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Intrathecal Drug Delivery for Intractable Pain: Identified Patient Satisfaction Survey Study Comparing Intrathecal Dose With Satisfaction, Pain Relief, and Side Effects

David M. Schultz, MD[1,2]; Caitlin H. Bakke, DO[1]; Hannah L. Ruble, MPH[1]; Collin S. Larmour, BS[1]; Jonathan M. Hagedorn, MD[3]; Alaa Abd-Elsayed, MD, MBA, MPH[4]

ABSTRACT

Objectives: Past studies have shown the efficacy of spinal targeted drug delivery (TDD) in pain relief, reduction in opioid use, and cost-effectiveness in long-term management of complex chronic pain. We conducted a survey to determine treatment variables associated with patient satisfaction.

Materials and Methods: Patients in a single pain clinic who were implanted with Medtronic pain pumps to relieve intractable pain were identified from our electronic health record. From November 2021 to February 2023, 973 patients with active TDD were identified; 564 completed the 23-question survey, and 560 were included in analyses. Most patients (96.4%) had intrathecal (IT) infusion admixtures containing bupivacaine and opioid. The survey compared satisfaction with IT medication dosages, pain relief, pain diagnosis, catheter tip location, side effects, mental clarity, physical functioning, and healthcare utilization. Outcomes were reported as proportions; $p < 0.05$ was considered significant.

Results: Most respondents reported good-to-excellent pain relief (63.8%), high satisfaction with TDD (80.7%), improvement in physical functioning (75.0%), and better quality of life (89.7%); 78.5% of respondents reported complete discontinuation or substantial reductions in systemic opioid use. There was a statistically significant relationship between satisfaction and IT medication dose ($p = 0.02$), with the average dose increasing with higher satisfaction groups. We found that patients on higher doses of IT opioids did not have more bothersome side effects ($p = 0.05$).

Conclusions: Our data show that the most satisfied respondents had higher IT doses, fewer side effects, and longer duration of TDD therapy. This suggests that higher dose IT admixtures are safe and effective at relieving pain and improving quality of life in patients with complex chronic pain whose condition has failed to respond adequately to other treatments. TDD may be an effective alternative to long-term systemic opioids for well-selected patients willing to accept the risks of invasive procedures.

Keywords: Chronic pain, intrathecal, IT opioid, pain pump, targeted drug delivery

INTRODUCTION

Intrathecal targeted drug delivery (TDD) through a programmable, fully implanted pump and intrathecal (IT) catheter system (Medtronic Synchromed, Minneapolis, MN) was first used in the early 1980s as a method for treating intractable pain.[1] Since then, many studies have shown the efficacy[2–6] and cost-effectiveness[7–10] of TDD in treating both cancer pain[11–13] and noncancer pain.[11–18]

As targeted spinal drug delivery evolves to become a more common option for pain control in refractory cases of complex chronic pain,[5,15,19] it is important to determine which components of TDD therapy correlate with the best outcomes and highest patient satisfaction. Many different opinions exist on IT dosing for TDD, from microdosing to Food and Drug Administration-approved monotherapy with morphine or ziconotide,[20,21] to recommendations for higher-dose spinal admixtures.[12] There also are varying

Address correspondence to: David M. Schultz, MD, Nura Pain Clinic, 2104 Northdale Blvd NW, Minneapolis, MN 55433, USA. Email: dschultz@nuraclinics.com

[1] Nura Pain Clinic, Minneapolis MN, USA;
[2] Department of Anesthesia, Critical Care and Pain Medicine, University of Minnesota, Twin Cities, MN, USA;
[3] Department of Anesthesiology and Perioperative Medicine, Division of Pain Medicine, Mayo Clinic, Rochester, MN, USA; and
[4] Department of Anesthesiology, University of Wisconsin, Madison, WI, USA

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opinions on which diagnoses are appropriate for TDD, the importance of catheter tip location, and the best site for pump pocket location.

Unfortunately, physicians lack data to make evidence-based decisions regarding optimal management of patients with TDD. Regarding dosing, most physicians would agree it is best to use the fewest spinal medications at the lowest doses possible to achieve pain relief.[12] Still, there is a paucity of data correlating dosages of IT medications with pain relief, side effects, mental clarity, physical functioning, healthcare utilization, and overall satisfaction with the therapy.

We hypothesized that the IT opioid-local anesthetic admixtures dosed at the higher end of Polyanalgesic Consensus Conference (PACC) guidelines[12] routinely used in our clinic contribute to the excellent pain relief and high patient satisfaction noted in our patients with TDD.[4] To investigate the relationship between the specifics of TDD therapy and overall patient satisfaction, we correlated management variables with identified patient responses to a 23-question satisfaction survey (Appendix 1).

MATERIALS AND METHODS

Patient Population

As in our previously published anonymous 2020 study,[4] we identified patients implanted with pain pumps who were being actively managed with TDD in our pain clinic practice. For our present study, we surveyed identified patients with initial implants between 1994 and 2022. At the time of the survey, 973 patients were actively managed with TDD by a team of specialized nurses and advanced practice providers supervised by a group of physician implanters. Patients referred to our pain clinic with refractory, disabling chronic pain in whom all other appropriate attempts at pain management have failed are considered for TDD. Most of these patients experienced inadequate pain relief from previous injections, surgeries, and trials or implants of neurostimulation systems, and were maintained on daily systemic opioids before pump implant. Of the 973 patients with active pain pumps in our practice, 564 responded to the survey (58.0%), and 560 were included in the analysis (57.6%). We discontinued surveying after 564 respondents because we considered this number adequate to provide clinically meaningful insights.

