

Inadvertent administration of intravenous anaesthesia induction agents via the intracerebroventricular, neuraxial or peripheral nerve route - A narrative review

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Submitted: 31-Dec-2023

Revised: 26-Feb-2024

Accepted: 02-Mar-2024

Published: 12-Apr-2024

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ABSTRACT

Intravenous (IV) medication administration error remains a major concern during the perioperative period. This review examines inadvertent IV anaesthesia induction agent administration via high-risk routes. Using Medline and Google Scholar, the author searched published reports of inadvertent administration via neuraxial (intrathecal, epidural), peripheral nerve or plexus or intracerebroventricular (ICV) route. The author applied the Human Factors Analysis and Classification System (HFACS) framework to identify systemic and human factors. Among 14 patients involved, thiopentone was administered via the epidural route in six patients. Four errors involved the routes of ICV (propofol and etomidate one each) or lumbar intrathecal (propofol infusion and etomidate bolus). Intrathecal thiopentone was associated with cauda equina syndrome in one patient. HFACS identified suboptimal handling of external ventricular and lumbar drains and deficiencies in the transition of care. Organisational policy to improve the handling of neuraxial devices, use of technological tools and improvements in identified deficiencies in preconditions before drug preparation and administration may minimise future risks of inadvertent IV induction agent administration.

Keywords: Complications, intracerebroventricular, intravenous induction agents, medication errors, neuraxial, peripheral nerve, regional anaesthesia, wrong route error

Access this article online
Website: https://journals.lww.com/ijaweb
DOI: 10.4103/ija.ija_1276_23
Quick response code


INTRODUCTION

Intravenous (IV) medication administration errors are intrinsic during the perioperative period because of multiple contributory factors within a complex and demanding environment.^[1] There are risks for substitution or wrong route administration errors for IV anaesthesia induction agents as these are kept ready along with other medications such as antibiotics, vasopressors and local anaesthetics.^[2,3] Inadvertent medications administered via neuraxial routes or into the intracerebroventricular (ICV) space can cause catastrophic consequences.^[4,5] There is a need to review the causes and outcomes following the accidental administration of an IV induction agent into the cerebrospinal fluid (CSF), epidural space or around peripheral nerves. It is also essential to understand the contributing factors for such potential high-risk incidents and the implementation of measures to prevent them. In this review, the

author investigates the clinical features following IV induction agent administration errors during neuraxial or peripheral nerve blockade or via the ICV route and their management and prevention strategies during the perioperative period.

METHODS

The author searched Medline and Google Scholar for published case reports on errors in inadvertent

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How to cite this article: Patel S. Inadvertent administration of intravenous anaesthesia induction agents via the intracerebroventricular, neuraxial or peripheral nerve route – A narrative review. *Indian J Anaesth* 2024;68:439-6.

IV anaesthesia induction agent administration via neuraxial (e.g. intrathecal, epidural), intracranial (e.g. ventricular) or peripheral nerve (e.g. nerve plexus) routes [Supplemental Files 1 and 2]. The author did not apply any restrictions for the search period or language. The last search was conducted in April 2023. The author manually searched references from the eligible articles to identify additional IV induction agent error reports. All identified articles describing the accidental administration of IV induction agents via the neuraxial or ICV route or during peripheral nerve blockade were evaluated for inclusion in the review.

For each error, the IV induction agent involved, the dose injected and the mode of administration were recorded on a standardised electronic form. The clinical scenarios, consequences, symptomatic or specific management measures, and outcomes were recorded. The results are described in terms of the number of errors and patients.

Based on James Reason's Swiss cheese model, a Human Factors Analysis and Classification System (HFACS) was used to identify human and systemic contributory factors. It describes failure at four levels: (1) organisational influences, (2) unsafe supervision, (3) preconditions for unsafe acts and (4) unsafe acts.

RESULTS

Thirteen reports (containing 14 patients) of accidental administration of IV induction agents via the epidural (eight patients), intrathecal (three), ICV (two patients) or brachial plexus (one patient) routes were identified [Supplemental File 1].^[6-18] Thiopentone was the most commonly administered drug through the epidural ($n = 6$), intrathecal (one patient) or axillary brachial plexus sheath (one patient) route.^[6-12] Propofol infusion was performed (with remifentanyl) via the lumbar drain intrathecally during posterior fossa neurosurgery^[13] or an access port placed in the right infraclavicular region into the ICV space.^[14] Etomidate was administered intrathecally during spinal anaesthesia^[16] or into the ICV space of a post-neurosurgical patient in the intensive care unit.^[15]

Table 1 and Supplemental File 2 summarise the IV induction agents involved, dose, route of administration, clinical features and outcomes. Pain, sedation and breathing difficulties were the main clinical features in awake patients.^[6-8,11,14] Intrathecal

thiopentone was associated with cauda equina syndrome.^[11] In three patients, the error was realised late in the presence of an epidural block or under general anaesthesia (GA).^[7,10,13]

