

Inadvertent intrathecal injections and best practice management

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Submitted 20 September 2016; accepted 25 September 2016; submission 9 June 2016.

Citation

Liu H, Tariq R, Liu GL, Yan H, Kaye AD. Inadvertent intrathecal injections and best practice management. *Acta Anaesthesiologica Scandinavica* 2016

doi: 10.1111/aas.12821

The intrathecal space has become an important anatomic site for medical intervention not only in anesthesia practice, but also in many other medical specialties. Undesired/inadvertent intrathecal injections (UII) are generally rare. There is tremendous variation in reported inadvertent administrations via an intrathecal route in the literature, mainly as individual cases and very small case-series reports. This review aims to identify potential sources of UII, its clinical presentations, and appropriate management. The inadvertent injectants are classified as anesthetic agents and pain medicines, chemotherapeutics, radiological contrast agents, antibiotics and corticosteroids, and miscellaneous chemical agents such as tranexamic acid. The clinical effects of UII are dependent upon inadvertent injectant(s) and dose being administered intrathecally, and can range from no adverse effect to profound neurological consequences and/or death. **Prompt cerebrospinal fluid (CSF) lavage** and cardiopulmonary support seem to be the mainstay of treatment. If serious consequences are anticipated, CSF lavage could be lifesaving. This review additionally provides some options for comprehensive management and preventing strategies.

Editorial Comment

In this topical review of inadvertent intrathecal injection, a wide selection of reported events and sequelae are presented, along with expert advice on managing complications or threatened complications, as well as some steps to try to avoid this misadventure.

Ever since Bier first injected cocaine into the intrathecal space in 1898,¹ the intrathecal space has become an important avenue for medical interventions not only in anesthetic practice, but also in many other medical specialties.² Many medications are intrathecally administered for the control of pain (local anesthetics, opioids etc.) and spasticity (such as baclofen).³ The intrathecal route is used for surgical anesthesia, post-operative analgesia, and analgesia for parturient in active labor.^{4–6} Drugs intended to be

administered intrathecally have to be delicately prepared and tested to ensure that the ingredients of the formulation (e.g. preservatives, adjuncts) would not be harmful and/or irritable to the nerve tissues.⁷ Agents with the potential to cause neurotoxicity are strictly prohibited from intrathecal use. The potentially dangerous adverse effects of intrathecal anesthesia/analgesia were first highlighted in 1947. **Two** healthy middle-aged men became **paraplegic** after spinal anesthesia for minor surgery. Their spinal

anesthesia was delivered by the same anesthesiologist using the same drug on the same day at the same hospital.⁸ The dreadful outcome was attributed to either the contamination of spinal needles or syringes during the sterilization/preparation process or **leakage of phenol** through invisible cracks in ampoule, in which the ampoules of local anesthetic had been immersed.⁸

Medication errors are not uncommon in medical practice. **Undesired/inadvertent intrathecal injection (UII)** is an important subset of medication errors. UII is **very rare** but it does occur and sporadic UII cases were reported in the literature. Abeysekera et al. studied 896 incidents related to drug errors in anesthesia practice. These errors were reported to the **Australian Incident Monitoring Study**.⁹ The **most common** type of error was during syringe and drug preparation which accounted for over half of the incidents, including 169 (18.9%) **involving syringe swaps** where the drugs correctly labeled but given in error, and 187 (20.8%) due to selection of the **wrong ampule or drug labeling errors**. **Incorrect route** of administration was the culprit in 126 (14.1%) incidents, 18 of 126 were UII incidents. The drugs most **commonly** involved were **neuromuscular blocking** agents, followed by **opioids**.⁹ Webster et al. carried out a survey in 2001 of 7794 anesthesiologists concerning frequency and nature of **drug administration errors in anesthesia practice**. Overall, **one drug administration error** was reported for **every 133 anesthetics**. The two **largest** individual categories of errors involved **incorrect doses** (20%) and **substitutions** (20%) with I.V. boluses of drug.¹⁰ Zhang et al. reported in 2013 a similar survey conducted in China ($n = 16,496$) and they found the largest categories of medication errors during anesthesia were omissions (27%), incorrect doses (23%), and substitutions (20%).¹¹ Fasting and Gisvold retrospectively reviewed anesthesia-related drug errors in a total of **55,426 procedures** over a span of 36 months in a single institution.¹² They found that **drug error** was **recorded** in 63 cases (0.11%). There were 28 **syringe swaps** and 9 **ampule swaps**. There were 8 'other wrong drug' cases and 18 cases where a wrong dose of the correct drug was given. The incidence of medication errors is probably more than previously

