# Transient Neurologic Symptoms: Etiology, Risk Factors, and Management

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Since its introduction in 1948, manufacturers report 5% hyperbaric lidocaine has been used for millions of spinal anesthetics. A predictable onset and limited duration of action have made lidocaine one of the most popular spinal anesthetics. Concern about the use of spinal lidocaine began in 1991 with published reports of cauda equina syndrome (CES) after continuous spinal anesthesia[1,2] and was heightened in 1993 when Schneider et al.[3] published a case report of 4 patients undergoing spinal anesthesia who postoperatively experienced aching and pain in the buttocks and lower extremities. This report will review the history, incidence, possible etiologies, risk factors, and treatment of transient neurologic symptoms (TNS) after lidocaine spinal anesthesia.

## History

The first prospective safety study of intrathecal lidocaine was performed by Phillips et al.[4] and published in 1968. A total of 10,440 patients (93% obstetric) undergoing spinal anesthesia with lidocaine was evaluated. The investigators concluded that lidocaine was safe for spinal anesthesia. Evaluation of this data shows that during the study period 284 patients complained of back pain after spinal anesthesia. Of these patients, 91 refused subsequent spinal anesthesia because of postspinal back pain.

After the safety study performed by Phillips, millions of patients underwent spinal anesthesia with 5% hyperbaric lidocaine without published report of apparent complications. Scrutiny of lidocaine began in 1991 with case reports documenting CES after continuous spinal anesthesia.[1,2] Of the initial reports of CES after continuous spinal anesthesia, 10 of 11 cases involved the use of lidocaine. It was postulated that the mechanics of microcatheters (which allowed pooling of local anesthetics at the lumbosacral nerve roots) in combination with supernormal doses of local anesthetics were the etiology of CES in these patients. Subsequently, at the direction of the Food and Drug Administration (FDA), spinal microcatheters were withdrawn from the United States market.

Concern over the use of single dose 5% hyperbaric lidocaine for spinal anesthesia began in 1993 when Schneider et al.[3] published a case report of 4 patients undergoing spinal anesthesia in the lithotomy position who postoperatively experienced aching and pain in the buttocks and lower extremities. Initial reports used the term transient radicular irritation (TRI) to describe this syndrome. Eventually the terminology was changed to TNS to better reflect the symptomatology and lack of definitive etiology. All of Schneider's patients recovered completely; nonetheless, subsequent editorials questioned the continued use of 5% hyperbaric lidocaine and suggested that a fresh appraisal of 5% hyperbaric lidocaine product safety by the appropriate regulatory agencies was in order.[5,6]

Since Schneider's initial case report, there have been many case reports and a few studies, both laboratory and clinical, from which we have learned a great deal about the incidence of TNS after spinal anesthesia. Prospective, randomized controlled studies[7-23] have shown a remarkable variability in the incidence of TNS among patients undergoing spinal anesthesia with lidocaine (Table 1). Clearly the incidence of TNS is highest after lidocaine spinal anesthesia versus other local anesthetics. As a result of these randomized studies, as well as an epidemiologic study by Freedman et al.,[24] we have learned that the incidence of TNS seems to vary with the type of surgery performed (Table 2). For example, patients undergoing surgery in the lithotomy position have an incidence of TNS of approximately 30% to 36%,[7,9,12] patients undergoing arthroscopic knee surgery an incidence of 18% to 22%,[8,10,15,16] and patients undergoing surgery in the supine position an incidence of 4% to 8%.[8,19]

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**Table 1. Randomized Controlled Studies Reporting TNS**