Following propofol ICV bolus^[14] or intrathecal infusion^[3] error, CSF aspiration and aspiration followed by drainage were performed, respectively. For seven patients, normal saline (NS), either 20, 25, 30, 40 or 80 ml (over 30 min), was administered to dilute medications from the epidural space^[6-9,17,18] or the axillary brachial plexus sheath.^[12]

Table 2 lists the contributing human and systemic factors. Syringe swaps involving 10, 20, 30 ml or an unknown size accounted for all epidural barbiturate errors.^[6-10,12,17,18] Lumbar drain-IV line confusion^[13] or assumption of the access port of the ICV device as IV access^[14] was related to two propofol errors. During rapid sequence induction, an etomidate error occurred due to confusion between the look-alike external ventricular drain (EVD) and central venous line tubing.^[15] Intrathecal etomidate error occurred during spinal anaesthesia due to an ampoule error.^[16] Double checking and non-Leur connectors could have prevented errors due to syringe swaps and neuraxial device-IV line confusion.

DISCUSSION

Although infrequent, inadvertent administration of IV induction agents is potentially catastrophic. Multiple contributing risk factors are related to accidental IV induction agent administration in the presence of neuraxial and ICV catheters or drains.

Hew *et al.*^[19] reported that IV induction agents were the second most common group of medications involved in epidural drug administration errors. However, recent evidence suggests that errors involving IV induction agents via neuraxial route are uncommon or infrequently published compared to tranexamic acid, cardiovascular drugs, potassium chloride and neuromuscular blocking drugs.^[4,5,20,21] Besides our analysis, one author reported propofol administration via EVD without further details.^[22] A ventriculostomy catheter was confused with a central line, and the child was nearly injected with propofol and rocuronium.^[22]

The precise incidences and types of errors associated with IV induction agent administration are unknown. Specifically, findings from several prospective studies demonstrate that the incidence of incorrect

Table 1: Clinical features and management of intravenous induction agent administration via high-risk routes

Author, year	Drug/dose/route	Sex/age Surgery	Clinical features	Investigations	Management	Outcome
Forestner <i>et al.</i> , 1975 ^[6]	Thiopentone 15 ml 2% (300 mg) Epidural (L)	M/59 Orthopaedic	Discomfort during injection, sedation Difficult to arouse	EMG on the day of the event was normal	Via two epidural catheters, LAs mixture with epinephrine, NS wash and methylprednisolone were injected. Surgery cancelled. The patient was shifted to ICU	No neurological sequelae
Cay, 1984 ^[7] Patient 1	Thiopentone 2.5% 10 ml (250 mg) Epidural (C)	M/33 Haemorrhoidectomy	Perineal pain, urinary retention, respiratory difficulty, delayed awakening	None reported	LAs to dilute thiopentone. Insertion of an epidural catheter for NS wash (1 l over 4½ h). GA was administered. Urinary catheterisation for 3 days	No neurological sequelae Follow-up at 3 months
Patient 2	Thiopentone 2.5% 20 ml Epidural (L)	F/22 LSCS	Inadequate top-up. No haemodynamic changes	None reported	Conversion to GA for LSCS Baby delivered 30 min after error. The baby required 3 min of assisted ventilation	No sequelae. Follow-up at 6 weeks
Brownridge, 1984 ^[8]	Thiopentone 2.5% 20 ml Epidural (C)	F/unknown Dilatation and curettage	Burning pain in legs and buttocks. Agitation	None reported	Epidural NS wash given	No neurological sequelae
Weigert <i>et al.</i> , 2000 ^[9]	Thiopentone 6 ml 2.5% (150 mg) Epidural (L)	F/46 Sigmoid colectomy	Error soon after GA induction. Cardiovascular status was stable	None reported	The bacterial filter was discarded. Eighty millilitres of NS was injected over 30 min into the epidural space. The epidural was kept, but not used. The following day, the epidural catheter was removed	No neurological sequelae
Huang <i>et al.</i> , 2006 ^[10]	Thiopentone 10 ml 2.5% Epidural (L)	M/76 Colorectal	GA was administered BP decreased to 60/40 mmHg from 160/90 mmHg	None reported	Fluid bolus, ephedrine. Dopamine and norepinephrine infusions. Surgery proceeded and was completed. Epidural catheter removed	Follow-up during hospitalisation
Abedini <i>et al.</i> , 2015 ^[11]	Thiopentone Dose unknown Intrathecal	M/unknown age Orthopaedic	No sensory or motor block. Cauda equina syndrome	MRI was normal EMG abnormal	Methylprednisolone (unknown dose) IV and 20% MgSO ₄ (unknown dose) IV for neuroprotection	No mention of follow-up
Tuohy <i>et al.</i> , 1982 ^[12]	Thiopentone 15 ml 2.5% Axillary sheath	M/17 Orthopaedic	Persistent pain and tenderness in the axilla for 2 days	None reported	40 ml LA injected into the axillary sheath, 40 ml of NS, left stellate ganglion block Surgery postponed. Dexamethasone IV. Elevation of the arm	Discharged on the same day. Follow-up at 4 weeks
Burbridge <i>et al.</i> , 2021 ^[13]	Propofol infusion 330 mg (intrathecal via lumbar drain)	F/51 Neurosurgery (posterior fossa tumour)	No neurological, haemodynamic or respiratory problems once the patient woke up	None reported	GA was maintained with sevoflurane 30 ml of white, opaque fluid drained from the lumbar drain. Surgery cancelled Tracheal extubation. The patient was shifted to ICU. After 2 days, CSF was drained 5 ml/h	No neurological sequelae No mention of follow-up
Tiefenthaler <i>et al.</i> , 2006 ^[14]	Propofol 1% 10 ml (100 mg) ICV	M/51 Procedure for chronic pain	Within seconds, the patient complained of severe neck pain Sedation	CSF examination on the next day is normal	Bag mask ventilation. Neck pain disappeared following withdrawal of approximately 20 ml of propofol, remifentanyl and cerebrospinal fluid. GA was administered	No neurological sequelae

