Retrospective Review

Post Dural Puncture Headache Following Intrathecal Drug Delivery System Placement

Stephanie A. Neuman, MD, Jason S. Eldrige, MD, Wenchun Qu, MD, PhD,
Eric D. Freeman, MD, and Bryan C. Hoelzer, MD

From: Department of
Anesthesiology/Pain Medicine,
Mayo Clinic, Rochester, MN

Dr. Neuman is a Pain Medicine
Physician with Anesthesiology/
Pain Medicine, Mayo Clinic,
Rochester, MN. Dr. Eldrige is
an Instructor in Anesthesiology/
Pain Medicine with Department
of Anesthesiology/Pain Medicine,
Mayo Clinic, Rochester, MN. Dr.
Qu is a Pain Medicine Fellow
in the Department of Physical
Medicine and Rehabilitation,
Mayo Clinic, Rochester, MN.
Dr. Freeman is a Pain Medicine
Fellow in the Department of
Anesthesiology/Pain Medicine,
Mayo Clinic, Rochester,
MN. Dr. Hoelzer is Assistant
Professor of Anesthesiology/Pain
Medicine in the Department of
Anesthesiology/Pain Medicine,
Mayo Clinic, Rochester, MN.

Address Correspondence:
Dr. Stephanie A. Neuman
Anesthesiology/Pain Medicine
Mayo Clinic
200 First St SW
Rochester, MN 55905
E-mail:
saneuman@gundluth.org

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Background: Placement of an intrathecal drug delivery system (IDDS) may provide substantial benefit to certain patients. However, placement of these devices is not without complications, and minimal data exist describing the rates of these complications. Specifically, there is a paucity of data describing the incidence of post dural puncture headache (PDPH) following IDDS placement.

Objectives: The aim of this study was to identify the incidence and treatment course of PDPH following placement of an IDDS in a retrospective review.

Study Design: Retrospective assessment of medical records.

Setting: Department of Pain Medicine and Anesthesiology, Mayo Clinic, Rochester, MN.

Methods: Following IRB approval, 319 IDDS surgical reports in 285 patients were identified retrospectively over a 20 year study time period. We report demographic information, number of dural punctures, techniques for sealing dural leak, details, and treatment course of PDPH in this population.

Results: Symptoms of PDPH were recognized in 73 individual cases (23% of total procedural volume). Younger patient age was the only statistically significant characteristic in predicting development of a PDPH. There were no statistically significant differences found in regards to other risk factors for PDPH development or treatment strategy employed. Seventy-nine percent of PDPH patients were successfully managed with conservative non-interventional therapies (bedrest, IV fluids, analgesics, antiemetics), while 21% required progression to epidural blood or fibrin glue patch procedures for full resolution of symptoms.

Limitations: Limitations include the retrospective design of the study as well as the potential for undocumented or improperly documented surgical techniques and/or events.

Conclusion: Though the development of PDPH after IDDS implantation was found to be fairly common (23% incidence), the majority of these patients had self-limited symptoms that resolved with conservative medical management. Epidural blood patch or application of epidural fibrin glue was therapeutically successful for the remainder of PDPH patients who were refractory to conservative measures.

Key words: Pain, intrathecal drug delivery system, pain pump, morphine, baclofen, postdural puncture headache, spinal headache

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The implantation of an intrathecal drug delivery system (IDDS) can provide significant pain and/or spasticity relief for patients with malignant pain, non-malignant pain, and those with intractable spasticity (1,2). Intrathecal drug delivery has commanded increasing interest and attention since the original observations of analgesia following neuraxial administration of morphine described by Behar et al (3) and Wang et al (4) in 1979. Since that time, many advances have been made with implantable IDDSs that have facilitated care for medically intractable pain and spasticity in particular (1-9). As IDDSs have matured technologically, there has also been significant growth in our pharmacologic knowledge, both in terms of drug choice and in understanding the sometimes complex interactions that govern which combinations and concentrations of drugs are most appropriate (1,2,6-8).