Survey

We administered a 23-question survey (Appendix 1) using self-reported, multiple-choice responses to examine satisfaction with TDD therapy in a single pain clinic practice with uniform standards for TDD management. We provided a paper survey to clinic patients with their consent at the end of their pump management visit. We examined patients' attitudes, behaviors, and outcomes surrounding TDD therapy by analyzing responses to survey questions and correlating these responses to the specifics of individual therapy recorded in the electronic health record (NextGen, Irvine, CA). We validated data mined from our electronic health record (EHR) with our ad hoc deidentified data collected in the Medtronic Product Surveillance Registry (PSR, NCT04873817) by temporarily reidentifying the PSR data and cross-referencing these with the data gleaned from our EHR. Data from the Medtronic PSR were initially gathered through chart review and patient interview per PSR study protocol and then entered into the Medtronic electronic data capture system, where they were audited for accuracy and completeness by Medtronic staff. The survey was identified and voluntary, and all survey data were deidentified once EHR review was complete. Patients did not receive compensation for survey completion. The protocol was reviewed by an institutional review board, which approved waiver of authorization for use and disclosure of protected health information.

Level of Satisfaction Based on Survey Responses

To identify broad correlations between satisfaction and the specifics of therapy, we divided subjects into low, medium, and high satisfaction groups based on survey responses. The principal investigator reviewed all survey questions and with team input determined the questions most indicative of overall patient satisfaction. We then created a "satisfaction index" based on the following four questions:

1. Overall, how do you feel about your pump? (Fig. 2)
2. How likely is it that you would recommend an implanted pain pump to a friend or colleague with chronic pain? (Fig. 3)
3. Do you feel the pump has improved your quality of life? (Fig. 4)
4. Would you have the pump implanted if you could go back and change your decision? (Fig. 5)

These four satisfaction questions were assigned ordinal weights, with responses indicating the most dissatisfaction receiving 0% satisfaction and those indicating the highest satisfaction receiving 100% on the index. These weighted scores were then averaged across all questions so that respondents who did not answer all questions could be included in the analysis. The average of the weighted scores was considered a ratio variable. Finally, the total range of responses was subdivided into low, medium, and high satisfaction groups for further analysis (Table 1).

Groups Based on IT Morphine Milligram Equivalents

One purpose of our study was to correlate the overall dose of IT opioid to pain relief and satisfaction, and we therefore needed a standard by which to compare overall IT opioid doses for our 560 respondents. This was problematic given not all subjects had the same IT opioid and some subjects had more than one opioid in their pump admixture. To standardize IT dosing among our typical spinal admixtures, we created a construct called IT morphine milligram equivalents (IMME), which we used to compare the potency of the three IT opioids used in our practice and to separate our subjects into low-, medium-, and high-dose TDD. Although there have been multiple attempts to characterize the pharmacoequivalence among morphine, hydromorphone, and fentanyl, there is a lack of consensus,[18,22–25] especially in relation to IT opioids. Based on our experience managing IT opioids over the past 30 years, we considered 1 mg IT morphine equivalent to 0.1 mg (100 mcg) IT fentanyl and 0.5 mg IT hydromorphone. Although most admixtures contained bupivacaine in a 1 mg to 1 mg ratio with IT morphine, 1 mg to 100 mcg ratio with fentanyl, and 0.5 mg to 1 mg ratio with hydromorphone, we did not factor bupivacaine into our IMME dosing equation. Therefore, our analysis selectively considered analgesic effects of opioid receptor blockade without considering the synergistic effects of bupivacaine neural blockade. Morphine was selected as the baseline IT opioid because it is common practice to convert systemic opioids into morphine milligram equivalents. We removed patients with terminal cancer from our analysis because of unusually high dosing with spinal admixtures containing opioid, local anesthetic, and ketamine in most of these patients.

Outcomes

The survey's primary objective was to determine overall patient satisfaction and pain relief, which was then used to group patients into three ordinal groups (low, medium, and high satisfaction). These groups were then compared with clinical and demographic information to determine whether there were any relationships between overall patient satisfaction and the specifics of therapy in the surveyed population.

We then correlated level of satisfaction and pain relief with IT dose (IMME) and further correlated both satisfaction and IT dose with multiple independent variables including side effects, mental clarity, physical functioning, improvement in quality of life, systemic opioid consumption, healthcare utilization, and comfort of the implanted pump.

In measuring overall patient satisfaction with TDD, we believed one of our four satisfaction questions—"How likely is it that you would recommend an implanted pain pump to a friend or colleague with chronic pain?"—was perhaps more important than the others given this single question is being increasingly used to calculate "Net Promoter Score" (NPS) as a measure of overall satisfaction in a wide variety of service industries, including healthcare. Although NPS is considered a valid measure of satisfaction with an experience, it has not been validated to measure satisfaction with a medical procedure. Because TDD is both a procedure and an experience over time, we believe the single NPS question provides insight into patient satisfaction with the overall experience of TDD. Nonetheless, there is currently no best-practice patient experience measurement tool, and the NPS question is simply one of four that we used to determine overall satisfaction in our study population.

Statistical Analysis

Survey responses were analyzed by investigators not involved in the generation of survey questions. Incomplete survey responses were included in the analysis, when appropriate. Some survey question responses were considered ordinal for interpretation and analysis, with the remaining survey responses classified as nominal.

Demographic data (age and sex) and clinical data (diagnosis, duration of therapy, medication dosage) were queried from our medical practice EHR from 2021 through 2023. Any indeterminate diagnoses were reclassified by the primary investigator. Diagnosis was considered nominal data, whereas age, duration of therapy, and medication doses were parametric continuous variables.

Survey responses were then correlated with the patient's demographic and clinical information, and these data were entered into one of the three satisfaction groups and analyzed for significant differences among satisfaction groups. Nominal data were analyzed using χ^2 tests of independence or Fisher's exact test when any group being investigated had an $n < 5$. Continuous variables were investigated using one-way analysis of variance (ANOVA) tests. For all statistical tests, α was set as 0.05, and β was set as 0.10. No significant differences were found among nominal variables. Significant findings of one-way ANOVA tests were further analyzed using post hoc *t*-tests with Bonferroni correction. Missing data were excluded from statistical analysis. Statistical tests were performed using RStudio (Posit team: Version 2023.6.1.524, statistical software; Boston, MA).