Contd...

Table 1: Contd...						
Author, year	Drug/dose/route	Sex/age Surgery	Clinical features	Investigations	Management	Outcome
Howell <i>et al.</i> , 2008 ^[15]	Etomidate 20 mg (10 ml) ICV (ventriculostomy catheter)	M/61 Post-op neurosurgery (Aneurysm clipping)	Loss of consciousness and became apnoeic Immediate tracheal intubation. Excellent intubating conditions	CT scan Cerebral angiography – vasospasm	20 ml of cerebrospinal fluid was aspirated from the ventriculostomy catheter and the catheter was left open to drain. Family informed	The management was withdrawn a few weeks later
Ahmadi <i>et al.</i> , 2023 ^[16]	Etomidate Unknown dose Intrathecal	F/73 Surgery was not mentioned	No neurological or haemodynamic symptoms or signs	None reported	Surgery cancelled The patient was monitored for 2 days Surgery was performed after 2 days	The patient was discharged
Wells <i>et al.</i> , 1987 ^[17]	Methohexital 5 ml 1% (50 mg) Epidural (L)	F/25 63 kg Gynaecology	An error during intraoperative top-up dose Post-op somnolent, drowsy and shallow respirations	None reported	Epidural NS, methylprednisolone, hyaluronidase intraoperatively. Post-op epidural used for pain management	No neurological sequelae Follow-up every day after discharge
Fukuda <i>et al.</i> , 1994 ^[18]	Thiamylal IV 3 ml 2.5% (75 mg) Epidural (L)	F/36 Gynaecology)	An error occurred during the test dose. Burning back pain – no motor or sensory changes	None reported	Epidural LA, hydrocortisone. GA was administered. Surgery was completed	No neurological sequelae Follow-up at 2 weeks

C=caudal, CSF=cerebrospinal fluid, CT=computerised tomography, EMG=electromyography, F=female, GA=general anaesthesia, ICU=intensive care unit, ICV=intracerebroventricular, IV=intravenous, L=lumbar, LA=local anaesthetic, LSCS=lower segment caesarean section, M=male, MRI=magnetic resonance imaging, NS=normal saline

Table 2: Contributory factors for intravenous induction agent administration errors identified using the Human Factors Analysis and Classification System framework

HFACS category	Contributory factors identified
Organisational influences	Safety climate/process: Deficiency in rules/norms/standards for syringe labels, ^[8,12] management of high-risk drains ^[13,15] and devices ^[14] Purchase of look-alike ampoules ^[16] and look-alike ventricular drain and central venous line tubing ^[15] Human resources management: The registered anaesthetic nurse prepared the drug and gave it to the trainee ^[11] ; the anaesthesia team changed at short notice ^[14]
Supervisory factors	Anaesthesia trainee doctor administered thiopentone prepared by a nurse ^[11] Prolonged unnoticed propofol infusion ^[13] Anaesthesia technician handed over an etomidate ampoule for spinal anaesthesia, instead of ropivacaine ^[16]
Preconditions for unsafe acts	LA and GA syringes were kept side by side ^[6-9,14,18] Ropivacaine and etomidate ampoules were kept side by side in the anaesthesia workstation ^[16] Haste: Urgent surgery, ^[7] soon after induction ^[18] Unlabelled syringes ^[8,10,12] Complacency ^[9] Failure to correct (during the procedure, the attending physician noticed the yellowish colour of the injectant and informed the trainee) ^[11] Poor team communication: ^[14] The anaesthesia team assumed infusion was going through the IV line ^[14] Inadequate handover: An error occurred by a reliever resident ^[17]
Unsafe acts	Skill-based errors ^[6-18] Perceptual errors: incorrect visual perception leading to poor judgement or misidentification of same-sized syringes, ^[6-9,10,12,17,18] ampoule, ^[16] intrathecal or intraventricular device ^[13-15] Failure to consider drug error as a cause for an inadequate epidural top-up ^[7]