| Author & Year | Type and No. of Patients Studied | Incidence of TNS | |
|---|---|---|---|
| Hampl 95 | 44 Gyn | 5% Lidocaine | 32% |
| | | 0.5% Bupivacaine | no TNS |
| Pollock 96 | 159 Arthroscopy/hernia | 5% Lidocaine | 16% |
| | | 2% Lidocaine | 16% |
| | | 0.75% Bupivacaine | no TNS |
| Hampl 96 | 50 Gyn | 5% Lidocaine | 32% |
| | | 2% Lidocaine | 40% |
| Liguori 98 | 60 Arthroscopy | 2% Lidocaine | 22% |
| | | 1.5% Mepivacaine | no TNS |
| Martinez 98 | 200 Mixed surgical | 5% Lidocaine | 4% |
| | | 5% Prilocaine | 1% |
| Salmela 98 | 90 Mostly GU | 2.5% Lidocaine | 20% |
| | | 4% Mepivacaine | 37% |
| | | 5% Bupivacaine | no TNS |
| Hampl 98 | 90 Gyn | 2% Lidocaine | 30% |
| | | 2% Prilocaine | 3% |
| | | 0.5% Bupivacaine | no TNS |
| Pollock 99 | 109 Arthroscopy | 2% Lidocaine | 16% |
| | | 1.0% Lidocaine | 22% |
| | | 0.5% Lidocaine | 17% |
| Hiller 99 | 60 Mixed | 5% Lidocaine | 27% |
| | | Gen Anesthesia | 3% |
| Hodgson 00 | 70 Arthroscopy | 5% Lidocaine | 31% |
| | | 10% Procaine | 6% |
| Keld 00 | 70 Mixed | 5% Lidocaine | 26% |
| | | .5% Bupivacaine | 3% |
| Ostgaard 00 | 100 GU | 2% Lidocaine | 14% |
| | | 2% Prilocaine | 1% |
| DeWeert 00 | 70 Mixed/supine | 2% Lidocaine | 3% |
| | | 2% Prilocaine | no TNS |
| Salazar 01 | 80 Supine ortho | 2% Lidocaine | 2.5% |
| | | 2% Mepivacaine | 2.5% |
| Lindh 01 | 107 Inguinal hernia | 2% Lid—early | 23% |
| | | 2% Lid—late | 23% |
| Philip 01 | 58 Postpartum tubal | 5% Lidocaine | 3% |
| | | .75% Bupivacaine | 7% |
| Aouad 01 | 200 C/Section | 5% Lidocaine | no TNS |
| | | .75% Bupivacaine | no TNS |

Abbreviations: Gyn, gynecologic; GU, genitourinary.

This observation makes it easier to explain the great variation reported in studies evaluating the incidence of TNS.

## Etiology

Possible causes of TNS include a specific local anesthetic toxicity,[5,6] needle trauma, neural ischemia secondary to sciatic stretching,[3] patient positioning, pooling of local anesthetics secondary to small gauge pencil-point needles,[25] muscle spasm, myofascial trigger points,[26] early mobilization, or irritation of the dorsal root ganglion.[27] Because few patients receiving intrathecal bupivacaine report TNS, it appears that TNS is not the result of having a subarachnoid block *per se*. Hence, epiphenomena of subarachnoid block (spinal needle placement, positioning for block placement surgery) are not the etiologic factors of TNS.[28]

Several investigators have assumed that TNS is a symptom of direct neurotoxicity. It is undeniable that local anesthetics exert significant neurotoxicity in the laboratory setting, and indeed lidocaine, tetracaine, and prilocaine appear more neurotoxic in animal models than bupivacaine and chloroprocaine.[29] Concentrations of lidocaine within the clinical useful range (1% to 5%) have been shown to inhibit nerve conduction in isolated frog sciatic nerve models.[30,31] However, one argument against local anesthetic toxicity as the etiology of TNS is that the factors that increase the incidence of TNS are not the same as the factors that increase the incidence of CES (known to result from local anesthetic toxicity). For example, the incidence of CES is increased by higher doses and concentrations of local anesthetics and by the addition of vasoconstrictors. None of these factors appear to increase the incidence of TNS. A recent study attempted to determine if TNS was the result of direct neurotoxicity of lidocaine, by evaluating a small number of volunteers with electromyography (EMG), nerve conduction studies, and somatosensory evoked potentials (SSEP) both before and during episodes of

**Table 2.** Incidence of TNS With Spinal Lidocaine by Type of Surgery

| Author & Year | Type and Number of Surgical Patients Studied | Incidence of TNS with Spinal Lidocaine |
|---|---|---|
| Hampl 95 | 44 Gyn | 32% |
| Hampl 96 | 50 Gyn | 36% |
| Hampl 98 | 90 Gyn | 30% |
| Pollock 96 | 100 Arthroscopy | 22% |
| Liquori 98 | 60 Arthroscopy | 22% |
| Pollock 98 | 109 Arthroscopy | 18% |
| Hodgson 00 | 70 Arthroscopy | 31% |
| Pollock 96 | 59 Hernia | 8% (single procedure, all supine) |
| Martinez 98 | 200 Mixed | 4% (various procedures and positions) |
| Salmela 98 | 90 Mostly GU | 20% (various procedures, most in lithotomy, some supine) |
| Hiller 99 | 60 Mixed | 27% (variety of procedures & positions) |
| Keld 00 | 70 Mixed | 26% (both supine & arthroscopy positions) |
| Ostgaard 00 | 100 GU | 14% (positions unknown) |
| DeWeert 00 | 70 Mixed supine | 20% (mostly supine, various procedures) |
| Salazar 01 | 80 Supine ortho | 2.5% (various procedures including arthroscopy, most supine) |

TNS. These volunteers had no changes in electrophysiologic testing even in areas susceptible to the effects of local anesthetic toxicity, such as the posterior nerve roots.[32]

The etiology of TNS remains the subject of ongoing laboratory and clinical research. It does appear that TNS is a syndrome associated predominately with the use of lidocaine spinal anesthesia, that decreasing the concentration from 5% to 0.5% does not decrease the incidence of TNS,[15] and that hyperosmolarity,[7] hyperbaricity, or the addition of glucose are not contributing factors. How surgical position may contribute to the development of TNS remains undetermined, but potential etiologies include musculoskeletal strain and sciatic stretching.