RESULTS

Diagnosis for Implant

Most patients reported satisfaction with TDD (80.7%), and we did not find a statistically significant relationship between diagnosis and satisfaction. The primary diagnosis for most patients with implants was spinal pain (78.4%), with 48 (8.6%) cervical spine pain, 81 (14.5%) thoracic spine pain, and 310 (55.6%) lumbar spine pain. The 59.1% of patients with spinal pain reported pain before and after spinal surgery and had an International Classification of Diseases, Tenth Revision diagnosis of postspinal surgery pain syndrome (M96.1). Thirty-five subjects (6.3%) had a high cervical catheter tip (C1–C2) location to treat head and face pain (Fig. 1). Of these patients, 32 were in the high-satisfaction group with none in the low-satisfaction group.

Overall Satisfaction

Regarding overall satisfaction, 41.7% of respondents (222/533) "loved their pump," and an additional 39.2% (209/533) stated their pump "helped them a lot and they were glad to have it" (Fig. 2). Only 1.3% of subjects (7/533) stated the pump was not helpful and were sorry to have had it implanted.

Single Question Measure of Satisfaction

In total, 538 subjects responded to our single NPS question: "Would you recommend an implanted pain pump to a friend or colleague with chronic pain?" Of these, 454 were promoters; 62

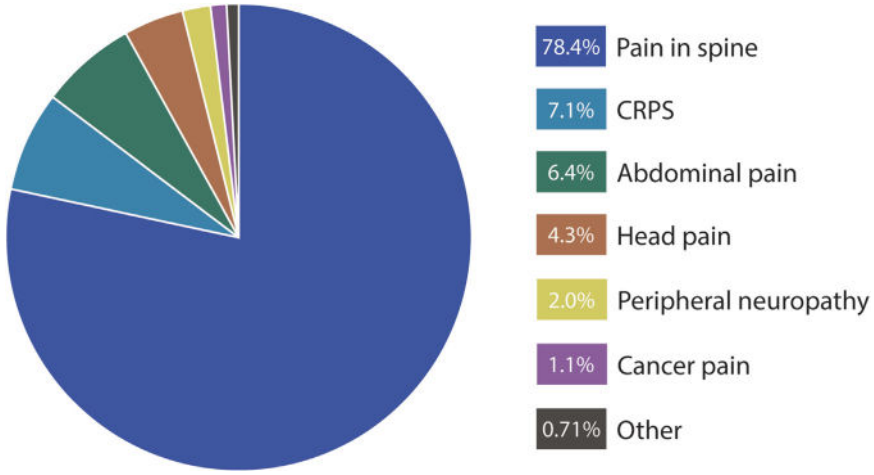

Figure 1. Primary diagnoses for implant of our surveyed patient population ($N = 560$). CRPS, complex regional pain syndrome.

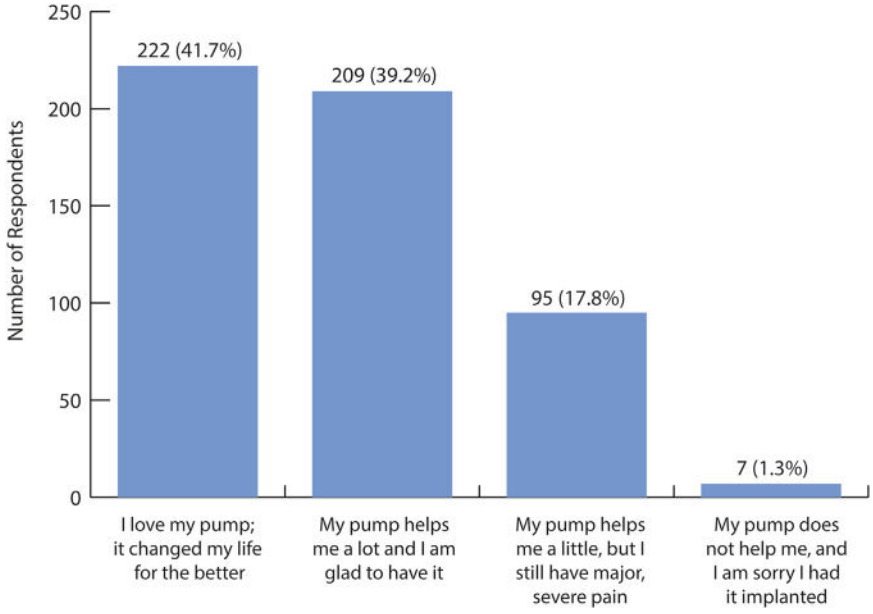

Figure 2. Overall, how do you feel about your pump? (n = 533).

were neutral, and 19 were detractors for a high NPS of 81 (Fig. 3). Although not validated as a single measure of satisfaction in health care, NPS scores >0 are considered good, >20 favorable, >50 excellent, and >80 in the top percentile.[26]

Quality of Life

Regarding quality of life, 49.5% of respondents (264/533) said this had very much improved because of their pump (Fig. 4); 40.2% (214/533) said their quality of life was moderately better because of their pump, and 9.4% (55/533) said their quality of life had not changed with the pump. No respondents said their quality of life was reduced because of the pump.

Would You Do It Again?

A total of 71.3% of respondents (377/529) said they would "definitely" have their pump implanted again if given the choice (Fig. 5); 21.4% (113/529) said they would probably have their pump reimplanted and were better off with it than without it, and 6.0% (32/529) said they would not or probably would not have their pump reimplanted.