GA=general anaesthesia, IV=intravenous, LA=local anaesthetic

route administration for IV induction agents may be around one in 150,000 [Table 3].^[23-29] If errors occur involving IV induction agents via routes other than those included in this analysis, they are more likely to be related to dose or substitution with other

medications.^[23-29] It is also noteworthy that several studies have found that IV induction agents are less commonly involved in operating room errors than other medications, including antibiotics, opioids, neuromuscular blocking drugs and cardiovascular

Table 3: Incidents and types of intravenous induction agent administration errors in various studies

Drug errors in anaesthesia studies: author, year Country	Prospective data collection for several anaesthetics	Number of drug administration errors analysed/number of IV induction agent errors	Type of error, number and IV induction agent involved
Webster <i>et al.</i> , 2001 ^[23] New Zealand	10,806	121 (including pre-errors)/5	Incorrect dose (2): Ketamine 1 (bolus), propofol 1 (infusion) Substitution (2): Thiopentone 1 (for cefuroxime), ketamine 1 (for remifentanyl) Omission (1): Propofol
Hingtong <i>et al.</i> , 2005 ^[24] Thailand	202,699	41/2	Not specified (2): Thiopentone 1, propofol 1
Yamamoto <i>et al.</i> , 2008 ^[25] Japan	27,454	48/5	Not specified (4) Incorrect route (1): ketamine (intended for IM, but given intravenously)
Llewellyn <i>et al.</i> , 2009 ^[26] South Africa	30,412	111 (including near misses)/5	Substitution (3): Not specified Repetition (1): Ketamine Incorrect route (1): Propofol (intra-arterial in place of intravenous)
Copper <i>et al.</i> , 2012 ^[27] USA	10,574	52 (including pre-errors)/3	Incorrect dose (1): Propofol Substitution (1): Thiopentone Omission (1): Methohexital
Zhang <i>et al.</i> , 2013 ^[28] China	24,380	179/19	Incorrect dose (11): (Propofol 9, ketamine 1, etomidate 1) Substitution (3): Ketamine 1 (for suxamethonium), etomidate 2 (for ketamine 1, for flurbiprofen axetil 1) Not specified (6): Propofol 6
Gariel <i>et al.</i> , 2018 ^[29] (paediatric) France	1400	40/3	Not specified (3): Propofol 2, ketamine 1

IV=Intravenous

drugs (e.g. vasopressors).^[23,25,26,30] Thiopentone errors will likely decline with its diminishing use in clinical anaesthesia practice.^[31]

Prevention: Correction of human and systemic factors

Organisational factors that can minimise the risk of IV induction agent errors via EVD and lumbar drain include robust policies and procedures to manage them in clinical locations, such as operating rooms, intensive care units, and radiology departments. Guidelines for managing EVDs and lumbar drain exist; however, compliance specifically for preventing drug errors via EVD or lumbar drain is minimal.^[32,33]

Measures to minimise inadvertent neuraxial medication administration have been discussed previously,^[4,5,20,21] and strategic interventions for prevention in the presence of EVD and lumbar drains are presented in Table 4.^[34] The anaesthesia providers must remember that errors concerning wrong route may occur if the IV induction agent is withdrawn in an NRFit (a non-Leur connector developed by Global Enteral Devices Supplier Association and approved by the International Organisation for Standardization) syringe or if the wrong bottle (e.g. propofol) is spiked with an NRFit administration set.

In the current analysis, latent proximal suboptimal preconditions in the working environment were present in several events [Table 2]. In these circumstances, the probability of error increases, particularly in haste, distraction and when the care transition occurs.

Multiple IV induction agent errors occurred during the transition of care by a single provider, from one anaesthesia provider to another or from a non-anaesthesia care provider to an anaesthesia care provider. Internal factors that affected continuity of care included lack of awareness (e.g. lack of situational awareness), lack of knowledge about the clinical condition (e.g., tunnelled catheters or invisible devices) and suboptimal practices (e.g., administering intrathecal drugs prepared by another colleague). The provider’s care and safety for a patient during clinical task transition were also influenced by multiple external factors, including inadequate handover, poor communication and coordination among team members, distraction, interruption and the level of supervision.

