

NEUROLOGICAL COMPLICATIONS ASSOCIATED WITH NEURAXIAL BLOCK : WHAT ARE THE CAUSES?

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Introduction

Complications of neuraxial block include technical failure; pruritis, nausea, and urinary retention; post dural puncture headache; hypotension, bradycardia and cardiac arrest; and neurological deficit. Of these complications, neurological sequelae can be most difficult to predict and treat. When permanent, they can be devastating for the patient. Fortunately, serious neurological complications following neuraxial block are rare. However, neurological deficit can also occur in other medical fields following similar procedures such as lumbar puncture and the injection of drugs or contrast media into the spinal canal.

The anaesthetic causes of neurological deficit can be summarized under four main headings: Direct trauma following needle insertion or injection, neurotoxicity of injected drugs, spinal haematoma formation and infection. Recently a number of important issues regarding these causes have appeared in the medical literature. In this article we review the more important issues raised by these recent reports.

Historical background

Spinal anaesthesia was first described by Corning in 1885,¹ and first performed in man using cocaine by Bier in 1898.² However, the technique was abandoned due to the unpleasant side effects. A number of less toxic local anaesthetic agents were subsequently developed, the most significant being procaine in 1904. However, it was not until Labat popularized the technique in 1923 in his book "Regional Anesthesia" that spinal anaesthesia became widely used.³ Spinal anaesthesia remained popular up until the 1940s because it provided high quality operating conditions. However, the discovery of new general anaesthetic agents, such as curare, turned the balance once again in favour of general anaesthesia. In the 1950's spinal anaesthesia was almost totally abandoned in Europe following a number of high profile court cases, the most notable being the Woolley

and Roe case.⁴ It was not until the late 1970's that spinal anaesthesia was reintroduced into clinical practice.

Labat's work published in 1923 included a number of side effects of spinal anaesthesia, including headache, cranial nerve palsy, retention of urine and anal incontinence. However, he did not report any cases of permanent nerve injury, such as foot drop or paralysis.³ It was not until a decade later that reports of more serious neurological sequelae began to appear. In 1936 seven New York patients were described with complication such as aseptic meningitis, poliomyelitis, lumbar radiculitis, cauda equine syndrome and transverse myelitis⁵ and in 1937 thirteen cases with cauda equina syndrome associated with the intrathecal use of duracaine and stovaine were reported.⁶ In 1945 three further cases of arachnoiditis were reported with the intrathecal use of procaine.⁷ The association of significant neurological injury with spinal anaesthesia was now established.

Despite these reports, the safety record of spinal anaesthesia was good considering the lack of intravenous fluid loading, the re-use of non-autoclaved needles, that surgeons often performed their own spinals and its use for upper abdominal surgery, or even thoracoplasty, thyroidectomy and craniotomy.

The most famous and influential cases of neurology injury following spinal anaesthesia was the Woolley and Roe case, which occurred at Chesterfield, England, in 1947. Two healthy middle-aged men, aged 56 and 45-years, both became paraplegic following spinal anaesthesia for relatively minor surgeries. The spinal anaesthetic was given by the same anaesthetist, using the same local anaesthetic (cinchocaine) on the same day.⁴ There was also a third unreported case in a patient with intestinal obstruction who died soon after surgery. At the court case 6-years later the judge accepted the suggestion that phenol, in which the ampoules of local anaesthetic had been kept, had contaminated the ampoules via a crack. However, subsequent explanation by the anaesthetist involved has suggested that acid descaling liquid used to clean the sterilizing pan for the needles and syringes had not been replaced that morning and may have contaminated the intrathecal injectate.⁸

The Woolley and Roe case had a major impact on anaesthetic practice throughout Britain, where spinal

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anesthesia was abandoned for over 20 years and was not reintroduced into clinical practice until the late 1970's. Woolley and Roe also proved to be a landmark medical negligence case. Presided over by one of most famous British Judges of recent times, Lord Justice Denning, his ruling on this case was to set a legal precedence for all medical claims cases that followed.