Despite the substantial expansion of our knowledge, implantable IDDS therapy is still associated with important morbidity, side-effects, and complications that may adversely affect our patients. A few of these potential risks include risk of drug toxicity, possibility of infection, formation of catheter-associated granulomas, development of hypogonadism, opioid-induced hyperalgesia, neurologic injury, bleeding risk, seroma formation, and persistent dural leak allowing cerebral spinal fluid (CSF) drainage (10-14). Surgically related morbidity, in particular, is of special interest because a study of the technique utilized may yield an understanding of how to minimize patient harm or discomfort. Post dural puncture headache (PDPH) is one such problem associated with IDDS implantation that is poorly understood, both in terms of frequency and response rate to different treatment algorithms (10-13).

Our investigation sets out to better understand the incidence of PDPH after IDDS implantation and to elucidate associated risk factors. Previously cited risk factors for the development of PDPH include young age, female gender, low body mass index (BMI), history of prior PDPH, history of chronic headache, increasing diameter of procedural needle, shape of needle tip, bevel orientation and insertion angle, stylet replacement, and operator experience (15). The incidence of PDPH after lumbar puncture or spinal anesthesia may be somewhere between 2% and 20%, and is likely influenced by patient age (15,16). PDPH incidence data for the IDDS population, however, appears to be lacking; a recent 2007 review article by Turner et al (17) notes that "7 [of 10] studies do not mention this complication, 2 mentioned it but did not provide data sufficient

to calculate the rate, and one reported that no patients had it." An earlier study by Kamran and Wright in 2001 (13) does report a PDPH incidence of 3.09% with IDDS implantation (3 out of 97 patients). However, the data presented are inadequate to identify risk factors, time course of symptoms, and treatment of PDPH (13).

OBJECTIVES

Though other papers exist that describe various treatment options for PDPH, we were able to describe treatment outcomes for PDPH after IDSS implantation over a 20 year retrospective review at a single academic center (16,18,19). The primary aim of our study was to determine the overall incidence of PDPH in patients undergoing placement of IDDSs, to identify any predisposing characteristics for development of PDPH, and to report on the success of therapeutic measures employed to treat PDPH.

METHODS

This retrospective cohort study is based upon a 20 year chart review of clinical experience at a large academic medical center (Mayo Clinic, Rochester, MN). Following appropriate institutional review board (IRB) approval, all patients who underwent placement of an IDDS during the period between June 1, 1989, and May 31, 2009, were included. The Mayo Clinic medical data retrieval service identified all patients who underwent implantation of an IDDS with the use of ICD-9 codes. The requirement for written informed consent was waived by the IRB.

Baseline data, including age, gender, race, diagnosis, type and purpose of IDDS placed, and number of dural punctures, were collected at the time of IDDS placement for all patients. Both written and electronic records were reviewed for each patient primarily by 2 of the authors. Development of a PDPH was assessed by reviewing the patient's inpatient and outpatient clinical notes for up to 3 weeks following IDDS implantation. Patient records were carefully evaluated to ensure the diagnosis was that of a PDPH and not of a headache secondary to migraine, tension headache, or other etiology. It was ensured that each patient had a postural component to the headache as well as met other classic diagnostic criteria (e.g., headache most commonly occurring within 24 – 48 hours of dural puncture, dull or throbbing in sensation, exacerbated with maneuvers that increase intracranial pressure, etc.). If PDPH was identified, the start date and end date of symptoms were recorded. Treatment and response to treatment

for PDPH was extracted from the inpatient progress notes, outpatient follow-up notes, and medication administration records until the headache resolved. All IDDS placement procedures were performed under fluoroscopic guidance via a paramedian approach at a single academic pain center by faculty or fellows supervised by faculty. Patients were observed in the hospital for a minimum of 24 hours after the procedure and followed up in clinic thereafter.

Demographic and baseline patient characteristics were analyzed. The primary analysis was on the incidence rate of PDPH within 3 weeks of IDDS placement. The secondary analysis was the assessment of risk factors and their potential contribution to PDPH. Risk factors analyzed included age, gender, race, BMI, diagnosis, number of dural punctures, and if purse string sealing was applied. Univariate analysis was conducted, using PDPH as the outcome and each potential risk factor as predicting variables. All predicting variables that were found to be statistically significantly associated with the PDPH were included in a final multivariate logistic regression model for assessment of relative risk and statistical significance. All tests were 2-sided at a 5% significance level. SAS version 9.1.3 (SAS Institute Inc, Cary, NC) was used for all analyses.

