Neurologic Complications After Neuraxial Anesthesia or Analgesia in Patients with Preexisting Peripheral Sensorimotor Neuropathy or Diabetic Polyneuropathy

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BACKGROUND: The risk of severe neurologic injury after neuraxial blockade is extremely rare among the general population. However, patients with preexisting neural compromise may be at increased risk of further neurologic sequelae after neuraxial anesthesia or analgesia.

METHODS: We retrospectively investigated 567 patients with a preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy who subsequently underwent neuraxial anesthesia or analgesia. Patient demographics, neurologic history, the indication and type of neuraxial blockade, complications, and block outcome were collected for each patient.

RESULTS: The majority of patients had chronically stable neurologic signs or symptoms at the time of block placement, with very few reporting progression of their symptoms within the last 6 mo. The type of neuraxial technique included spinal anesthesia in 325 (57%) patients, epidural anesthesia or analgesia in 214 (38%) patients, continuous spinal anesthesia in 24 (4%) patients, and a combined spinal-epidural technique in four (1%) patients. Overall, two (0.4%; 95% CI 0.1%–1.3%) patients experienced new or progressive postoperative neurologic deficits, in the setting of an uneventful neuraxial technique. In these patients, the neuraxial block may have contributed to the injury secondary to direct trauma or local anesthetic neurotoxicity around an already vulnerable nerve. Sixty-five (11.5%) technical complications occurred in 63 patients. The most common complication was unintentional elicitation of a paresthesia (7.6%), followed by traumatic (evidence of blood) needle placement (1.6%) and unplanned dural puncture (0.9%). There were no infectious or hematologic complications.

CONCLUSIONS: The risk of severe postoperative neurologic dysfunction in patients with peripheral sensorimotor neuropathy or diabetic polyneuropathy undergoing neuraxial anesthesia or analgesia was found to be 0.4% (95% CI 0.1%–1.3%). Clinicians should be aware of this potentially high-risk subgroup of patients when developing and implementing a regional anesthetic care plan.

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Peripheral sensorimotor neuropathies may occur secondary to a variety of underlying etiologies, including metabolic, autoimmune, infectious, or hereditary abnormalities. Of these etiologies, diabetes mellitus is the most common cause of systemic polyneuropathy. The frequency of diabetic polyneuropathy ranges from 4% to 8% at the time of initial presentation, to approximately 50% in patients with chronic disease. Ultimately, all asymptomatic patients will likely be found to have abnormalities of nerve conduction (1,2). Patients with underlying, chronic neural compromise secondary to ischemic (peripheral vascular disease or microangiopathy), toxic (chemotherapy), or metabolic (diabetes mellitus) abnormalities may be at an increased risk of further neurologic injury because of a physiologic "double-crush."

The double-crush phenomenon suggests that patients with preexisting neural compromise may be more susceptible to injury when exposed to a secondary insult at another site (3) (Fig. 1). Secondary insults may include a variety of mechanical (needle- or catheter-induced trauma), ischemic (epinephrine-induced vasoconstriction), or toxic (local anesthetic neurotoxicity) risk factors often associated with regional anesthetic techniques. Osterman (4) emphasized that not only are two low-grade insults along a peripheral nerve worse than an injury at a single site, but that the damage of dual-injury exceeds the expected additive damage caused by each isolated insult. Furthermore, the secondary insult may occur at *any* point along the neural transmission pathway. As a result, the performance