Incidence

The true incidence of neurological complications arising from neuraxial block is difficult to define. In a retrospective review of 11,574 spinal blocks administered between 1948 and 1960 there were no serious nerve injuries related directly to performing spinal block reported.⁹ The majority of neurological injuries acquired intra-operatively are either related to the surgical operation, patient positioning, pre-existing disease or others causes like tourniquets. Of recent US legal claims for intra-operative nerve injury, 61% occur during general anaesthesia and were mainly ulnar nerve and brachial plexus injuries secondary to positioning.¹⁰

In a more recent survey of 71,053 regional anaesthetic procedures performed in France, 24 neurological injuries followed spinal block, an incidence of 6 in 10,000 and 6 following epidural block, an incidence of 2 in 10,000.¹¹ These injuries included 6 cases of paraplegia and 1 case of cauda equine syndrome. In a survey of insurance claims from Finland taken over a 7-year period, from an estimated 720,000 procedures, 23 neurological injuries followed spinal block and 6 followed epidural block, an overall incidence of 0.4 in 10,000.¹² These two reports occurred in the mid 1990's and, when compared to previous data, suggest a significant recent increase in the incidence of severe neurological injuries in association with neuraxial block.

Direct trauma to the spinal cord:

In 2001, Reynolds reported 7 cases of unilateral sensory loss (L4-S1) with foot drop (n=6) and urinary dysfunction (n=3) in patients receiving spinal block.¹³ All but one of these cases involved obstetric patients. In all these cases a fine gauge pencil point needle was thought to have been inserted at the L2-3 level, and pain was experienced during needle insertion. Subsequent MRI scan in 6 cases showed damage to the lower spinal cord, with conus formation, indicating that the needle must have accidentally penetrated the spinal cord. In her review of these cases, Reynolds highlighted the difficulty that anaesthetists have, in accurately determining the spinal level when performing neuraxial block, even when Tuffier's line is used.¹⁴ An error of 1-2 interspaces is common. Reynolds recommended that only the L4-5 level be used for spinal block in order to minimize the risk of spinal cord

trauma. She also suggested that the increased obstetric use of epidurals, which are usually inserted at a higher lumbar level, may have resulted in a recent trend to use higher lumbar inter-spaces for spinal block. Such a change in routine practice may explain the recent perceived increase in serious neurological injuries following spinal block. Furthermore, she also recommended extreme caution when pain is reported during spinal puncture or intrathecal injection.

A number of recent cases of paraplegia have also been reported following the use of thoracic epidural block¹⁵⁻²⁰ (Table 1). A common feature in many of these cases was that the patient was anaesthetized and unconscious when the epidural was sited, so important warning signs of pending spinal injury, such as pain and paraesthesia, were unavailable. One such case from Germany resulted in so much public debated that professional guidelines regarding the use of thoracic epidurals were produced.¹⁹ Recommendations included no epidural being inserted above the L1-2 level in an anaesthetized patient and thoracic epidurals should only be inserted when their use can be fully justified. For example, the routine use of a thoracic epidural for an open cholecystectomy is difficult to be justified.

Table - 1 : Published cases where paraplegia followed thoracic epidural placement.

Author	Year	Source	Case
Oswalt	1989	ASRA News	68y woman left foot drop
Hetland	1998	Norway	3-cases, one paraplegic
Bromage	1998	Reg Anesth	Paraplegic
Mayall	1999	Anaesthesia	69y man paraplegic
Grüning	1999	Anaesthesia	Paraplegic
Kao	2004	Taiwan	81y woman paraplegic

Neurotoxicity of spinal agents:

The potential for neurotoxicity when using local anaesthetics is well recognized and was highlighted in the 1950's by the Woolley and Roe case. To evaluate the potential toxicity of local anaesthetic drugs, the early pioneers of local anaesthesia relied on self experimentation and clinical experience. Only in recent years have suitable animal models of spinal cord toxicity been available and the toxicity of the commonly used spinal anaesthetic agents fully evaluated.