imagined. UII is also most likely under-reported for various reasons. This review is aimed at identifying the potential agents of UII, their clinical presentations, their management options, and strategies to prevent or minimize the incidence of UII.

Anesthetic agents and pain medications

Intrathecal drug therapy is often effective for patients with chronic and cancer pain. By delivering the drugs via an intrathecal route, the risk of side effects of analgesics may be significantly decreased due to the substantially smaller doses required when compared to drugs given systemically.¹³ However, there is a risk of inadvertently administering too large doses intrathecally.

Epidural anesthesia: inadvertent spinal anesthesia

Both opioids and local anesthetics are typically used in neuraxial labor analgesia, surgical anesthesia, and post-operative analgesia. An epidural catheter can be unknowingly placed in or migrate into the intrathecal space. The **dose required** in the **epidural** vs. the **intrathecal** space differs by approximately a **factor of 10**.¹⁴ The clinical consequences of unintended intrathecal injection depend upon the amount of local anesthetic agent or other medications introduced into the CSF. While smaller amounts may result in numbness of the lower extremities, or higher but acceptable spinal blockade level may ensue, larger doses could potentially lead to a dangerously high spinal or total spinal anesthesia, manifesting as respiratory distress, hypotension, cardiac arrest, and/or fetal distress.¹⁵ A large dose of opioid into the subarachnoid space may potentially depress respiratory center leading to serious hypoxemia and fetal bradycardia in obstetric patients.¹⁶

Neuromuscular blocking drugs

The effect of **intrathecally** administered muscle **relaxant** is **not well-understood**. Understandably, if neuromuscular blocking drugs are delivered intravenously for a sufficient time and dose they will eventually enter the cerebrospinal

fluid (CSF) and reach certain levels in the CSF. Szenohradszky et al. used a **rodent model** to study the potential pharmacologic effects of neuromuscular blocking drugs (NMBDs) delivered intrathecally. They examined the effects of intraventricular infusion of NMBDs such as atracurium, pancuronium, and vecuronium in anesthetized rats. They found NMBDs directly injected into the CSF can cause **dose-dependent CNS excitation and seizures**.¹⁷ However, other clinical case reports in **humans** described a **lack of serious side effects** after intrathecal NMBD. Zirak et al. have published a case report where atracurium was administered intrathecally to a 38-year-old woman. The patient had no sensory or motor abnormality immediately post-operatively or within the first month postoperatively.¹⁸

Labetalol

Balestrieri et al. described an accidental intrathecal injection of 15 mg **labetalol** via a spinal catheter in a patient undergoing a post-partum tubal ligation. The spinal catheter was removed immediately after the procedure. She did **not suffer** apparent adverse neurologic effects.¹⁹

Sodium thiopentone

Abedini et al. described an UII case of sodium thiopentone by an anesthesia resident in a patient scheduled for tibia surgery under spinal anesthesia. The attending anesthesiologist noticed the yellowish color of the injectant; the drug ampule was checked and it was found that a nurse had accidentally prepared an injection of sodium thiopentone instead of 0.5% bupivacaine. Methylprednisolone and 20% magnesium sulfate were given intravenously in attempt to offer some neuroprotection, however, the patient developed **cauda equina syndrome** in a few **hours**.²⁰

Antitumor chemical agents

Currently, **methotrexate**, **cytarabine**, **hydrocortisone**, **prednisone**, and **ThioTEPA**, are all approved for **intrathecal chemotherapy**.^{21,22} A number of chemotherapy regimens have simultaneous

intrathecal and intravenous combinations of anti-cancer drugs. Therefore, it is possible that a chemotherapeutic drug intended for the intravenous route can be accidentally administered intrathecally.