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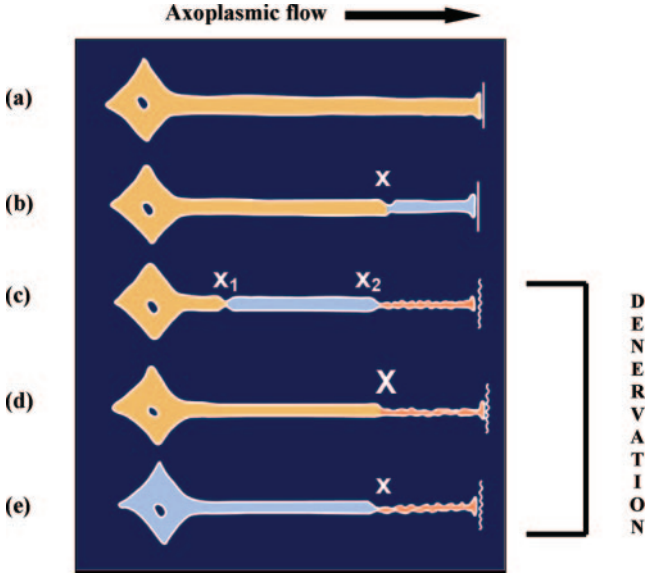


Figure 1. The "Double-Crush" Phenomenon. Axoplasmic flow is indicated by the degree of shading. Complete loss of axoplasmic flow results in denervation (c,d,e). (a) Normal neuron. (b) Mild neuronal injury at a single site (x) is insufficient to cause denervation distal to the insult. (c) Mild neuronal injury at two separate sites (x_1 and x_2) may cause distal denervation (i.e. "Double Crush"). (d) Severe neuronal injury at a single site (X) may also cause distal denervation. (e) Axon with a diffuse, preexisting underlying disease process (toxic, metabolic, ischemic) may have impaired axonal flow throughout the neuron which may or may not be symptomatic; but predisposes the axon to distal denervation following a single minor neural insult at x (i.e., "Double Crush").

of neuraxial techniques in patients with preexisting peripheral sensorimotor neuropathies may theoretically increase their risk of a double-crush injury. The aim of this investigation was to examine the frequency of new or progressive neurologic complications in patients with preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy who subsequently underwent neuraxial anesthesia or analgesia.

METHODS

After IRB approval and informed written consent, the medical records of all patients at the Mayo Clinic from the period 1988–2000 with a history of peripheral sensorimotor neuropathy or diabetic polyneuropathy who underwent a subsequent spinal or epidural anesthetic were retrospectively reviewed. Neurologic diagnoses were limited to those of the peripheral nervous system, and did not include patients with a diagnosis of central nervous system (CNS) pathology. All patients underwent electrodiagnostic testing and/or had confirmation of their neurologic diagnosis by a neurologist or neurosurgeon before study inclusion.

Demographic data (age, gender, height, and weight), the date of each neurologic diagnosis, and the character of neurologic symptoms (motor deficits, sensory deficits, paresthesias or dysesthesias, and hyperreflexia) at the time of spinal or epidural anesthesia were collected for each patient. Neurologic symptoms at the time of their procedure were further classified as: 1) acute (exacerbation of symptoms within the last 30 days); 2) subacute (exacerbation of symptoms within the last 1–6 mo); or 3) chronic/stable (no change in symptoms within the last 6 mo).

Indications for neuraxial anesthesia or analgesia (surgical anesthesia, labor analgesia, or postoperative analgesia only), surgical procedure (orthopedic, urologic, general/abdominal, cesarean delivery) and neuraxial technique (single-injection spinal, continuous spinal, epidural, combined spinal/epidural) were recorded. Details of each neuraxial technique, including awake placement (yes or no), approach (midline, paramedian, both), number of attempts, and local anesthetic(s) used were collected. The use of epinephrine or other local anesthetic additives was also documented. Technical complications occurring at the time of block placement, such as difficulty identifying the epidural space, difficulty advancing an epidural or subarachnoid catheter, traumatic block placement (evidence of blood), unplanned dural puncture, difficulty obtaining cerebral spinal fluid, paresthesia elicitation, or unintended "total" or "high" spinal were all identified. Block efficacy was categorized as: 1) satisfactory (surgery performed without additional intervention); 2) unilateral anesthesia or analgesia; 3) segmental or incomplete anesthesia or analgesia; or 4) no block/block failure.