With the development of safe and reliable local anaesthetic agents, such as bupivacaine and lignocaine, autoclaving and disposable equipment, spinal block in recent

times was considered a safe technique and devoid of any serious neurotoxicity. However, in the 1990's lignocaine 5% became popular as a spinal agent for day case surgery. Early clinical trials attested to its safety,²¹ but this was later disproved by reports of permanent neurological injury following spinal lignocaine 5% and the use of microcatheters.^{22,23} The use of micro-catheters to deliver intrathecal top-ups and infusions was stopped, but the use of spinal lignocaine 5% continued. Cases of transient low back pain with abnormal sensations in the buttocks and legs, or transient radicular irritation, 24 hours after injecting lignocaine intrathecally were reported.²⁴⁻²⁶ Subsequent clinical trails found a 20-25% incidence of transient radicular irritation following spinal lignocaine²⁷⁻³⁵ [(Table 2). Data collected from animal models showed that lignocaine was more neurotoxic in clinically used concentrations than the other commonly used spinal agents, such as bupivacaine or ropivacaine³⁶⁻⁴⁸ (Table 3). However, experimental data also showed that high concentrations of any local anaesthetic agent on nerves fibres could cause irreversible damage. Bupivacaine and ropivacaine are used intrathecally in sufficiently low concentrations to avoid neurotoxicity, but this is not true for lignocaine 5% and its use spinally is difficult to justify.

Table - 2: Publications that estimated the incidence of transient neurological symptoms or radicular irritation following local anaesthetic block.

Author	Year	Source	Lignocaine	Bupivacaine	Other
Pollock	1996	Anesthesiology	16%		
Salmela	1998	Acta Anesth Scand	20%	0%	37% (mepivacaine)
HAMPL	1998	Anesthesiology	32%	0%	3% (prilocaine)
Pollock	1999	Anesthesiology	16-22%		
Hodgson	2000	Reg Anesth Pain Med	31%		6% (prilocaine)
Keld	2000	Acta Anesth Scand	26%	3%	
Tong	2003	Anesthesiology	18-21%		
Silvanto	2004	Anesth Analg	16%		
Cramer	2005	Euro J Anesth	23-27%		
<i>Medians</i>			20-25%	< 1%	

Apart from local anaesthetic drugs, a number of other agents are given intrathecally either as sole agents or adjuncts to local anaesthetics. Experimental data on the neurotoxicity of many of these agents are limited. Opiates appear to be safe, but the safety of most other agents is

questionable⁴⁹ (Table 4). It is also often forgotten that the drug preparations often contain additives like sodium metabisulphate, methylparaben or sterilizing solutions and these additives can also be potentially neurotoxic. Routine autoclaving and the use of disposable equipment have reduced the risk of contamination. Many intrathecal drugs are now also provided in preservative free form.

Table - 3 : Laboratory studies showing the toxicity of different local anaesthetic agents.

Author	Year	Source	Animal	Intrathecal drug(s)	Outcome
Bainton	1994	Anesthesiol	Frog n.	Lidocaine 5%	Irreversible conduction loss
Lambert	1994	Anesthesiol	Frog sciatic n	Lidocaine, tetracaine	Irreversible conduction loss with higher concentrations.
Kanai	1998	Anesth Analg	Crayfish	Lidocaine	Irreversible conduction loss
Takenami	2000	Masui	Rat	2% tetracaine	Mild pathological changes in the posterior roots and posterior column
Hashimoto	2001	Anesthesiol	Rat	Epineprine & lidocaine	Neurotoxicity of lidocaine increased by addition of epineprine
Malinovsky	2002	Anesthesiol	Rabbit	Ropivacaine	No neurotoxicity
Kishimoto	2002	Anesthesiol	Rat	Prilocaine vs. Lidocaine	Similar toxicity
Yamashita	2003	Anesth Analg	Rabbit	Ropivacaine vs. others	Toxicity: lidocaine = tetracaine (amethocaine) > bupivacaine > ropivacaine
Takenami	2004	Reg Anesth Pain Med	Rat	Mepivacaine, prilocaine vs lidocaine	Toxicity: lidocaine > mepivacaine = prilocaine
Sakura	2005	Anesth Analg	Rat	Lidocaine vs. bupivacaine	Bupivacaine less toxic in equipotent doses than lidocaine (lignocaine)
Takenami	2005	Reg Anesth Pain Med	Rat	Bupivacaine vs. lidocaine	Bupivacaine less toxic on post roots
Muguruma	2006	Anesthesiol	Rat	Bupivacaine (Enantiomers of)	Neurotoxicity similar
Muguruma	2006	Anesth Analg	Rats	Epidural lidocaine	Epidural lidocaine cause dose-dependant neurotoxicity.