Management: Removal and dilution of IV induction agent from neuronal spaces

No specific therapy is available to counteract the neurological sequelae of neuraxial, ICV or intrabrachial

Table 4: Prevention of inadvertent drug administrations via external ventricular and lumbar drains (adopted and modified with permission from ISMP, United States of America)^[34]

Device design:

- Non-Leur connectors for EVD and LD drains and any associated stopcocks or ports

Organisation responsibility:

- Establish a policy for the safe management of EVD and LD
- How to operate open and closed systems, trained staff (nurse, physician) required, staff education (please see below), dedicated, clearly labelled lines, and IV poles for the system mount
- Drug administration procedure in the presence of EVD/LD

During insertion:

- When placing an EVD, if the catheter exits from any location other than the scalp, avoid subcutaneous tunnelling near common central venous access sites, for example, the clavicle or neck
- Affix a prominent and colourful label near the distal end of the CSF tubing setup to distinguish it from other medical tubing (including IV lines)
- Consider labelling if a stopcock is used for a system

While *in situ*:

- Equipment for EVDs and LDs and pumps for venous lines should be placed on separate IV poles
- Avoid threading EVD and LD through a gown
- Use identifiable labels on all lines and pumps if there are multiple lines and pumps

Before drug administration:

- Perform a safety check and identify the access port for IV injections and other lines or drains attached to the patient
- Read label of ampoules and syringes
- Double-check (with another person or using barcode scan technology) drugs before withdrawal and administration
- Trace all access lines and injection ports to their origin before administration
- Whenever possible, staff familiar with EVD/LDs should be involved in the checking process to reduce the risk of wrong route drug administration
- Aspirate before injection, if possible, to confirm the route of administration

Transfer with devices:

- A pre-transport screening checklist might be helpful. The receiving staff should be provided with all details and advice to ensure the patient's safety
- A standardised handover process

Staff education:

- For new/temporary/locum staff, skills assessment during induction. Regular mandatory skills review for compliance with the safe use of EVD/LDs. Organisational awareness of staff who infrequently encounter EVD/LDs
- Educate providers and staff to recognise the signs and symptoms of different accidental intraventricular administration from the published case reports (e.g. IV induction agent, chemotherapeutic agents, contrast media and phenytoin)

CSF=Cerebrospinal fluid, EVD=External ventricular drain, ISMP=Institute for Safe Medicine Practices, IV=Intravenous, LD=Lumbar drain

plexus IV induction agent administration errors. Once an error is recognised, management depends on several factors, including route, drug administered, clinical scenario, and signs and symptoms. Figure 1 highlights an approach to managing the accidental administration of an IV induction agent. Individual patients may require variable interventions.

For intrathecal or ICV route errors, immediate CSF aspiration, drainage or lavage is a logical step to remove the drug from CSF if there is a drain or catheter *in situ* [Figure 1].^[14,20,21] Recently, Koning *et al.*^[35] have suggested a guide for the removal of unintended drugs following accidental administration via a percutaneous lumbar approach. In humans, cerebrospinal lavage appears beneficial in accidental intrathecal tranexamic acid^[20] and potassium chloride^[21] errors and inadvertent intrathecal injection of local anaesthetics secondary to epidural catheter

misplacement.^[36-38] Time, initial and total volume of CSF removed are some determinants of the quantity of the drug removed.^[13,35,39]

The strategies for epidural route errors included dilution with local anaesthetics, NS or both, epidural or systemic steroids to prevent neurotoxicity and other symptomatic management [Table 1, Supplemental File 2].^[6-9,17,18] However, the utility of all these empirical rescue measures is complex to evaluate from the analysed reports. For epidural route barbiturate errors, seven of the eight patients received epidural saline washout in variable quantities. In humans, crystalloid (normal saline or Ringer's lactate) washout resulted in epidural local anaesthetic motor and sensory block regression.^[40] The optimal quantity may be 30–45 ml, as lower volumes may not be adequate and large volumes are likely to cause side effects, including raised epidural pressure.^[9,41] Saline