New or progressive postoperative neurologic deficits (motor or sensory deficits, painful paresthesias, or bowel or bladder dysfunction) were identified in the daily progress notes of the primary surgical service and/or the Anesthesia Pain Service. Complications were also noted during the patient's 2, 4, or 6 wk surgical follow-up visit. The presence of infectious (neuraxial abscess) or hematologic (neuraxial hematoma) complications was also documented. All complications were followed until complete resolution, or until the last documented date of evaluation.

RESULTS

Five hundred sixty-seven ($n = 567$) patients were identified as having a preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy, and subsequently undergoing neuraxial anesthesia or analgesia. All patients had a single neurologic diagnosis, with no evidence of coexisting spinal canal or CNS pathology (Table 1). Patient demographics included a mean patient age of 68 ± 14 yr, height of 171 ± 10 cm, and weight of 83 ± 18 kg. Gender distribution was 385 (68%) males and 182 (32%) females. At the time of surgical anesthesia, an established neurologic diagnosis had been present at a mean of 4 ± 5 yr (range: 0–42 yr). Sensory deficits and painful paresthesias or dysesthesias were the most common neurologic findings, followed by motor deficits and hyperreflexia (Table 1). Nearly all patients had chronically stable neurologic signs or

Table 1. Neurologic History of 567 Patients with Peripheral Sensorimotor Neuropathy or Diabetic Polyneuropathy

Neurologic feature(s)	No. of patients	%
Neurologic diagnosis		
Peripheral sensorimotor neuropathy	293	52
Diabetic polyneuropathy	274	48
Neurologic history[a]		
Motor deficits	230	42
Sensory deficits	481	87
Pain/dysesthesias	412	74
Hyperreflexia	37	7
Disease state at time of block placement		
Acute exacerbation (<30 days)	25	4
Subacute exacerbation (1–6 mo)	39	7
Chronic/stable (>6 mo)	503	89

[a] Neurologic history data were missing for 15 patients. Percentages are based upon those patients with available data.

symptoms (motor or sensory deficits, dysesthesias, paresthesias, or hyperreflexia) at the time of block placement, with very few reporting progression of their symptoms within the last 6 mo (Table 1).

The type of neuraxial blockade, indications for block placement, and timing of local anesthetic use are described in Table 2. The majority of patients ($n = 440$; 82%) had successful placement of their neuraxial technique at a single interspace with a single needle pass. Overall, there were 65 (11.5%) technical complications in 63 patients. The most common complication was the unintentional elicitation of a paresthesia, followed by traumatic (evidence of blood) needle placement and unplanned dural puncture (Table 2). There were no documented cases of infectious (neuraxial abscess) or hematologic (neuraxial hematoma) complications.

Two (0.4%; 95% CI 0.1%–1.3%) patients experienced new or progressive postoperative neurologic deficits when compared with preoperative findings. Complication rates were similar after both spinal (0.3%; 95% CI 0.01%–1.6%) and epidural (0.5%; 95% CI 0.01%–2.6%) anesthesia. The first patient with a complication was a 77-year-old female who underwent a cemented bipolar endoprosthesis placement for a left femoral neck fracture. She had a 12-yr history of Type II diabetes mellitus, with bilateral peripheral neuropathy manifested as distal upper and lower extremity numbness. She was also diagnosed with diabetic autonomic neuropathy 3 yr before her femoral neck fracture. The spinal anesthetic (bupivacaine 0.75%, 15 mg and 1:200,000 epinephrine) was uneventful and required two needle redirections without an elicited paresthesia. Postoperatively, the patient experienced persistent urinary retention which improved, but was still present after 5 yr. She also complained of left lower extremity pain throughout her hospitalization. After a comprehensive evaluation by internal medicine, urology, and orthopedics, the complication was suspected to be an exacerbation of her diabetic peripheral neuropathy, with the role of the spinal being unclear.