## Risk Factors

Clinical studies to date have attempted to determine which patients may be at risk for the development of TNS. Lidocaine spinal anesthesia, the lithotomy position, and ambulatory surgical status[24] have all been determined to be important predictors of the development of TNS. Additional factors that may contribute to the development of TNS are arthroscopic knee surgery and obesity. It has yet to be determined conclusively if ambulatory surgery status contributes to the development of TNS. In the epidemiologic study by Freedman,[24] outpatient status was shown to be a significant risk factor for the development of TNS. A recent study[21] randomized inguinal hernia patients to early (immediate) or late (12 hours) ambulation after 100 mg, 2% hyperbaric lidocaine spinal anesthesia. These investigators reported no difference in the incidence of TNS (23%) between the groups.

One group of patients recently evaluated for the presence of TNS are obstetric patients. Despite the concern that pregnant patients may be at increased risk for neurologic deficits or pain after spinal anesthesia, randomized controlled trials have shown a low incidence of TNS in women undergoing cesarean delivery (0% to 8%)[23] or postpartum tubal ligation (3%).[22] The incidence in these patients seems consistent with other studies of nonpregnant patients undergoing surgery in the supine position.

## Treatment

Several randomized studies have included descriptions of the characteristics of TNS reported by patients experiencing the syndrome. The majority of patients experience bilateral symptoms in the anterior or posterior aspects of their thighs, which they describe variously as burning, aching, crampy, or radiating. Approximately one half of the patients report that the pain radiates down into their lower extremities and 50% to 100% report symptoms of lower back pain. When asked to rate their pain on a scale of 1 to 10, the average number is 6.2 (range, 1 to 9).[8,15] Most patients report an onset within 12 to 24 hours after surgery and a duration between 6 hours and 4 days. The onset of this syndrome is markedly different from that of back pain after chloroprocaine epidural anesthesia, which occurs immediately upon resolution of the epidural block and is confined to the lower back without a radicular component. No reported patients with TNS have had abnormal neurologic exams or motor weakness. Thus, if a patient presents with an abnormal neurologic exam or motor weakness, other possible etiologies, such as an epidural hematoma or nerve root damage, must be eliminated (Table 3).

Despite the transient nature of this syndrome, it has proven to be very uncomfortable for patients and extremely difficult to treat effectively. Current treatment options for TNS remain limited to traditional classes of medications and some interven-

**Table 3.** Differential Diagnosis of TNS

| Syndrome | Onset-Duration | Symptoms | Treatment |
|---|---|---|---|
| TNS | 6-36 hr after spinal or epidural anesthesia/1-7 days | Unilateral or bilateral pain in the anterior or posterior thighs ± extension into legs, ± back pain | NSAIDs |
| | | | Opioids |
| | | No motor weakness | Warm heat |
| | | No neuroabnormalities | Trigger point injections |
| Chloroprocaine back pain | Immediate onset after epidural regression/1-4 hr | Low back pain following chloroprocaine epidural in doses greater than 30 cc | Epidural fentanyl |
| | | | NSAIDs |
| | | | Opioids |
| Epidural hematoma | 0-2 days | Muscle weakness, radicular back pain, sensory deficit | MRI, neurosurgical consult, surgical decompressive laminectomy |
| Epidural abscess | 2-7 days | Backache, progressive neurologic symptoms, ± fever | Antibiotics, possible surgical drainage |
| Spinal nerve injury | 0-2 days/1-12 weeks | Pain during insertion of needle or catheter, pain on injection, paresthesia, pain and numbness over distribution of nerve root | May need EMG to assess baseline neurologic status |
| Anterior spinal artery syndrome | Immediate | Postoperative painless paraplegia | If secondary to vasospasm may respond to vasodilating drugs and hypertensive therapy |
| Adhesive arachnoiditis | 0 months | Pain on injection, variable degree of neurologic deficit, often progressive with pain and paraplegia | Diagnosis by CT, MRI or myelography. No effective treatment |
| Cauda equina syndrome | 0 days | Loss of bowel and bladder function, paraplegia, motor weakness, sensory loss | No effective treatment |

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

tional therapy. Unfortunately, most reports of effective therapy are predominantly anecdotal. Current therapeutic options include opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, and symptomatic therapy (Table 4).