Reduction in Systemic Opioids

Before referral for pain pump trial and implant, most study subjects had been treated with daily systemic opioids. Although patients often experience pain relief with systemic opioids, unacceptable side

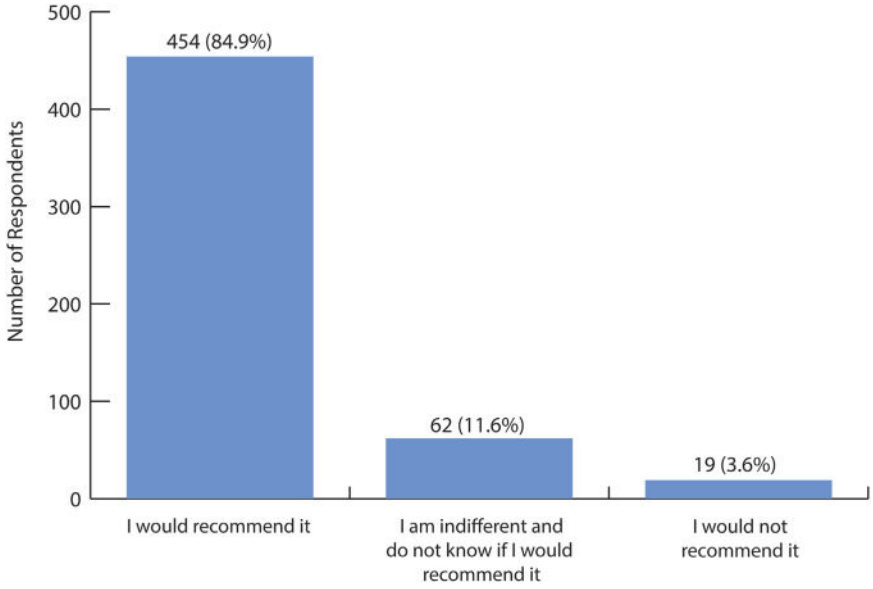

Figure 3. How likely is it that you would recommend an implanted pain pump to a friend or colleague with chronic pain? (n = 538). NPS calculation: NPS = ([number of promoters]/[total respondents]) − ([number of detractors]/[total respondents])

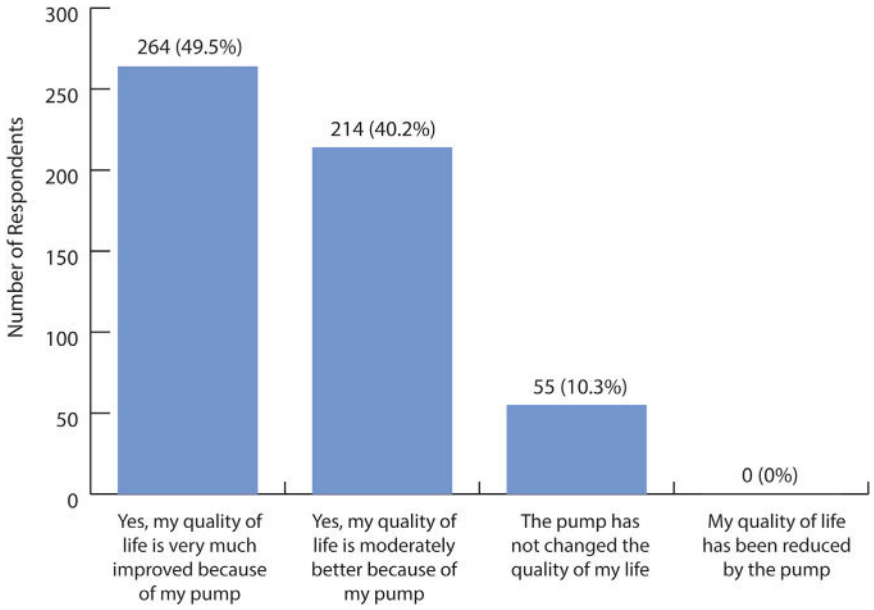

Figure 4. Do you feel the pump has improved your quality of life? (n = 533).

effects motivate many of them to seek an alternative method of pain management. At our clinic, we take over opioid prescribing after referral and taper systemic opioids as much as feasible for TDD candidates before IT trial. Nonetheless, many patients are unable to discontinue or dramatically reduce systemic opioids before implantation. In these cases, we gradually reduce systemic opioids after implant as pain relief is achieved with IT medications. In our present study, 78.5% of patients (388/494) tapered systemic opioids to low levels, and 50.2% (248/494) discontinued them completely or almost completely after pump implant (Fig. 6).

Side Effects

A statistically significant relationship was found with one-way ANOVA between IMME dose and severity of side effects (p = 0.0484), although post hoc testing did not find significant differences among groups. Interestingly, respondents who reported severe side effects had a lower average IMME dose (15.2 ± 11.9 mg/d) than those reporting no significant side effects, minor and tolerable side effects, or bothersome but manageable side effects (20.2 ± 10.8, 18.1 ± 10.1, and 18.0 ± 10.9 mg/d, respectively).