Table 2. Block Characteristics in 567 Patients with Peripheral Sensorimotor Neuropathy or Diabetic Polyneuropathy Undergoing Neuraxial Anesthesia or Analgesia

Block characteristic	No. of patients	%
Neuraxial blockade		
Spinal	325	57
Continuous spinal	24	4
Epidural	214	38
Combined spinal-epidural	4	1
Indication		
Labor analgesia	8	1
Postoperative analgesia only	52	9
Surgical	507	90
Orthopedic	320	56
Urologic	104	18
Intraabdominal	46	8
Cesarean delivery	4	1
Other	33	6
No. of attempts required[a]		
One	440	82
Two	80	15
Three or more	16	3
Unknown	31	—
Local anesthetic use[b]		
Intraoperative	519	92
Postoperative	55	10
Epinephrine use	224	40
Technical complications	65	11.5
Unable to reach epidural space	1	0.2
Failure to advance catheter	3	0.5
Unplanned dural puncture	5	0.9
Failure to obtain CSF	3	0.5
Unintended "high" spinal	1	0.2
Traumatic (blood)	9	1.6
Paresthesia	43	7.6
Block efficacy		
Satisfactory	558	98.4
Unilateral	0	0.0
Patchy or segmental	2	0.4
No block (block failure)	7	1.2
Neurologic complications	2	0.4

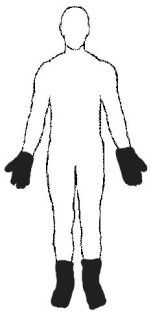
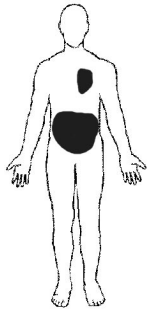
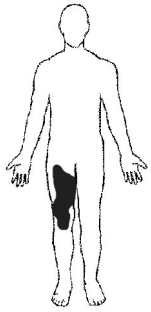
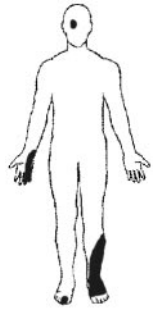
CSF = cerebral spinal fluid.

[a] The number of attempts required was not available for 31 patients. Percentages are based upon those patients with available data.

[b] Seven patients received both intra- and postoperative local anesthetics.

The second patient was a 70-year-old male who underwent an aorto-bifemoral bypass and bilateral lumbar sympathectomy for severe peripheral vascular disease under a combined epidural and general anesthetic. The patient had a 12-yr history of Type II diabetes mellitus with bilateral lower extremity numbness (electromyography studies confirmed a generalized sensorimotor neuropathy), and a 4-yr history of diabetic autonomic neuropathy. The epidural was placed preoperatively (bupivacaine 0.5%; total 31 mL intraoperatively) combined with an uneventful general anesthetic. Intraoperatively, the aortic cross-clamp was placed distal to the renal arteries, with no

Table 3. Types of Neuropathies Associated with Diabetes

	Distal sensory and sensorimotor polyneuropathy	Autonomic neuropathy	Lumbar thoracic nerve root disease	Mononeuropathies
Common names	Diabetic neuropathy		Asymmetric proximal neuropathy Diabetic amyotrophy Diabetic thoracic polyradiculopathy	Cranial mononeuropathy Peripheral mononeuropathy Mononeuropathy multiple
Clinical signs and symptoms	Most common type of diabetic neuropathy Classic "stocking-glove" sensory loss Progressive loss of sensory axons	Insidious presentation Postural hypotension Gastroparesis Enteropathy Often undiagnosed Co-exists with other types of neuropathies	Unilateral pain in leg or abdomen Injury to nerve roots and axon degeneration Weakness and atrophy in one or more nerve root Minimal sensory loss More common in elderly patients Coexisting peripheral neuropathy common Occurs in patients with long history of diabetes	Dysfunction of single nerve root Either insidious or acute onset Often painful Frequencly cranial nerve III, median nerve or peroneal nerve No relationship to duration of diabetes
Pathology	Multifactorial	Multifactorial	Inflammatory component Vasculitis and ischemia?	Inflammatory component Vasculitis and ischemia?
Diagram				