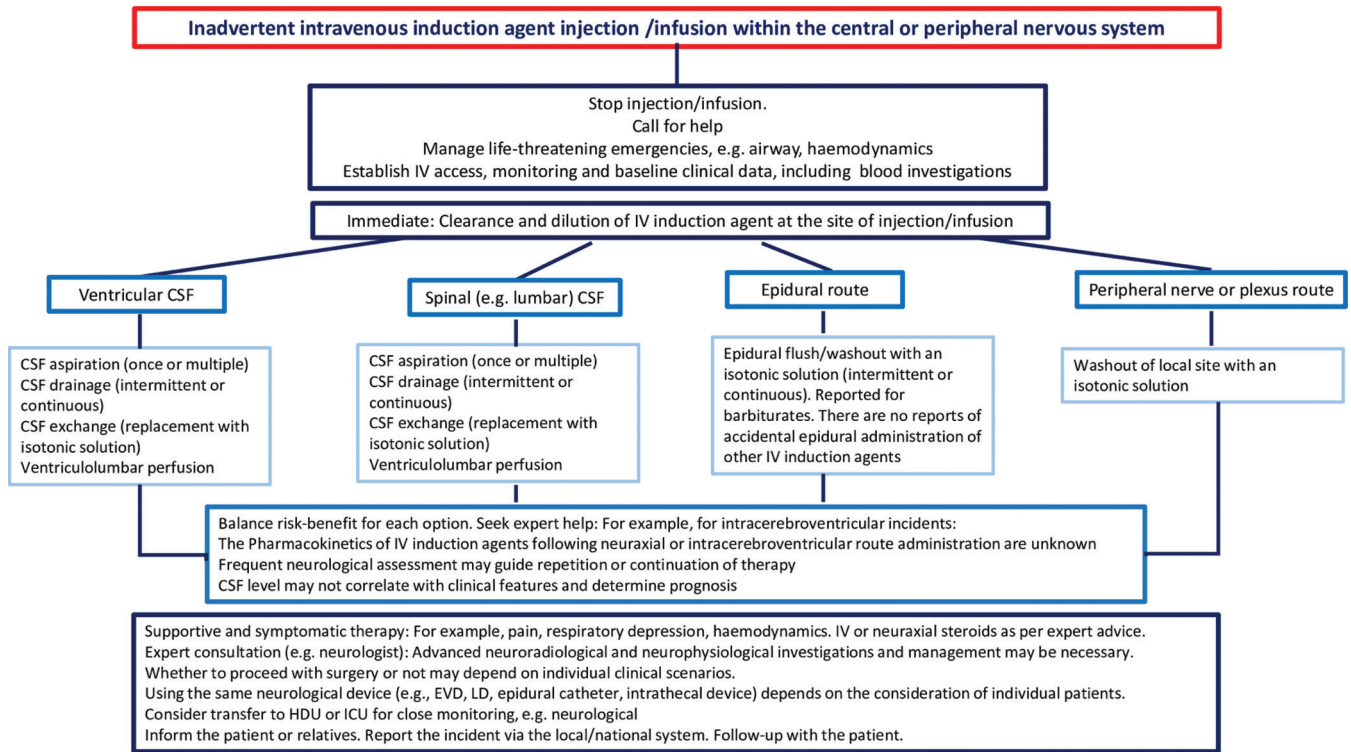


Figure 1: An approach to manage accidental administration of intravenous induction agents via the central or peripheral nervous system routes CSF = cerebrospinal fluid, EVD = external ventricular drain, HDU = high-dependency unit, ICU = intensive care unit, IV = intravenous, LD = lumbar drain

washout may have spread the administered barbiturate to more segments, providing a larger vascular area for absorption. In addition, acidic (pH 5.0) NS could lower epidural thiopentone pH and increase the unionised quantity for vascular uptake. While epidural saline was most likely not associated with any harm in the current review, epidural potassium chloride error analysis demonstrated the spread of neurological damage following epidural saline administration.^[21]

Limitations

The review included inherent impediments to the analysis based on non-standardised details in case reports. The incidents are limited in number and occur under diverse clinical circumstances. Some case reports did not provide evidence or insight into specific systemic contributory factors, such as local guidelines for handling intrathecal, epidural or intraventricular devices or drains.

CONCLUSION

The current review adds to the knowledge of rare IV anaesthesia induction agent administration errors via high-risk routes and highlights contributing systemic factors. HFACS suggests multifactorial contributing factors require changes to minimise