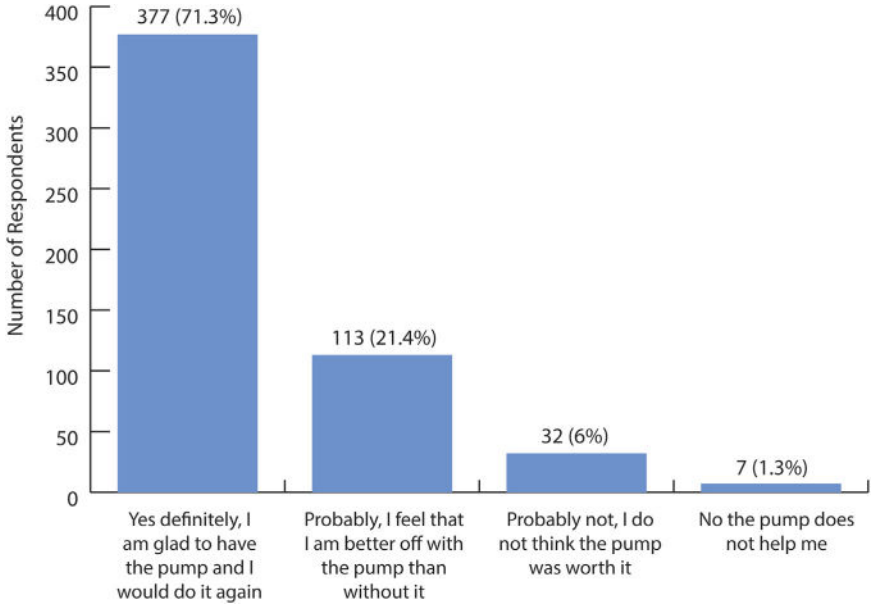

Figure 5. Would you have the pump implanted if you could go back and change your decision? (n = 529).

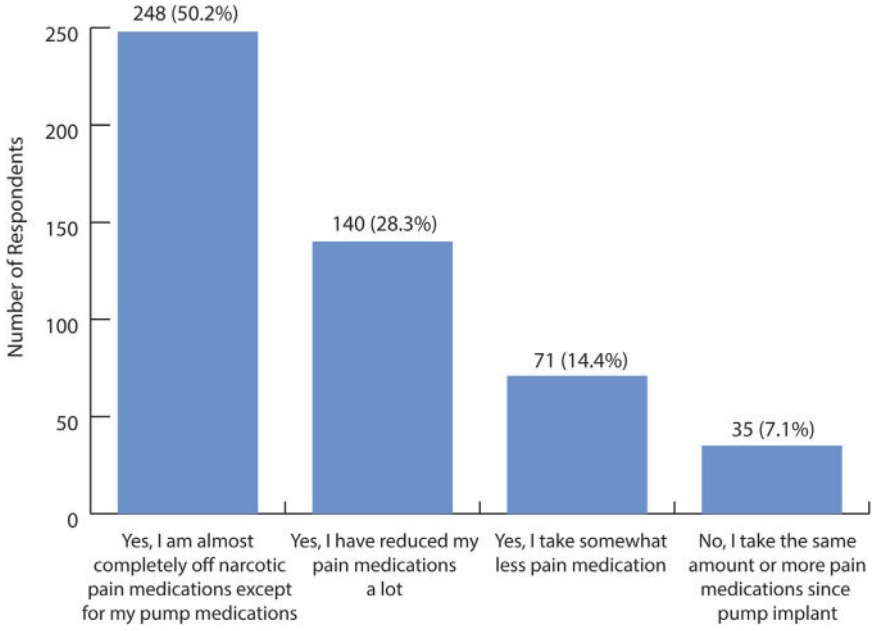

Figure 6. Has your pain pump helped you to reduce your oral or skin patch opioids? (n = 494).

Moreover, 57.1% of respondents (296/518) said they experienced no significant side effects from TDD (Fig. 6). Another 25.1% (130/518) experienced side effects that were minor and tolerable. Only 3.9% (20/518) experienced side effects causing major problems (Fig. 7).

Side effects were not problematic for most subjects (Appendix 2 presents further analysis).

Mental Clarity, Sleep, Physical Activity, and Healthcare Utilization

Most subjects denied somnolence or mental impairment; 78.6% of respondents (428/544) felt clear-headed without mental clouding, and only 1.3% (7/544) felt mentally impaired from TDD. No subjects acknowledged overdoses or car accidents related to TDD. 71.0% (382/538) were much or somewhat more awake than at preimplant systemic opioid management; 51.9% (276/532) slept better, with only 5.3% (28/532) reporting worsened sleep. 75.0% (399/532) rated physical activity as much or somewhat better. 32.3% (141/436) reported being able to return to work either part- or full-time; 63.7% (278/436) noted no impact on their ability to return to work; 3.9% (17/436) noted their ability to work had been reduced by the pump. 82.3% of respondents (431/524) denied emergency department visits or hospitalizations for pain-related issues since implant and an additional 12.4% (65/524) admitted to less hospital care after implant than before.

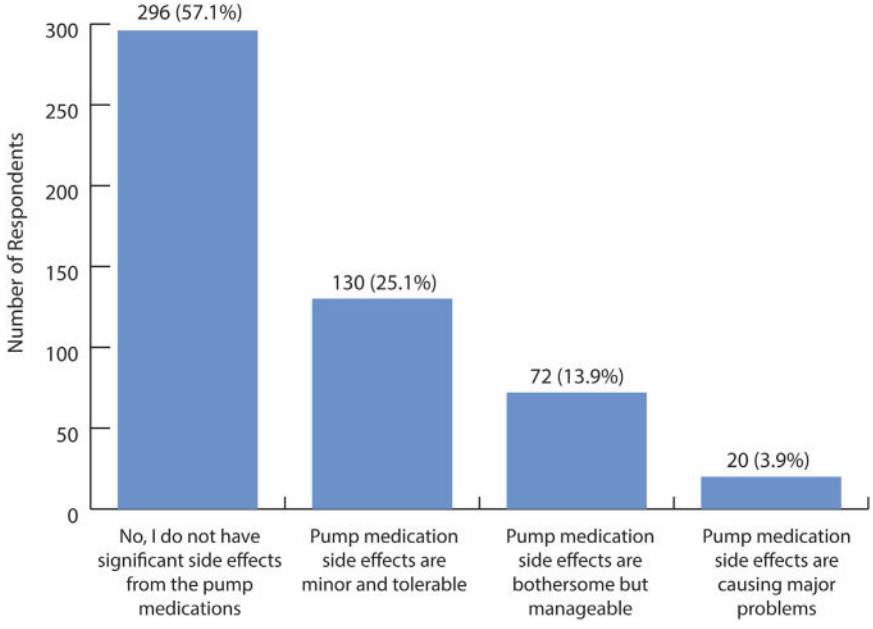

Figure 7. Have side effects from the pump medications been a problem? (n = 518).