Vincristine

Vincristine is a naturally occurring alkaloid used in chemotherapeutic regimens for acute lymphoblastic leukemia, non-Hodgkin's lymphoma, and other malignancies. Vincristine has serious **neurotoxic** effects and can result in **fatal myeloencephalopathy** if accidentally injected intrathecally.²³ There are a number of case reports about UII of vincristine, and the overwhelming majority of these cases ended in death.^{24–29} A few other reported **nonfatal cases** **suffered ascending paralysis and paraplegia**.^{30–33}

Vindesine

Vindesine is also an antimitotic vinca alkaloid used in chemotherapy for a variety of malignancies.³⁴ A few UII cases of Vindesine have been described in the literature.³⁵ Tournel et al. report a 25-year-old female being treated for non-Hodgkin's lymphoma was accidentally given vindesine intrathecally. The error was recognized immediately and a spinal cord washing was performed through **CSF lavage with isotonic saline**. The patient suffered **progressive paralysis and finally died** 6 weeks later.³⁶

Bortezomib

Bortezomib is a proteasome inhibitor used in the treatment of multiple myeloma, mantle-cell lymphoma, and other malignancies. Three fatalities due to Velcade (bortezomib) being accidentally given intrathecally instead of the intended intravenous route have been reported by the European Medicines Agency.^{37,38} The **fatal** events occurred when intrathecal chemotherapy was scheduled at the same time as bortezomib to be intravenously administered.³⁹

Methotrexate

Intrathecally administered methotrexate has an established role in the prevention and treatment

of meningeal involvement of childhood acute lymphoblastic leukemia and non-Hodgkin's lymphoma. However, several cases of accidental overdose were reported in the literature that resulted in permanent neurological damage or even death.^{40,41}

Bleomycin

Bleomycin, a glycopeptide antibiotic, is used subcutaneously or intravenously in the treatment of Hodgkin's lymphoma, non-Hodgkin's lymphoma, testicular cancer, ovarian cancer, and cervical cancer. Loebermann et al. reported a 39-year-old male being treated for chronic myeloid leukemia accidentally received 30 mg of bleomycin intrathecally. Timely CSF lavage with normal saline, an iatrogenic pneumoencephalus was induced to further remove CSF, and intravenous corticosteroid treatment resulted in a favorable outcome with no major side effects.⁴²

Anthracycline antibiotics

Doxorubicin is a chemotherapeutic agent belonging to the anthracycline family. It can treat particular types of leukemia. Arico et al. reported a female patient with acute lymphoblastic leukemia, who was accidentally given doxorubicin intrathecally. The patient developed severe, life-threatening acute encephalopathy with high-pressure hydrocephalus. Prompt ventriculoperitoneal shunting led to complete reversal of hydrocephalus with progressive disappearance of the acute encephalopathy.⁴³

Daunorubicin is another anthracycline antibiotic used for cancer therapy. A 3 year old female inadvertently received a 17 mg daunorubicin intrathecally. The error was recognized about 1 h after the injection. She was managed by CSF lavage with barbotage technique (repeated injection and aspiration). In addition, intrathecal hydrocortisone was also given. CSF drainage was allowed for 36 h with a subarachnoid catheter. Only 5.6 mg (33%) of the dose was recovered from the CSF. The patient developed progressive destruction of the nervous system, presumably caused by intrathecal daunorubicin, and the patient ultimately became comatose with a flaccid paraparesis, areflexia, and ascending progressive bulbar palsy.⁴⁴

Corticosteroids & antibiotics

Methylprednisolone

Methylprednisolone is often used for treating chronic back pain via epidural injection. Its inadvertent injection into the intrathecal space is associated with complications such as adhesive arachnoiditis.⁴⁵ Methylprednisolone has also been injected intrathecally in patients suffering from post-therapeutic neuralgia and complex regional pain syndrome. However, the efficacy of intrathecal methylprednisolone in neuropathic pain has been contradictory due to uncertain safety.⁴⁶ Lima et al. studied the clinical and histological changes, associated with the injection of methylprednisolone into the intrathecal space of 14 dogs, and in a randomized, double blinded, controlled clinical trial. There was no clinically observable difference in the group that received methylprednisolone, except histological evidence of meningeal thickening and lymphocytic infiltrates.⁴⁵