drug administration errors via high-risk routes. These data indicate that double-checking and non-Leur connectors for neuraxial and ICV catheters or drains may prevent future adverse events. Immediate CSF withdrawal and epidural saline washout may limit the neuronal damaging actions of IV induction agents.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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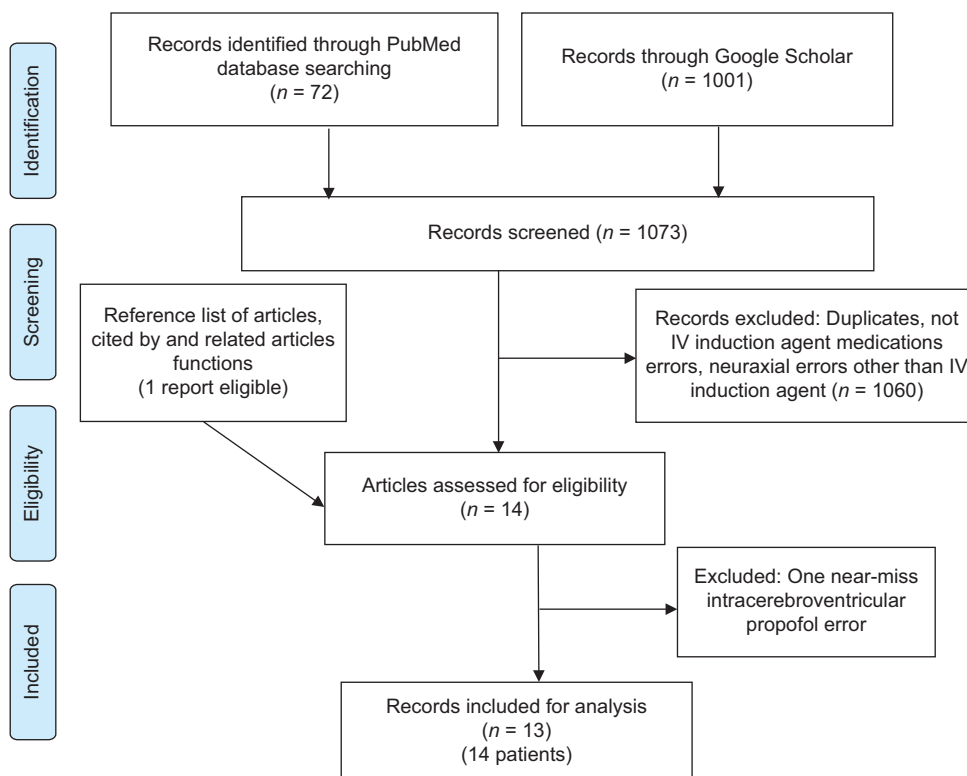
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SUPPLEMENTARY MATERIAL

Supplemental File 1: Search strategy for PubMed and Google Scholar



Supplemental Figure: Search strategy. Preferred Reporting Items Systematic Reviews and Meta-analyses- intravenous (IV) induction agent error search flowchart

PubMed search:

("subarachnoid"[TIAB] OR "intrathecal"[TIAB] OR "spinal"[TIAB] OR "epidural"[TIAB] OR "neuraxial"[TIAB] OR "intracerebroventricular"[TIAB] OR "lumbar drain"[TIAB] OR "ventricular drain"[TIAB] OR "lumbar"[TIAB] OR "intraventricular"[TIAB] OR "ventriculostomy"[TIAB] OR "Brachial plexus"[TIAB] OR "lumbar plexus"[TIAB] OR "interscalene"[TIAB] OR "axillary" [TIAB] OR "supraclavicular"[TIAB] OR "infraclavicular"[TIAB] OR "femoral"[TIAB] OR "fascia iliaca"[TIAB] OR "three-in-one"[TIAB] OR "sciatic"[TIAB] OR "popliteal"[TIAB] OR "adductor canal"[TIAB] OR "saphenous"[TIAB] OR "ankle"[TIAB] OR "intercostal"[TIAB] OR "paravertebral"[TIAB] OR "erector spinae"[TIAB] OR "pectoral"[TIAB] OR "transverse abdominis plane"[TIAB] OR "peribulbar"[TIAB] OR "retrobulbar"[TIAB] OR "subtenon"[TIAB] OR "Penile"[TIAB])

AND

("accidental"[TIAB] OR "inadvertent"[TIAB] OR "unintentional"[TIAB] OR "drug errors"[TIAB] OR "medication errors"[TIAB] OR "drug error"[TIAB] OR "medication error"[TIAB] OR "adverse reaction"[TIAB])

AND

("Thiopentone"[TIAB] OR "Thiamylal"[TIAB] OR "Methohexitone"[TIAB] OR "Propofol"[TIAB] OR "Etomidate"[TIAB] OR "Ketamine"[TIAB] OR "Thiopental"[TIAB] OR "Methohexital"[TIAB])

Google Scholar search:

Search in the title using the terms:

- epidural (medication name)
- intrathecal (medication name)
- neuraxial (medication name)

Medication name: Thiopentone, Thiopental, Propofol, Ketamine, Etomidate, Methohexitone, Methohexital, Thiamylal

Results:

- Epidural thiopentone: five (two duplicates, three excluded)
- Intrathecal thiopentone: one (duplicate)
- Neuraxial thiopentone: one (excluded)
- Epidural thiopental: 10 (three duplicates, seven excluded)
- Intrathecal thiopental: one (excluded)
- Neuraxial thiopental: 0
- Epidural thiamylal: one (duplicate)
- Intrathecal thiamylal: 0
- Neuraxial thiamylal: 0
- Intrathecal methohexitone: 0
- Neuraxial methohexitone: 0
- Intrathecal methohexital: 0
- Neuraxial methohexital: 0
- Epidural methohexital: 0
- Epidural methohexitone: two (duplicates)
- Epidural propofol: 222 results (all excluded)
- Intrathecal propofol: 71 results (all excluded)
- Neuraxial propofol: five (all excluded)
- Epidural ketamine: 478 (all excluded)
- Intrathecal ketamine: 185 (all excluded)
- Neuraxial ketamine: six (all excluded)
- Epidural etomidate: eight (all excluded)
- Intrathecal etomidate: five (one included, four excluded)
- Neuraxial etomidate: 0