RESULTS

We reviewed 319 surgical cases performed on 285 unique patients, including all primary IDDS placement and/or revision surgeries. Baseline patient characteristics are listed, along with the medical indication for device placement (Table 1 and Fig. 1). Additionally, we

Fig. 1. Clinical indication for IDDS implantation.

Table 1. Patient demographics and univariate analysis for predicting headache.

Variable	Frequency (285)	Percent	Point Estimate	95% Confidence Interval
Age				
18–39	56	19.7	4.4	2.0 – 9.9
40–59	127	44.6	2.9	1.4 – 5.8
≥60	102	35.8	Reference	
Gender				
Women	117	41.1	1.2	0.7 – 2.0
Men	168	59.0	Reference	
BMI				
Normal and Underweight	140	49.1	1.7	0.8 – 3.4
Overweight	81	28.4	1.6	0.7 – 3.5
Obese	64	22.5	Reference	
Diagnosis				
Cancer Pain	154	54.0	0.4	0.2 – 0.7
Chronic Pain	31	10.9	0.2	0.1 – 0.6
Spasticity	100	35.1	Reference

recorded a number of other surgical factors for each patient that is relevant to discuss. Ninety-one point nine percent of IDDS patients required only one dural puncture, while some patients required 2 (5.4%), 3 (1.5%), 4 (0.8%), or 6 (0.4%) dural punctures prior to successful catheter threading. The vast majority of the surgical cases utilized 15-gauge needles (80%) to access the intrathecal space, and only 20% of implants were performed with 18-gauge needles. Data in Table 2 denotes the frequency of use of purse string sutures, and reports the overall incidence of PDPH for our entire retrospective review (Fig. 2).

To further examine the influence of gender, age, IDDS indication, use of purse string suture, and BMI on PDPH development, we used logistic regression to statistically analyze the data (Tables 1 - 3). Of the aforementioned variables, only young age was shown to be a statistically significant risk factor for PDPH (specifically Table 3 and Fig. 3). Other factors, includ-

Table 2. Procedural characteristics and univariate analysis for predicting PDPH.

Variable	Frequency (319)	Percent	Point Estimate	95% Confidence Interval
Post Dural Puncture Headache				
Yes	73	22.9		
No	246	77.1		
Purse String Suture				
No	201	63.0	0.7	0.4 - 1.3
Yes	118	37.0	Reference	

Table 3. Risk factors assessed with logistic regression for PDPH after IDDS implantation.

	Effect	Point Estimate	95% Confidence Intervals
Gender			
	Female vs Male	1.2	0.7 - 2.1
Age			
	18 - 39 vs ≥ 60	3.0	1.3 - 7.2
	40 - 59 vs ≥ 60	2.2	1.1 - 4.6
Diagnosis			
	Cancer Pain vs Spasticity	0.6	0.3 - 1.0
	Chronic Pain vs Spasticity	0.3	0.1 - 0.9

ing surgical techniques with smaller needle gauge size and use of a purse string suture, were not shown to be clinically significant in lessening the risk of PDPH.

Once PDPH symptoms developed, there were a variety of therapies instituted in this patient population. Conservative measures of bedrest and medication administration (analgesics, caffeine, and/or antiemetic therapy) were the most common therapies, followed closely by use of intravenous fluid hydration (Fig. 4). Approximately one in 5 patients (21%) required procedural intervention in the form of an epidural blood patch (EBP) or epidural fibrin glue patch (EFP). In all cases, the patients who required these interventional epidural patches had full resolution of symptoms afterwards; 2 patients, however, did require a second epidural patch procedure in order to achieve lasting relief.