Rifampin

Rifampin is a potent broad-spectrum antibiotic. It is usually administered orally. Senbaga et al. reported a patient accidentally receiving 600 mg of rifampin instead of vancomycin via an intrathecal catheter. Fortunately, the patient did not show any reaction to the intrathecal rifampin except his urine turning orange-colored, which is typical of rifampicin administration systemically.⁴⁷

Contrast agents

Myelography is routinely performed safely using nonionic water-soluble radiographic contrast media. However, ionic contrast media may get accidentally injected intrathecally and result in severe and fatal neurotoxic reactions related to their hyperosmolality and ionic characteristics. Ionic contrast media are therefore strictly contraindicated for all radiologic applications involving CNS such as myelography.⁴⁸

Meglumine diatrizoate (Diatrizoic acid)/Amedetrizate

Undesired/inadvertent intrathecal injections of meglumine diatrizoate, an ionic contrast medium,

can result in a syndrome of ascending spasms, convulsions, myoclonus, respiratory distress, and tonic-clonic seizure, which can lead to death if not recognized and managed in a timely fashion.^{49–51} The patient's response was dependent upon the neurotoxicity, LD50, and the dose of the contrast agent administered. There was a patient successfully managed with anticonvulsant therapy, CSF drainage, and elective paralysis.⁵² Hilz et al. described an interesting patient who had UII of 10 ml meglumine diatrizoate and the patient was initially stable, gradually deteriorated neurologically, later exhibited myoclonus and jerky movements of the lower extremities, and ultimately death.⁵³ Sam et al. reported a case of life-threatening myoclonus after UII of 60% meglumine diatrizoate.⁵⁴ Intrathecal meglumine diatrizoate may also induce rhabdomyolysis and myoglobinuria, which could be successfully managed with midazolam and vecuronium. A case reported by Chirumumila was a 50-year-old female for spine surgery and accidentally injected with meglumine diatrizoate intrathecally. She progressively developed ascending, rigid, jerky, intermittent involuntary movements of both lower limbs. She had 60 ml CSF drainage, which successfully saved the patient from potentially life-threatening sequelae.⁵⁵ Nakazawa reported two cases of successful management of patients with accidental intrathecal amidetrizate (Urografin) by CSF lavage and intravenous administration of thiopentone.⁵⁶ Thiopentone provides a high degree of sedation and is highly effective as an anticonvulsant.

Gadolinium

Gadolinium is sometimes used to confirm needle epidural placement. Gadolinium can cause severe neurotoxicity and seizures if injected intrathecally in laboratory animals. Kapoor et al. reported injecting high dose of gadolinium epidurally, which was complicated by a wet tap necessitated an epidural blood patch for PDPH. Shortly after the autologous blood injection, the patient developed mental status changes and grand-mal seizures which was likely secondary to spreading epidural gadolinium into the intrathecal space.⁵⁷

Ioxithalamate

A patient who accidentally had intrathecal ioxithalamate recovered completely after a combination therapy of aggressive control of seizures, mechanical ventilation, neuromuscular paralysis, systemic steroid, CSF lavage, and prophylactic antibiotics.⁵⁸

Other chemical agents

Glutaraldehyde

Glutaraldehyde is an organic compound used to sterilize medical instruments and as a fixative for histological preparations. Davis et al. described a case of inadvertent injection of glutaraldehyde intrathecally in a 64-year-old diabetic man. The patient suffered hypotension and coma with subsequent death 5 days after the procedure. Postmortem examination revealed fixation of the outer cortical shell of the spinal cord and brain stem.⁵⁹

Potassium chloride

During routine spinal anesthesia, an ampule of potassium chloride, instead of bupivacaine, was mistakenly opened and inadvertently administered into the subarachnoid space of a patient who subsequently developed pain, cramps, and ultimately led to death within 2.5 h of injection.⁶⁰ Another case reported by Dias et al. was a 62-year-old man who developed severe pain, cramps, paraplegia, and pulmonary edema after unintended injection of potassium chloride into the subarachnoid space. The patient was managed by CSF lavage with 0.9% saline and other supportive measures, and recovered well without obvious permanent neurological injury.⁶¹