Pump Size, Location, and Comfort

Overall, 88.2% (494/560) of respondents had 40cc pumps implanted in the upper buttock; 89.0% (463/520) stated the pain pump was comfortable regardless of location; 77.1% of survey respondents (401/520) had upper buttock pumps and liked their pump location, and 11.9% (62/520) had abdominal pumps and liked their pump location. Overall, 90.7% of respondents (497/548) reported that pump pocket discomfort was not a problem, and 75.6% (409/541) were happy with the size of their pump; 9.2% (50/544) wanted a larger pump to prolong refill intervals, and 16.0% (87/544) wanted a smaller pump for better comfort.

Bolus Dosing

In total, 82.2% of patients (444/540) had bolus dosing incorporated into their pump programming; 70.4% of respondents (370/525) said boluses were very helpful, and an additional 14.6% (77/525) said they were somewhat helpful.

Election to Discontinue TDD

When subjects were asked whether they would like to discontinue TDD therapy, 96.5% (467/484) answered, "No, my pump helps me enough, so I want to keep it." Only 3.5% of respondents (17/484) said they wanted their pump turned down and removed.

IMME and Patient Satisfaction

We found that across our surveyed population, the average IMME per day was 19.2 ± 10.7 mg. One-way ANOVA analysis found significant differences in IMME dose among groups ($p = 0.02$). Descriptive analysis shows that the average IMME dose decreased with lower patient satisfaction. However, post hoc comparisons found no statistically significant differences among the groups. Although the data suggest a relationship between satisfaction and IMME dosing, we cannot determine directionality. One-way ANOVA detected significant differences ($p = 0.05$) in dosage among patients reporting varying severities of side effects (Table 1).

The patients who reported major side effects had an average IMME of 15.2 ± 11.9. Those with bothersome but manageable side effects had an IMME of 18.0 ± 10.9, and respondents with minor and tolerable side effects had an IMME of 18.1 ± 10.1. The population reporting no significant side effects averaged the highest IMME of 20.2 ± 10.8. One-way ANOVA detected significant differences in IMME among respondent groupings.

We did not detect a statistically significant relationship between physical activity and IMME, nor any statistically significant relationships between changes in physical functioning and IMME dosing. Only 13 patients reported increased somnolence, and there was no statistically significant correlation of somnolence with IMME.

Demographic and Clinical Variables Related to Satisfaction

The only variable found to have a statistically significant relationship with our satisfaction index was the number of months since implant ($p = 0.001$). Our *t*-tests showed significant differences between low and medium and low and high satisfaction groups but not between medium and high satisfaction groups. This implies that satisfaction improves over time after implant and/or that patients who are satisfied with their pump continue therapy. The remaining variables were not significantly related to our satisfaction construct (Table 2).

DISCUSSION

Our data show that most of our survey respondents rate their pain relief as good to excellent, with high rates of self-reported clinical benefits such as improved physical function, better quality of life, systemic opioid reduction, few bothersome side effects, and less emergency healthcare utilization. In our surveyed population, patients on higher IT doses tended to have better pain relief, whereas patients on lower doses tended to have less pain relief. This suggests that higher IMME doses may be associated with better pain relief without an increase in the frequency or severity of side effects. Our findings support the use of TDD as an alternative to systemic opioid use for well-selected patients with intractable chronic pain willing to accept the risks of the invasive procedures involved in trialing, implanting, refilling, and managing pain pumps over time. We discuss the risks, history, and evolution of TDD as an alternative to systemic opioids further in Appendix 3.

Regarding TDD drawbacks and challenges, patients must be informed of risks before implantation, and well-trained, specialized staff must actively work to maximize therapeutic benefits while minimizing potential harm over time. The implantation of a TDD system requires minimally invasive surgery that carries inherent risks associated with surgery, surgical anesthesia, and the potential for postoperative infection. Once implanted, IT doses must be adjusted as systemic opioids are decreased, which can take several weeks or months. Furthermore, a robust clinical infrastructure is essential to ensure that patients with implanted pumps are regularly monitored for therapeutic efficacy and that their pumps can be safely accessed and reprogrammed for refills or admixture adjustments by trained personnel. In addition, there may be currently unknown risks associated with long-term intrathecal infusion of compounded, off-label IT admixtures and there are logistical considerations regarding the delivery of these admixtures to the clinic before pump refill visits. These challenges may pose significant barriers for providers looking to transition patients from systemic opioids to TDD therapy but can be overcome with

Table 1. Comparing IMME With Satisfaction in Patients Surveyed ($N = 560$).

Medications	Dosing in low- satisfaction group ($n = 22$)		Dosing in medium-satisfaction group ($n = 102$)		Dosing in high- satisfaction group ($n = 436$)		*p* Value
	Mean	SD	Mean	SD	Mean	SD	
IMME*	15.5	10.5	17.1	10.4	19.8	10.7	0.018
Bupivacaine (mg)	9.92	5.34	12.7	24.5	11.8	6.25	0.57

*IT IMME of hydromorphone, fentanyl, and morphine (mg).

Table 2. Correlating Satisfaction to Age, Sex, Diagnosis for Implant, Months Since Implant, and Pump Pocket Location (N = 560).