Discussion

The primary goals of our study were to identify the incidence, treatment course, and associated risk factors for development of PDPH following placement of an IDDS. In our 20 year retrospective review, we report that symptoms of PDPH were recognized in 73 individual cases (23% of total procedural volume). Of the recognized cases of PDPH, 79% (n = 58) were amenable to management with conservative non-interventional therapies, while 21% (n = 15) of cases required progres-

sion to an EBP or EFP. Thus, EBP or EFP was required in 4.7% (15/319) of all IDDS placements for complete resolution of PDPH symptoms.

Younger patient age was the only statistically significant characteristic in predicting development of a PDPH in both univariate analysis and logistic regression. The 18 – 39-year-old group was found to be over 4 times more likely to develop a PDPH than the > 60-year-old age group. Similarly, the 40 – 59-year-old age group was almost 3 times more likely to develop a PDPH than their older counterparts in the > 60-year-old age group. Although univariate analysis demonstrated that patients who underwent placement of the IDDS for spasticity had a significantly higher rate of developing a PDPH than those who underwent placement for cancer or chronic pain, this did not hold true when performing logistic regression analysis. This finding in univariate analysis was likely confounded by age, as patients who require IDDS placement for spasticity are often younger.

It has long been thought that other specific patient characteristics such as female gender and low BMI are also significant risk factors for development of a PDPH following dural puncture. To our surprise, we were unable to demonstrate this even when combining these characteristics. Furthermore, it is commonly believed that placement of a purse string suture may prevent

development of a PDPH. However, our findings suggest that this surgical technique may bear no role in PDPH occurrence.

Lastly, our study reports a higher incidence of PDPH (23%) than some previously published estimates. Kamran's and Wright's 2001 review of IDDS complications (13), for instance, describes a spinal headache incidence of only 3.06%. However, Kamran's and Wright's paper (13) excludes 25 patients (out of 122 patient cases reviewed for the study) due to loss of follow-up or transfer of care. These data, coupled with the greater number of patients reviewed in our retrospective examination, imply that the true incidence of PDPH after IDDS implantation may have been significantly underappreciated in the past.

LIMITATIONS

Our study certainly has some limitations. Undocumented surgical techniques and surgeon-specific preventative measures (e.g., restyling, use of a purse string suture, abdominal binder placement postoperatively, intravenous fluid bolus postoperatively) may have been performed by the multiple surgeons placing these systems. However, given the fact that the large number of surgeons were from only 2 separate medical specialties (fellowship-trained pain physicians and neurosurgeons), we conclude that variance in technique was not likely to be clinically significant in regards to patient outcome. Another potential criticism is that some surgical reports may not have properly documented the number of dural punctures required for successful intrathecal catheter deployment. Consequently, our ability to comment on the number of dural punctures being a predictor for development of PDPH is potentially limited.

CONCLUSION

In conclusion, our 20-experience demonstrates that nearly 23% of IDDS cases develop PDPH symptoms after surgical implantation. However, the majority of PDPH

cases (79%) respond favorably to conservative medical therapy. Approximately 21% of PDPH patients eventually require interventional procedures (epidural blood or fibrin glue) for relief, and the vast majority of these patients (88%) have full resolution of symptoms following one EBP. The results of our study are not germane to the clinical decision-making process for selecting which patients will benefit most from IDDS placement. However, our clinical review may facilitate a better understanding of the procedural risks involved for patients and provide therapeutic guidance to interventionalists treating patients that develop PDPH following IDDS implantation.

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Dr. Eldrige helped design the study, collect data, and prepare the manuscript. Dr. Eldrige also approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.

Dr. Qu helped design the study, collect data, analyze data, and prepare the manuscript. Dr. Qu also approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.

Dr. Freeman helped design the study and collect data; and also approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.

Dr. Hoelzer helped design the study, collect data, analyze data, and prepare the manuscript; and also approved the final manuscript and attests to the integrity of the original data and the analysis reported in this manuscript.