Magnesium sulfate

Magnesium sulfate (MgSO_4) is sometimes used as an analgesic adjuvant along with opioids and local anesthetics in the subarachnoid space, usually in very small doses.^{62–64} Gilani et al. described a case that patient was erroneously administered 700 mg of MgSO_4 (3.5 ml of 20% solution) intrathecally.⁶⁴ The patient initially

described feeling warmth and cutaneous anesthesia. The patient's surgery was done under general anesthesia with subsequent prolonged neuromuscular blockade and lethargy, ultimately extubated about 10 h later after muscle strength improved. The patient favorably recovered and did not develop neurological symptoms, headache, or backache.⁶⁴

Methylene blue/fluorescein

Previously, methylene blue was occasionally administered to trace sources of CSF leaks. This practice is no longer acceptable, as methylene blue can cause radiculomyelopathy.^{65, 66} Sharr et al. described a 59-year-old man who had 6 ml unbuffered methylene blue injected intrathecally to localize the source of CSF rhinorrhea. He became shocked and developed a mild paraparesis, which subsequently progressed to a total paraplegia.⁶⁷ Similarly, fluorescein has also been employed to determine the exact site of CSF leaks, but it is not without complications. Alkan et al. reported a patient who was injected fluorescein intrathecally and later suffered amnesia, and grand mal seizure, followed by low-back pain spreading through the right leg. The patient was treated with aggressive hydration, CSF drainage, intravenous corticosteroids, and anticonvulsant drugs and recovered without sequelae.⁶⁸ Other authors reported a delayed absence seizure following an intrathecal fluorescein injection.⁶⁹ Therefore, appropriate caution should be exercised when intrathecal fluorescein is administered.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent. Hatch reported a female for cesarean section delivery had 2 ml tranexamic acid intrathecally. She immediately complained of severe back pain followed by muscle spasm and tetany. General anesthesia was then induced but the patient's muscle spasm and tetany persisted despite the use of non-depolarizing muscle relaxant. Later the patient developed hemodynamic instability, ventricular tachycardia, and status epilepticus.⁷⁰ Kaabachi also reported a case of inadvertent intrathecal tranexamic acid instead of bupivacaine.⁷¹ Yeh et al. also reported

a patient who had intrathecal tranexamic acid and developed convulsions and refractory ventricular fibrillation.⁷² The prognosis was good in these cases when managed promptly with support of hemodynamic and respiratory systems, and promptly given anticonvulsants.^{73,74} CSF lavage promptly would be advisable to minimize potential morbidity and/or mortality.⁷⁵

Table 1 is a summary of the reported cases and the drugs inadvertently injected into intrathecal space and their clinical manifestations and outcomes.

Management

The mainstay of management of patients with an UII is CSF lavage and cardiopulmonary support. The documented case reports seemed to have shown the effectiveness of such a management strategy. However, one must be cautious in using case reports to guide management and best practice strategies. Ideally, a large-scale randomized clinical trial (RCT) should be performed to address the effectiveness and safety of this technique. Unfortunately, it is very difficult to conduct such a clinical trial due to the sporadic incidence and emergent nature.⁷⁶

The management of inadvertent intrathecal Vincristine is the most extensively studied and reviewed in the literature. Even though most reviews are specific to vincristine, they can potentially be extrapolated to other situations involving inadvertent intrathecal administration. While the optimal management of this complication is unknown, emergency CSF lavage remains the principal management based on literature reviews.

CSF lavage

CSF lavage involves direct CSF aspiration and CSF replacement. CSF lavage is done via a spinal catheter or spinal needle. CSF is aspirated slowly at the volume of 10–20 ml at a time and replaced with an equal volume of preservative-free normal saline. How much CSF volume can be safely replaced? Some reports replaced 40ml,^{77,78} and one report replaced 75ml CSF volume.⁷⁹ CSA lavage has to be done under absolute sterile conditions. Any introduction of a pathogen/chemical irritant into the subarachnoid

Table 1 UII drugs/agents and their clinical manifestations and outcomes.