prolonged periods of intraoperative hypotension. Approximately 6 h postoperatively, the patient was found to have left lower extremity sensory loss and flaccid paralysis, and slight worsening of his right lower extremity numbness. The epidural infusion (fentanyl 5 mcg/mL, without local anesthetic) was discontinued. Imaging excluded a neuraxial hematoma, and re-exploration of the surgical site yielded no surgical etiology. The differential diagnoses by the neurology and neurosurgical services included ischemic cauda equina versus traumatic lumbar plexus lesion (during epidural placement). Electromyography performed 6 mo later revealed evidence of residual severe chronic left lumbar plexopathy superimposed on a generalized sensorimotor peripheral neuropathy. The patient was diagnosed with a lumbar plexopathy of unclear etiology, and although he had a 50% resolution of symptoms at 1 yr, he continued to have a persistent left peroneal neuropathy 10 yr later.

DISCUSSION

The severe, persistent, neurologic complications described in this study are extremely rare complications of neuraxial blockade (5,6). Moen et al. (5) reported 127 (0.008%) severe neurologic injuries after 1,510,000 neuraxial blocks. Permanent neurologic damage was observed in 85 (67%) patients. Similarly, Auroy et al. (6) reported 12 (0.03%) serious neurologic complications after 35,439 spinals and 5561 epidural anesthetics. All but three patients recovered fully within 3 wk. However, it has been suggested that when compared with the general population, patients with preexisting neural compromise, including peripheral sensorimotor neuropathy and diabetic polyneuropathy, may be at an increased risk of perioperative nerve damage after regional blockade (7–10).

The pathophysiology of diabetic polyneuropathy is multifactorial and not completely understood. Any disruption in the supply of essential components (blood, oxygen, adenosine triphosphate, glucose) to the axon can cause distal axonal degeneration. Proposed mechanisms include sorbitol deposition within the nerve secondary to glucose accumulation, local tissue ischemia in sensory and autonomic nerve fibers as a result of endoneurial hypoxia, abnormal tissue repair mechanisms caused by excess glucose, and mitochondrial dysfunction in the dorsal root ganglia (11,12). Pathologically, there is evidence of a variety of abnormalities in both large and small nerve blood vessels, subsequently leading to multifocal fiber loss.

These microvascular changes, associated neurologic abnormalities, and evidence of nerve fiber injury suggest that ischemia may be a likely pathophysiologic mechanism (12).

There are several types of neuropathies associated with diabetes, each classified into a distinct clinical syndrome (Table 3). Distal symmetric sensorimotor polyneuropathy is the most common syndrome, and is often considered synonymous with the term diabetic neuropathy. Diabetes mellitus may also injure the nerve roots at one or more high lumbar or thoracic levels. Affected patients are typically older, have coexisting peripheral polyneuropathy, and may have weakness and atrophy in the distribution of one or more contiguous nerve roots. It is common for elderly, diabetic patients to present with more than one distinct clinical syndrome. Importantly, although loss of axons is most prevalent in the peripheral nerve trunks, there may be concomitant, undiagnosed involvement of the spinal cord (13,14). Whether this spinal cord involvement is a primary or secondary event is unclear. It has been speculated that damage to peripheral nerves may cause the spinal cord to shrink and subsequently die back; alternatively, the initial damage may be at the level of the CNS, with the peripheral nerves being affected secondarily (13).