Coagulation & neuraxial block

Haematoma formation within the spinal canal can cause permanent paralysis. In the patient with normal coagulation, the incidence of spinal haematoma following neuraxial block is very low, 1 in 150-200,000,^{50,51} being similar to that of spontaneous spinal haematoma formation. However, the risk of haematoma formation and paraplegia following neuraxial block in the anti-coagulated patient, or patient with impaired clotting, is well recognized. In a review of 61 case reports in which epidural haematoma followed spinal or epidural block, 68% of patients had a coagulation disorders and 41% received heparin. Of these 61 patients, 87% subsequently suffered permanent neurological deficit.⁵²

Class	Drug	Experimental data	Intrathecal use
Opioids	Morphine, Fentanyl,	Extensive laboratory & clinical studies	Safe
α_2 agonists	Clonidine	Extensive studies	Safe
Acetylcholine	Neostigmine	Limited data	Probably safe
GABA agonists	Midazolam Baclofen	Conflicting results	Controversial Probably safe
NMDA antagonists	Ketamine Amitriptyline	Limited data Needs further investigation	Probably safe Best avoided
NSAIDs		Needs further investigation	Best avoided
Steroids		Lack of objective evidence regarding safety	Best avoided
Adjuvants	Adrenaline, Phenylephrine, Glucose	No evidence of neurotoxicity Poorly studied Used clinically, no evidence neurotoxicity	Safe Probably safe Safe
	Antioxidants Preservatives Excipients	Despite concerns regarding past preparations, most seem safe for human use.	

However, taking aspirin, or receiving subcutaneous heparin, does not put the patient at any substantially greater risk when spinal or epidural block is performed.⁵³ Neuraxial block can also be used in the patient who requires intra-operative heparinization provided accepted and well established guidelines are followed.⁵⁴ One should wait at least 1-hour after performing a spinal or placing a catheter before starting heparinization; wait 2 to 4-hours after cessation of heparinization before removing a catheter; and wait 1-hour after removal before recommencing

heparinization. One should also check 2-hourly for evidence of paralysis. The majority of patients with an epidural haematoma will present with back pain and progressive neurological deficit. Any case of suspected haematoma requires an urgent CT, or MRI, scan. Surgical decompression needs to be performed within 8-hours to prevent permanent neurological loss.

In the mid 1990's a new heparin formulation was introduced into clinical practice as a prophylaxis against venous thromboembolism called low molecular weight heparin. It differed from conventional heparin because it was more predictable and did not require regular monitoring. The introduction of low molecular weight heparin was followed by a spate of case reports in North America (n=40) of epidural haematoma following neuraxial block (incidence: 1:3000 epidurals) and resulted in a FDA public health warning (December 1997) recommending that low molecular weight heparin should be stopped at least 12 hours before performing any neuraxial block. However, the risk of epidural haematoma following neuraxial in Europe with low molecular weight heparin was much lower. This discrepancy was explained by differences in dosage. In North America up to 8000 IU/24h was given, whereas in Europe the dosage was limited to 4000 IU/24h. The risk of haematoma was also increased by the concurrent use of anti-platelet drugs, such as aspirin or other non-steroidal anti-inflammatory drugs.