One of the most successful classes of drugs for treating TNS has been the NSAIDs. Patients generally report good pain relief with these drugs. Ibuprofen, naproxen, and ketorolac have all been used successfully. If significant muscle spasm is an accompanying component of TNS, patients may experience therapeutic benefit from the addition of muscle relaxants, such as cyclobenzaprine. Symptomatic therapy, including leg elevation on pillows and heating pads, may provide an additional measure of patient comfort.

In addition to systemic medications, there have been case reports describing the use of trigger point injections to treat TNS after lidocaine spinal anesthesia.[26] In the first case report to describe this therapy, the patients were treated 2 weeks after their spinal anesthetic. It is very difficult to determine if the symptoms that these patients were experiencing 2 weeks postoperatively were TNS or more classic muscle spasm that may have been initiated by TNS. Nonetheless, trigger point injection is a relatively easy therapy to administer with few risks; thus it is a good option for patients who are uncomfortable enough that they will like to return to the hospital or outpatient clinic for treatment.

Because current treatment options for TNS are not always successful, prevention of the syndrome is important. Total abandonment of the use of spi-

**Table 4. Treatment Options for TNS**

| Drug | Mechanism of Action | Efficacy for TNS |
|---|---|---|
| Opioids | Bind with opioid receptors at many sites in the CNS, increases pain threshold, alters pain perception, inhibits ascending pain pathways | Moderate |
| NSAID | Inhibits prostaglandin synthesis by decreasing the activity of the enzyme cyclo-oxygenase which results in decreased formation of prostaglandin precursors | Best currently available |
| Muscle relaxants | Reduces tonic somatic motor activity influencing both alpha and gamma motor neurons | Effective if muscle spasm is present |
| Symptomatic therapy (warm heat, positioning) | May relax muscle spasm and decrease muscular strain | Moderate relief |
| Trigger point injections | Provides analgesia, relaxes the muscles and increases blood flow to the area | Very experimental but low risk, effective if muscle spasm is present |

Abbreviation: CNS, Central nervous system.

nal lidocaine is probably not warranted; however, careful patient selection is crucial. For example, the primary risk factors for the development of TNS are lidocaine spinal anesthesia in ambulatory patients undergoing lithotomy or knee arthroscopy.[24] Thus avoidance of lidocaine spinal anesthesia in these patients is justified. However, the incidence of TNS after lidocaine spinal anesthesia in a patient undergoing inguinal hernia repair is between 4% to 8%,[8] perhaps an acceptable risk, because few other effective short-acting spinal agents are available. Unfortunately, dilution of lidocaine does not appear to decrease the incidence of TNS. Several studies have shown that dilution of lidocaine from 5% to concentrations as low as 0.5% will not consistently decrease the incidence of TNS.[15] The selection of alternative spinal anesthetics for high-risk patients is not an easy one. No ideal alternative exists. Procaine, mepivacaine, bupivacaine, and prilocaine have all been evaluated.

Procaine may have an incidence of TNS that is less than lidocaine, but with the trade-offs of less reliable anesthesia, increased nausea, and pruritus when combined with fentanyl.[16] Mepivacaine has been used routinely in Europe for spinal anesthesia as a 4% hyperbaric concentration. The true incidence of TNS with mepivacaine is controversial. Liguori et al.[10] reported no TNS with the 1.5% solution in patients receiving spinal anesthesia for arthroscopy, while Salmela et al.[13] reported a 37% incidence with the 4% solution in patients undergoing urologic surgery. Bupivacaine is associated with virtually no incidence of TNS, but even in very low doses may lead to longer discharge times than lidocaine. Prilocaine, perhaps the best alternative, is not available for spinal anesthesia in the United States market.[12] Potentially, the ideal alternative will be very low doses of spinal local anesthetics combined with opioids. Further studies are needed to fully evaluate the clinical utility of these combinations.

When a patient complains of symptoms after central neuraxial block, other more serious causes of leg and back pain must be eliminated (Table 3). Once other possible etiologies (hematoma, abscess, CES) have been eliminated, treatment may begin. The best initial treatment is NSAIDs, with warm compresses and comfortable positioning. If patients do not respond to these therapies, treatment with oral opioids, muscle relaxants, physical therapy, or transcutaneous electrical nerve stimulation (TENS) may be added. For the patient willing to return to the hospital because of intense discomfort, trigger point injections may be performed. After other potential etiologies have been eliminated, reassure the patient that these symptoms, although uncomfortable, are transient in nature and typically will resolve within 1 to 4 days.

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