Characteristic	n (%)	Low satisfaction n = 22 (4%)	Medium satisfaction n = 102 (18%)	High satisfaction n = 436 (78%)	p Value*
Age					0.30
	59.1 ± 12.6	55.6 ± 11.0	58.3 ± 112.7	59.5 ± 12.7	
Sex					
Male	214 (38)	9 (41)	45 (44)	156 (36)	0.28
Female	350 (63)	13 (59)	57 (56)	280 (64)	0.39
Diagnosis					
Abdominal pain	36 (6)	0	10 (10)	26 (6)	
Cancer	6 (1)	0	0	6 (1)	
CRPS	40 (7)	4 (18)	8 (8)	28 (6)	
Head pain	24 (4)	0	4 (4)	20 (5)	
Cervical spine pain	48 (9)	1 (5)	9 (9)	38 (9)	
Thoracic spine pain	81 (15)	6 (27)	12 (12)	63 (14)	
Lumbar spine pain	310 (55)	10 (46)	56 (55)	244 (56)	
Peripheral neuropathy	11 (2)	1 (5)	3 (3)	7 (2)	
Other†	4 (0.7)	0	0	4 (0.9)	
Mo since implant					0.001
	76.9 ± 68.6	37.7 ± 30.0	62.9 ± 65.9	82.2 ± 69.5	
Pump location					0.62
Abdominal	69 (12)	2 (9)	16 (16)	51 (12)	
Buttock	451 (81)	17 (77)	83 (81)	351 (81)	

CRPS, complex regional pain syndrome.

*p Value between satisfaction groups was found to be 2.2×10^{-16}.

†Other includes four patients with the following respective primary diagnoses: angina pectoris with documented spasm, multiple sclerosis, paraplegia, and quadriplegia.

appropriate clinical infrastructure, clinician knowledge, and realistic patient expectations.

Regarding side effects after pump implant, 57% of survey respondents denied TDD side effects and an additional 25% stated TDD side effects were minor and tolerable. The most common side effect reported was constipation, although this may be due, at least in part, to the effects of continued systemic opioid use after beginning TDD. Owing to the limitations of our data set, we were unable to correlate systemic opioid use with side effects.

The high satisfaction and good-to-excellent pain relief for patients with TDD in our present identified survey study are similar to results from our previously published anonymous 2020 TDD patient satisfaction survey.[4] The positive survey responses echo the verbal praise for TDD we have been hearing from patients with implanted pumps over the past three decades. We rarely hear such consistently positive feedback from our patients with implantable neurostimulation systems or about any of the other pain management interventions we offer. Importantly, pain pumps in our clinic are implanted in our patients with the most complex chronic pain who have failed to respond adequately to any other treatment.

In our present study, most study subjects were treated with daily systemic opioids before IT trial and pump implant. We recommend tapering systemic opioids by ≥50% before TDD trial, but some of our patients are only able to taper slightly or not at all. We usually proceed with implant regardless, with the clear understanding that we will taper systemic opioids once pain relief is established with TDD.

The high rate of satisfaction noted with IT bolus dosing is not surprising since the ability to self-administer additional pump medication as needed provides maximal control to the patient and reduces the need for oral pain medication to treat breakthrough pain. Patients with low satisfaction tended to be on lower IMME doses than did respondents in the medium and high satisfaction groups ($p = 0.02$). Although there may be a positive relationship between higher IMME dosing and increased satisfaction and between lower IMME and lower satisfaction, this relationship did not reach statistical significance. A potential explanation for the lower satisfaction observed in the lower IMME group is that, in our clinical practice, many patients receiving lower IMME despite inadequate pain relief are maintained on low IT doses owing to unacceptable side effects from increasing their IT medication. When TDD side effects occur, our first response is often to reduce IMME and treat pain using short-term increases in systemic opioids. Therefore, patients with low satisfaction and low IMME may be those most susceptible to severe side effects from IT medications.

Regardless of IMME or satisfaction level, when less satisfied patients were asked whether they would like their pain pump turned down and removed, only 17 subjects (4%) responded yes. This coincides with PSR data showing that the rate of pump reimplant at end of battery life is >95%.[5] The comparable published surgical explant rate for neurostimulation systems is 24%,[27] with a 38% explant rate at 10 years after rechargeable battery depletion.[28]

Regarding pump size, we believe 40cc pumps improve convenience and safety by reducing the frequency of pump refills given inadvertent "pocket fill" and/or pump programming errors can lead to massive opioid overdose.[29] Buttock pocket sites also render refills more stable and safe because the pump overlies firmer tissue rather than soft abdominal viscera.[30] In addition, surgery with the patient in the prone position is much easier and reduces operating times, which may, in turn, reduce infection rates.[30,31] Buttock pump pockets also make catheter revision surgeries much easier because surgery occurs with the patient prone, and the pump and catheter are in close approximation. We therefore implant most of our patients (88.2%) with 40cc pumps into an upper buttock pocket (Fig. 8a).

Anecdotally, we hear more patient complaints about neurostimulation pulse generator pockets than about pain pump pockets, despite the larger pump device size. This may be secondary to the local anesthetic effect of intrathecal bupivacaine creating a sensory blockade of pain impulses from the pump