UII drugs	Clinical manifestation/Consequences
Vincristine	Death, paralysis, paraplegia ³⁰
Vindesine	Paralysis ³⁶
Local anesthetics (much larger doses)	High or total spinal, hypotension, respiratory depression, coma, death
Opioids (much larger dose)	Respiratory depression
Labetolol	No significant problem ¹⁹
Atracurium	No significant problem ¹⁸
Sodium thiopentone	Cauda equina syndrome ²⁰
Bortezomib	Death ^{37,38}
Methotrexate (overdose)	Death or permanent neurologic injury ^{40,41}
Bleomycin	No major complications after comprehensive treatment ⁴²
Doxorubicin	Severe, life-threatening acute encephalopathy with high-pressure hydrocephalus ⁴³
Daunorubicin	Comatose with a flaccid paraparesis, areflexia and, ascending progressive bulbar palsy ⁴⁴
Methylprednisolone	Adhesive arachnoiditis ⁴⁵
Rifampin	No significant problem ⁴⁷
Meglumine diatrizoate	Syndrome of ascending spasms, convulsions, myoclonus, respiratory distress and tonic-clonic seizure, death. ^{49,50} Neuroleptic malignant syndrome ⁵⁰
Amidetrizate (Urografin) ⁵⁵	
Gadolinium	Severe neurotoxicity and seizures ⁵⁷
Ioxithalamate	No neurological deficit after CSF lavage ⁵⁸
Glutaraldehyde	Hypotension, coma, death ⁵⁹
Potassium chloride	Pain, cramps, paraplegia, pulmonary edema, death ^{60,61}
Magnesium Sulfate	Feelings of warmth, cutaneous anesthesia, prolonged neuromuscular blockade, and lethargy ⁶⁴
Methylene Blue (larger dose)	Shock, paraparesis, total paraplegia ⁶⁷
Tranexamic acid	Severe back pain, muscle spasm and tetany, hemodynamic instability, ventricular tachycardia, status epilepticus ⁷⁰
	Convulsions and refractory ventricular fibrillation ⁷²

space may lead to meningitis or encephalitis. CSF lavage must be performed as soon as possible after UII. Pongudom reported that in 16 patients who had CSF lavage, 56.3% survived 30 days or more and 37.5% had survived more than 6 months.⁸⁰ The most appropriate management of patients with UII of an ionic contrast agent is the removal of the inadvertently injected ionic contrast either by CSF lavage or drainage.⁸¹ One great advantage of CSF lavage is if used appropriately **CSF lavage does not seem to have any major complications** in a clinically indicated emergency situation. In light of the limited clinical experience and information on CSF lavage, clinicians need to balance the risks and potential benefits on a case-by-case basis before using CSF lavage.

CSF drainage and ventriculolumbar perfusion: The **management of accidental slight overdose is done by immediate lumbar drainage alone. Higher overdoses** will necessitate CSF **lavage** or other procedures as ventriculolumbar perfusion.^{82,83}

Fresh frozen plasma (FFP) has also been suggested as **adjunct** to the **CSF replacement solution** if UII drug is **vincristine**. FFP is believed to rapidly **bind vincristine**, thus reducing its potential neurotoxicity.⁸⁴

Anti-neurotoxic and neuroprotective agents, such as pyridoxine, folic acid, glutamic acid, and corticosteroids have also been used in case of neurotoxic agents involving drugs such as vincristine. Unfortunately some patients still have experienced significant neurological deficit, including paraparesis and tetraparesis.⁸⁵

Muscle relaxation and anticonvulsant therapy are also recommended in a review of the literature.^{52,72–74}

Other management such as intravenous fluid infusion, diuresis, sedation, have also been reported.⁴⁹ Intramuscularly administered folinic acid (leucovorin) has been shown to reduce methotrexate neurotoxicity and improve survival in a few individual case reports following inadvertent intrathecal methotrexate

Table 2 Management options for undesired/inadvertent intrathecal injections.