Infection and neuraxial block

The incidence of spinal canal infection following neuraxial block is very low and quoted rates are 1 in 680,000 for obstetric patients and 1.2 in 100,000 for the general population.⁵⁵ Epidural abscess due to *staphylococcus* infection is the main cause and accounts for 83% of the cases. The incidence is increased if an indwelling catheter is used for more than 24-hours.⁵⁶ Post dural puncture meningitis occasionally occurs and is caused by gram negative organisms or streptococcus.

A recent case of fatal post dural puncture meningitis was reported in a young woman who received an epidural for labour.⁵⁷ The first attempt to site the epidural at the L3/4 level resulted in a dural puncture. The epidural and catheter were resited at the level above. The patient gave birth to a healthy male infant by normal vaginal delivery. However, she developed a fever soon after the delivery and required intensive care admission. A lumbar puncture performed 15-hours later confirmed the diagnosis of meningitis. The offending organism was a common mouth commensal *streptococcus viridens*. Two other similar cases involving obstetric patients of post dural puncture meningitis were reported in 2000 and 2002.^{57,58} Baer performed a thorough and extensive review of the literature identifying

similar anaesthetic, medical or radiology cases.⁵⁷ She highlighted a lack of awareness of post dural puncture meningitis amongst those treating these patients, suggesting that a greater awareness of the condition may have led to earlier definitive treatment and thus less mortality. The causative organism was *streptococcus viridens* in at least 49% of cases. The source of infection could be isolated to the physician's oral and nasal cavities in several cases and the risk of infection increased if the physician had an upper respiratory tract infection because of the increase in nasal secretions.

Anaesthetists need to be more aware of the risk of post dural puncture meningitis when performing spinal or epidural block. There are currently no well recognized aseptic guidelines for performing neuraxial block or regional anaesthesia procedures in general. Guidelines do exist in other areas of anaesthetic practice, such as central venous line insertion. The use of full antiseptic precautions, including skin preparation, caps and face masks, gloves and hand washing, seems advisable.

Conclusions

The incidence of serious neurological complications following spinal and epidural block is low and about 1-2 in 10,000. However, it may have increased in recent years. The placement of a spinal or epidural needle can injure the spinal cord. The lowest possible lumbar inter-space should be used to avoid hitting the spinal cord. The use of thoracic epidurals must be justified and the patient should be awake so he can report any "alert events" suggestive nerve injury such as paraesthesia or pain. The choice of intrathecal drug is important because of the risk of neurotoxicity. Lignocaine 5% has a high reported incidence of transient neurological symptoms and is best avoided. Bupivacaine appears free from neurotoxicity in clinically used doses. There is limited evidence to support the intrathecal use of other classes of drug, but spinal opiates appear to be safe. Patients on low molecular weight heparin are at high risk of developing epidural haematoma and paraplegia. The heparin should be stopped at least 12 hours prior to performing neuraxial block. A case of fatal post dural puncture meningitis was recently reported. The causative organism came from the anaesthetist's nasal or oral cavity. Full aseptic precautions including wearing a face mask should be used to prevent contamination of cerebrospinal fluid with *streptococcus viridens*.

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Front Inside Cover – Colour	Rs. 30,000/-
Back Inside Cover – Colour	Rs. 30,000/-
Centre Two pages – Colour	Rs. 55,000/-
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Inside Full Page – Colour	Rs. 25,000/-
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Classified Advertisements

Cost of each B/W advertisement in each issue for Professionals and Hospitals	
2 x 3 inch	Rs. 4000/-
3 x 5 inch	Rs. 8000/-
Half Page	Rs. 10000/-

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Size of Journal Page size :	26 cms x 19 cms Print Area :22 cms x 15.5 cms
Frequency	Bi-Annual
Advertisement Material	Good art work or +ve film with proof.

Payments By Demand Drafts favouring 'Editor, SAARC Journal of Anaesthesia' payable at Belgaum, Karnataka, INDIA

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