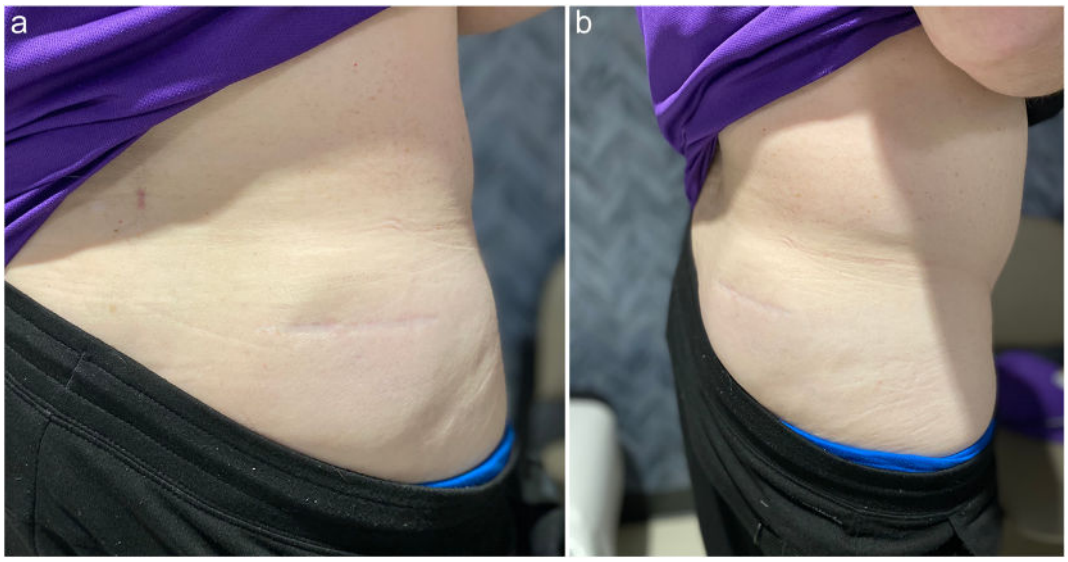

Figure 8. a. Pictured is a patient with TDD with a 40cc pump implanted into a right upper buttock pocket site. b. Profile view of the same right upper buttock pump pocket site.

pocket. Our patients receive an average of 11.9 ± 11.8 mg of IT bupivacaine per 24 hours but rarely report numbness or weakness and function normally with ambulation and driving.

Most would agree that microdosing is wonderful when it works. But what if pain is poorly controlled with low-dose IT medication? As healthcare providers, our primary directive is to reduce suffering in our patients without causing harm rather than to prescribe the least amount of medication. Our study shows minimal harm with increasing IT dosing up to reasonable limits outlined in PACC[12] guidelines until pain relief is achieved. Except for the increasingly rare occurrence of catheter tip granuloma, there is no published evidence that commonly used admixtures of IT pump medications have caused damage to the spinal cord or toxicity to the body's organs over time.[12] In our 30-year history of implanting and managing IT pain pumps, we have had no cases of organ or spinal cord injury from IT medications, even in patients with terminal cancer being treated with high-dose ketamine-containing admixtures. Our survey results provide additional evidence that TDD is safe and efficacious with manageable side effects whether IT doses are high or low.

Limitations

Limitations of our study include the lack of anonymity, self-selection bias, and survivorship bias. Perceived lack of anonymity could bias subjects toward positive responses. Self-selection bias may have affected our data because highly satisfied/highly dissatisfied patients are more likely to take a voluntary survey than are apathetic patients. Survivorship bias (a successful subgroup is considered typical of the entire group) could have contributed to bias because most patients gradually increase their IT medication dose until they achieve therapeutic efficacy. We did not use statistical methods to control for time effects. It is possible that these biases caused our data to be skewed toward high satisfaction, with 78% of our subjects in the high-satisfaction group and only 4% in the low-satisfaction group. Lastly, this is a single-center study, and results may have differed if a multicenter study had been performed, given differences in patient populations and clinical care guidelines.

CONCLUSIONS

IT drug delivery provides a safe and effective alternative to long-term pain management with systemic opioids in patients with refractory chronic pain who have failed to find relief with all other interventions. However, managing patients on IT medication requires a minimally invasive surgical procedure, regular percutaneous pump refills, and specialized clinical infrastructure and patient care. Although lower-dose IT medications are preferable if pain relief is adequate, we found higher-dose IT medication admixtures to be associated with improved satisfaction and better pain relief, without evidence of increased side effects, mental impairment, or therapy complications.

Authorship Statements

David M. Schultz designed the study and survey questions, prepared the manuscript draft, and conducted patient recruitment, literary research, and continued review/editing of the manuscript draft. Data collection, data analysis, graph development, and manuscript writing/editing were conducted by Collin S. Larmour. Hannah L. Ruble and Caitlin H. Bakke performed data collection and entry, literary research, manuscript writing/editing, and graph development. Alaa Abd-Elsayed assisted with data analysis, manuscript editing and responding to reviewers. Jonathan M. Hagedorn assisted with manuscript editing and responding to reviewers. David M. Schultz, Alaa Abd-Elsayed, Collin S. Larmour, Caitlin H. Bakke, and Hannah L. Ruble all reviewed and approved the submitted version of the manuscript.

Conflict of Interest

David M. Schultz has received consulting fees from Medtronic and Abbott, unrelated to this manuscript. Alaa Abd-Elsayed has received consulting fees from Medtronic, Avanos, Curonix, and Averitas. The remaining authors report no conflict of interest.

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SUPPLEMENTARY DATA

To access the supplementary material accompanying this article, visit the online version of *Neuromodulation: Technology at the Neural Interface* at www.neuromodulationjournal.org and at https://doi.org/10.1016/j.neurom.2024.11.006.

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COMMENT

More clinical studies support the use of off-label and compounded medications in intrathecal drug delivery for chronic pain. As much as we need more robust clinical controlled studies, this study is helpful in further increasing our clinical experience and knowledge in intrathecal drug delivery systems. I would combine study outcomes with the current polyanalgesics consensus panel and other references on intrathecal drug delivery for chronic pain (Kim PS, Staats PS, Deer TR, Iadarola MJ, Mannes AJ. Intrathecal drug delivery for cancer pain. In: *Nervous System Drug Delivery: Principles and Practice*. Academic Press; 2019:501–520; Deer TR, Pope JE, Hayek SM, et al. The Polyanalgesic Consensus Conference (PACC): recommendations on intrathecal drug infusion systems best practices and guidelines. Neuromodulation. 2017;20:96–132. https://doi.org/10.1111/ner.12538).

Philip Kim, MD
Bryn Mawr, PA, USA