncture Headache

Ben J. P. Crul, M.D., Ph.D.,\* Bastiaan M. Gerritse, M.D.,† Robert T. M. van Dongen, M.D., Ph.D.,‡  
Hennie C. Schoonderwaldt, M.D., Ph.D.§

RECENTLY we reported the successful treatment of persistent cerebrospinal fluid leak during long-term intrathecal catheterization with the epidural injection of fibrin glue (Tissucol, duo 500; Immuno AG, Vienna, Austria) in three patients with preterminal cancer who had severe pain.<sup>1</sup> In this case report, we describe the successful treatment of persistent postdural puncture headache in a woman after spinal anesthesia.

### Case Report

A 29-yr-old woman was scheduled for ligament repair of the right knee and removal of osteosynthesis material in the right tibia under spinal anesthesia. After three attempts, lumbar puncture with a 25-gauge pencil-point needle was successful. Spinal anesthesia was instituted with 3.5 ml bupivacaine (plain), 0.5%. Anesthesia and surgery were uncomplicated. Six hours after surgery, the patient experienced a neck ache radiating into the occipital region accompanied by nausea and vomiting. Sitting up aggravated the symptoms. Because of these problems, the patient was kept in the hospital for one night. She was sent home the next and advised to remain in bed, drink fluids, and take acetaminophen orally.

Her headache did not subside, so it was decided on day 2 after surgery to administer an epidural injection of 10 ml autologous blood between spinal levels L3 and L4. During injection, the patient experienced severe back pain radiating to her left leg. After this therapy, the headache pain lessened. She tried to resume work 8 days after surgery.

\* Professor of Pain Management, Institute for Anesthesiology.

† Staff Member in Anesthesiology, Institute for Anesthesiology.

‡ Staff Member in Pain Management, Institute for Anesthesiology.

§ Staff Member, Department of Neurology.

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Address reprint requests to Prof. Dr. Crul: Institute for Anesthesiology, University Hospital Nijmegen, Geert Grooteplein 10, 6500 GM Nijmegen, The Netherlands. Address electronic mail to: B.Crul@anes.azn.nl

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This resulted in a full recurrence of her pain, nausea, vomiting, and dizziness, forcing her to interrupt her work as a physical therapist. After another week at home, the patient had not improved, so she was referred to a neurologist, who could not identify any other causes of her symptoms and confirmed the diagnosis of postdural puncture headache. Because the patient was reluctant to have another epidural blood patch, full bed rest for 3 weeks and an ample fluid intake and acetaminophen (as needed) were again advised. Although the patient complied with this regimen, she continued to have posture-related headache, nausea, vomiting, and dizziness.

These problems were still present 5 weeks after surgery. She was readmitted to the hospital for clinical observation and treatment. Epidural blood patches were repeated twice, but with no improvement. Because of this situation, which was characterized as "desperate" by the patient and her treating physicians, neurosurgical repair by laminectomy and duraplasty was considered.

Our University Hospital Pain Clinic was asked for a consultation. Magnetic resonance imaging showed a small midline hernia of the intervertebral disc between the third and fourth lumbar vertebra, without compression of the contents of the dural sac. We advised the intravenous use of adrenocorticotrophic hormone,<sup>2</sup> but that had no beneficial effect. Given the seriousness of the patient's problems, the imminence of a neurosurgical intervention, and the good results obtained with epidural injection of fibrin glue in patients with persistent leak of cerebrospinal fluid, an analogous approach in this patient was proposed.

She was informed about the scarce experience with the technique, and we emphasized the fact that no data were present about specific risks. After the patient gave her consent, an epidural injection between levels L3 and L4 was performed with 3 ml fibrin glue. To identify the epidural space, the loss-of-resistance technique was applied using a 18-gauge Tuohy needle. During the (slow) injection of fibrin glue, the patient was in the left recumbent position. Again, she experienced some backache with irradiation to her left leg.

During the first 24 h after injection, the patient remained in a horizontal recumbent position. She was asked to avoid coughing and Valsalva maneuvers during the first 24 h. A stool softener was administered orally.

After 24 h, the patient was mobilized. Her posture-related headache had disappeared fully. In addition, nausea and dizziness were absent. Gradually, she resumed her daily activities. No recurrence of postdural puncture headache-related complaints occurred. In a follow-up telephone call 7 months after surgery, she reported that her headache had not returned and she no complaints attributable to the injection of fibrin glue.

## CASE REPORTS

**Discussion**

Fibrin glue is a preparation of pooled human plasma obtained from plasmapheresis. It is prepared by mixing two solutions. The first one contains fibrinogen, factor XIII, fibronectin, aprotinin, and plasminogen; the second one contains thrombin and calcium. When these solutions are mixed, fibrinogen is converted to fibrin monomers, which aggregate and form a gel.<sup>3</sup> Fibrin glue has a high tensile strength and tolerates highly moist environments. The fibrin clot forms a temporary biological seal of the dura until healing occurs.<sup>4</sup> Fibrin glue is widely applied in otology and neurosurgery as a method to achieve a watertight dural closure.<sup>5</sup> It has proved to be a satisfactory technique for stopping cerebrospinal fluid leakage in a series of 20 consecutive craniofacial resections with dural defects.<sup>6</sup> Percutaneous fibrin sealing also has been applied successfully in cases of subcutaneous cerebrospinal fluid fistulae after operations to the brain and the spinal cord,<sup>7</sup> thereby obviating repeated operation. Fibrin glue clots do not retract, because of the lack of corpuscular blood components. The fibrin in the clot also has a special affinity for collagen fibers. There are no signs of an inflammatory response. Dural specimens examined after application of fibrin glue showed a clot adhering to the epidural side.<sup>8</sup>

Using a product of biological origin implies a potential risk of viral infection. However, no cases have been documented of viral transmission using fibrin glue (as manufactured by Immuno AG). The manufacturer uses a recombinant DNA technique to identify viral contamination, which allows detection of very low viral load.<sup>9</sup>

The routine treatment of cerebrospinal fluid leak after dural puncture consists of initial conservative symptomatic treatment with progression to epidural injection of autologous blood, which can be repeated if necessary.<sup>10-12</sup> Since the epidural blood patch was intro-

duced,<sup>13</sup> it has been applied widely and safely. Further examination of the epidural fibrin glue injection technique is necessary to place this treatment within the therapeutic armamentarium.

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