The two patients experiencing severe postoperative neurologic complications in this review were both elderly patients with significant preoperative neurologic symptoms. Given the extent of their symptoms and the concomitant autonomic neuropathy, it is likely that these patients may have had both distal symmetric sensorimotor polyneuropathy, as well as undiagnosed (subclinical) proximal neuropathy. This may have increased their risk of a double-crush injury after exposure to a neuraxial technique. Although the etiology of the postoperative complications is unclear, both patients had postoperative symptoms suggestive of cauda equina syndrome. The cauda equina is poorly vascularized and therefore extremely sensitive to ischemic injury (15). Cauda equina syndrome involves the lumbosacral nerve roots and is characterized by bowel and bladder dysfunction, perineal sensory loss, and lower extremity motor weakness (16). Two large, independent reviews of complications after neuraxial blockade found a similar incidence of cauda equina syndrome after spinal and epidural anesthesia or analgesia (5,6). Although toxicity was presumed to be the cause, an undiagnosed preexisting deficit (spinal stenosis or proximal neuropathy) could not be excluded. Moen et al. (5) reported 32 cases of cauda equina syndrome and four cases of paraparesis, all of which were permanent. All of the paraparetic patients and nine of the cauda equina patients were retrospectively (one patient diagnosed preoperatively) diagnosed with spinal stenosis. It is important to note that most patients presented in these two reviews had an uneventful neuraxial block with a relatively nontoxic local anesthetic dose.

Abnormal local anesthetic diffusion and subsequent neurotoxicity may have been the contributing factors to the observed neurologic complications in our series. Toxicity differs greatly among local anesthetics; lidocaine and tetracaine may produce deficits when administered in clinically used concentrations, whereas bupivacaine is considered the least neurotoxic. Even though hyperbaric lidocaine is most often associated with neurotoxicity, all local anesthetics are potentially neurotoxic (17). Using rats injected with streptozotocin to induce diabetes, Kalichman and Calcutt (9) concluded that local anesthetic requirements are decreased in diabetic animals, and therefore the risk of local anesthetic toxicity and subsequent nerve injury is increased. The authors hypothesized that diabetic nerve fibers may be more susceptible to the toxic effects of local anesthetics for two reasons: 1) they are exposed to larger concentrations of anesthetics because of decreased bloodflow; and 2) the nerve is already "stressed" by chronic ischemic hypoxia (9). This has been supported clinically with preliminary data, which demonstrate that the percentage of successful blocks is significantly higher in the diabetic population when compared with nondiabetic patients (18). Finally, it is possible that epinephrine may have a pathogenic role in the development of neurotoxicity after regional anesthesia. Epinephrine alone, or when combined with a local anesthetic, may significantly reduce nerve blood flow (19). Alterations in neural blood flow may lead to both structural and functional changes to nerve fibers. This may have a significant impact on diabetic nerves, as they are more vulnerable to ischemia when compared to nondiabetic nerve fibers (20,21).

Importantly, the limitations of this retrospective investigation must be recognized. First, there may be a selection bias, in that neuraxial blockade was used in a relatively selected group of diabetic patients, the majority of whom were neurologically stable (89% chronically stable or nonprogressive) during the preceding 6 mo. Second, the duration of postoperative follow-up was limited to 6–8 wk. Neurologic deterioration occurring beyond this point, although unlikely, could not have been reliably identified. Finally, the logistics of performing of a retrospective investigation make it difficult to reliably capture all minor or subclinical complications. This limitation may result in a lower incidence of minor, unrecognized complications, or adverse events that may otherwise appear in prospective studies.

In summary, this retrospective study evaluated the neurologic complications after neuraxial anesthesia or analgesia in patients with preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy. Of the 567 patients studied, two (0.4%; 95% CI 0.1%–1.3%) experienced new or progressive postoperative neurologic deficits when compared with preoperative findings. Although the role of the neuraxial blockade is unclear, it was likely not the primary cause of the

postoperative neurologic deficit in either of these patients. Rather, it may have been a contributing factor in an already vulnerable nerve. Therefore, we conclude that the risk of severe postoperative neurologic injury in patients with preexisting peripheral sensorimotor neuropathy or diabetic polyneuropathy undergoing neuraxial anesthesia or analgesia is relatively uncommon. However, the risk appears to be higher than that reported for the general population (5,6). Clinicians should be aware of this potentially high-risk subgroup of patients when developing and implementing a regional anesthetic care plan.

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