Management options	Indications/UII drugs
CSF lavage ^{76,77,81}	Most drugs, CSF lavage is generally very safe. Large dose of local anesthetics, opioids, Sodium thiopentone, vincristine, Large dose methotrexate, bortezomib, meglumine diatrizoate
CSF drainage/ventriculolumbar perfusion ^{82,83}	Amidetrizate (Urografin), methotrexate
Cardiopulmonary support	All UII cases if necessary
Observation	NMBDs, labetolol
Steroids ^{20,42}	Sodium thiopentone, ²⁰ Bleomycin ⁴²
Intravenous sedatives ⁴⁹	
Magnesium ²⁰	Sodium thiopentone, Trenaxamic acid
Iatrogenic pneumoencephalus ⁴²	Bleomycin
Ventriculoperitoneal shunting ⁴³	Doxorubicin ⁴³
Elective paralysis ⁵²	Meglumine diatrizoate
FFP added to CSF replacement ⁸⁴	Vincristine
Anti-neurotoxic & neuroprotective agents: pyridoxine, folic acid, glutamic acid ⁸⁵	Vincristine ⁸⁵
Patient's postural change ⁵⁸	If UII injectant is hyperbaric, head up to minimize cephalad migration of the drug, or vice versa.

NMBDs, neuromuscular blocking drugs.

administration.^{86,87} Intrathecal administration of carboxypeptidase G2 (CPDG2), an enzyme that inactivates methotrexate, has also been reported.⁸⁸

All the treatment options are summarized in Table 2.

Preventive strategies

Undesired/inadvertent intrathecal injections is a preventable medical error. The best management of UII is preemptive by developing effective strategies of prevention and incorporating them as standard operation and daily routine clinical practice. A study of 1089 'preventable' critical events revealed human lapses as the leading cause of errors in anesthesia mishaps and medical practice in general.⁸⁹ Jensen et al. provided

Table 3 General prevention of medication errors.

Targeting human factors	Emphasize training focusing on potential medication errors Heighten individual alertness on medication errors Read drug vial prints or bottle label before drawing any drug Label all drug syringes and write legibly Read syringe label before giving any drug Use checklist and double checking mechanism
Improving equipment & technology	Barcode drug bottle/vial and syringe Color-coded drug, vial, bottle, and syringe Unique connector for drug bottle and syringe Barcode reading & confirming mechanism

Table 4 Specific strategies to prevent/minimize undesired/inadvertent intrathecal injection.

Place only intrathecal drug(s) on the counter or anesthesia cart/procedure table
Read the labels of all vials/bottles before drawing into syringe(s)
Calculate the intrathecal dose and only draw to the exact amount to the syringe for spinal injection
Double checking before injection
Checklist for the operator and teammate(s)
Read the labels of syringe(s) or vial(s) before administration
Pay attention to medication's physical characteristics, like color, clarity, smell, etc.

some recommendations for preventing drug administration errors during anesthesia with focuses on syringe labeling and double-checking mechanisms.⁹⁰ Tighe also proposed a 10-step systematic solution for preventing incorrect intrathecal injection.⁹¹ Merry et al. have advocated that labeling greatly contributes to the safety of medication administration in anesthetic practice. They suggest the use of pre-printed labels or pre-filled syringes would reduce the number of steps involved and thereby decrease the risk of an inadvertent injection.⁹² They also suggest the use of bar codes and other cognitive aids.⁹³

The advocated preventive measures are summarized in Tables 3 and 4.

In summary, medical error is believed to be the third leading cause of death in the United States.⁹⁴ Unfortunately, we still see potentially disastrous medical errors occur in relatively safe

procedures such as intrathecal drug administration and spinal anesthesia. The solutions will almost surely be multifaceted. Prioritizing patient safety over OR efficiency and turnover times, focusing training on potential medications errors, heightening individual alertness on medication errors, adopting checklist and double-checking mechanisms, and many other preventive strategies.⁹⁵ Effective institutional and society guidelines must also be developed and strictly reinforced. A **root cause analysis** of any inadvertent intrathecal injection should be undertaken to highlight the fundamental cause of the error and thus improve the health care system for a better and safer care in the future.^{96,97} While errors are inevitable in any endeavor with human involvement, with due cautions they can surely be reduced to a minimum level.

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