REFERENCES

1. Stearns L, Boortz-Marx R, Du Pen S, Friehs G, Gordon M, Halyard M, Herbst L, Kiser J. Intrathecal drug delivery for the management of cancer pain: A multidisciplinary consensus of best clinical practices. *J Support Oncol* 2005; 3:399-408.
2. Wallace M, Yaksh TL. Long-term spinal analgesic delivery: A review of the pre-clinical and clinical literature. *Reg Anesth Pain Med* 2000; 25:117-157.
3. Behar M, Magora F, Olshwang D, Davidson JT. Epidural morphine in treatment of pain. *Lancet* 1979; 1:527-529.
4. Wang JK, Nauss LA, Thomas JE. Pain relief by intrathecally applied morphine in man. *Anesthesiology* 1979; 50:149-151.
5. Benzon HT, Raj PP. *Raj's Practical Management of Pain*. 4th edition. Mosby-Elsevier, Philadelphia, 2008.
6. Deer TR, Prager J, Levy R, Rathmell J, Buchser E, Burton A, Caraway D, Cousins M, De Andres J, Diwan S, Erdek M, Grigsby E, Huntoon M, Jacobs MS, Kim

- P, Kumar K, Leong M, Liem L, McDowell li GC, Panchal S, Rauck R, Saulino M, Sitzman BT, Staats P, Stanton-Hicks M, Stearns L, Wallace M, Willis KD, Witt W, Yaksh T, Mekhail N. Polyanalgesic Consensus Conference 2012: Recommendations for the management of pain by intrathecal (intraspinale) drug delivery: Report of an interdisciplinary expert panel. *Neuromodulation* 2012; 15:436-466.
7. Deer TR, Smith HS, Burton AW, Pope JE, Doleys DM, Levy RM, Staats PS, Wallace MS, Webster LR, Rauck RL, Cousins M. Comprehensive consensus based guidelines on intrathecal drug delivery systems in the treatment of pain caused by cancer pain. *Pain Physician* 2011; 14:E283-312.
8. Deer TR, Smith HS, Cousins M, Doleys DM, Levy RM, Rathmell JP, Staats PS, Wallace M, Webster LR. Consensus guidelines for the selection and implantation of patients with noncancer pain for intrathecal drug delivery. *Pain Physician* 2010; 13:E175-213.
9. Loeser JD, Bonica JJ. *Bonica's Management of Pain*. 3rd edition. Lippincott Williams & Wilkins, Philadelphia, 2001.
10. Coffey RJ, Owens ML, Broste SK, Dubois MY, Ferrante FM, Schultz DM, Stearns LJ, Turner MS. Mortality associated with implantation and management of intrathecal opioid drug infusion systems to treat noncancer pain. *Anesthesiology* 2009; 111:881-891.
11. Crul BJ, Delhaas EM. Technical complications during long-term subarachnoid or epidural administration of morphine in terminally ill cancer patients: A review of 140 cases. *Reg Anesth* 1991; 16:209-213.
12. Follett KA, Naumann CP. A prospective study of catheter-related complications of intrathecal drug delivery systems. *J Pain Symptom Manage* 2000; 19:209-215.
13. Kamran S, Wright BD. Complications of intrathecal drug delivery systems. *Neuromodulation* 2001; 4:111-115.
14. Ruan X. Drug-related side effects of long-term intrathecal morphine therapy. *Pain Physician* 2007; 10:357-366.
15. Bezov D, Lipton RB, Ashina S. Post-dural puncture headache: Part I diagnosis, epidemiology, etiology, and pathophysiology. *Headache* 2010; 50:1144-1152.
16. Basurto Ona X, Martinez Garcia L, Sola I, Bonfill Cosp X. Drug therapy for treating post-dural puncture headache. *Cochrane Database Syst Rev* 2011; 10:CD007887.
17. Turner JA, Sears JM, Loeser JD. Programmable intrathecal opioid delivery systems for chronic noncancer pain: A systematic review of effectiveness and complications. *Clin J Pain* 2007; 23:180-195.
18. Gerritse BM, van Dongen RT, Crul BJ. Epidural fibrin glue injection stops persistent cerebrospinal fluid leak during long-term intrathecal catheterization. *Anesth Analg* 1997; 84:1140-1141.
19. Raj PP. *Interventional Pain Management: Image-guided Procedures*. 2nd edition. Saunders/Elsevier, Philadelphia, PA, 2008.