Other searches:

Reference list of the articles (one additional report found)

'Related articles' and 'cited by' functions on Google scholar

Supplemental file 2

Supplemental Table: Clinical details, features and management of intravenous induction agent administration errors

Author, year Country	Drug Dose Route	Age/sex Surgery	Clinical features	Investigations	Management	Outcome
Forestner <i>et al.</i> , 1975 ⁽⁶⁾ USA	Thiopentone 15 ml 2% (300 mg) Epidural L3–L4	59/M Orthopaedic (fracture hip fixation)	Discomfort during injection of thiopentone through the epidural needle. Incorrect syringe (in place of a syringe containing intended local anaesthetic mixture with epinephrine) picked up and drug injected Epidural catheter passed The error was realised when the patient was found sedated The patient was responsive, but incoherent and difficult to arouse Local anaesthetic with epinephrine injected – surgical block to T8 The sensory block was gone in 2 h. After that, no pain, paraesthesia or numbness	EMG on the day of event was normal	Following the error, a 15-ml mixture of LAs with epinephrine injected via an epidural catheter (bupivacaine 0.5% 7.5 ml+lidocaine 1.5% 7.5 ml+1:1000 epinephrine 0.1 ml) Surgery cancelled Second epidural catheter was inserted at L1–L2 Epidural lavage from the lower catheter was unsuccessful Epidural saline 25 ml via second (upper) catheter Methylprednisolone 125 mg in 10 ml saline through the lower catheter Lower epidural catheter removed The patient was shifted to ICU	No neurological sequelae The surgery was performed under GA 5 days later
Cay, 1984 ⁽⁷⁾ Australia Patient 1	Thiopentone 2.5% 10 ml (250 mg) Epidural caudal In place of bupivacaine 0.5%	30/M Haemorrhoidectomy	No neurological pain on injection more than expected with caudal procedure. The drug tray was checked. Error noticed Forty millilitres of local anaesthetic was injected through the same caudal needle Pain improved, but signs of a very high epidural block over the next 10 min. Drowsy. Respiratory difficulties. Immediate GA was administered Surgery was uneventful. Two hours after induction, the patient woke up, and tracheal extubation was done Pain in the anus at 4 h. Difficulty in passing urine for the next 3 days. No motor or sensory problems after 48 h.	None reported	20 ml 0.5 bupivacaine and 20 ml 1.0% lignocaine were injected to dilute thiopentone immediately after the error GA administered – IV thiopentone 250 and suxamethonium The epidural catheter was inserted at the end of surgery at the L3–L4 space. One litre of NS was administered over 4.5 h After that, the epidural catheter was removed Urinary retention needed catheterisation	No neurological sequelae No sequelae at 3 months follow-up

Contd...

Supplemental Table: Contd..

Author, year Country	Drug Dose Route	Age/sex Surgery	Clinical features	Investigations	Management	Outcome
Patient 2	Thiopentone 2.5% 20 ml (500 mg) Epidural L3-L4 In place of 20 ml 0.5% bupivacaine with adrenaline 1:200,000	F/22 LSCS	She received multiple top-ups of local anaesthetic (10 ml 0.25% bupivacaine) during labour of 9 h. For LSCS top-up, thiopentone was given in error The 'error' top-up did not increase the level of analgesia higher than T10 and did not cause haemodynamic changes. Over the next 15 min, the patient became drowsy Surgery started 20 min after thiopentone 'top up' for LSCS. Error realised when it was decided to convert the inadequate block to GA Complete neurological examination at 24 h revealed no motor, sensory or reflex abnormalities	None reported	GA was administered for LSCS Baby delivered 30 min after error. The baby required 3 min of assisted ventilation Apgar score 3 at 1 min, 7 at 5 min and 9 at 10 min. No other abnormalities in the baby	No neurological sequelae At 6 weeks, follow-up of the mother and baby revealed no neurology problems
Brownridge, 1984 ⁽⁶⁾ Australia	Thiopentone 2.5% 20 ml (500 mg) Epidural caudal In place of 2% prilocaine	Unknown age/F Dilatation & curettage	Burning pain in legs and buttocks. Despite this, the injection continued. 20 ml given Second syringe was connected to IV, and 10 ml was administered. The patient became agitated. Error realised	None reported	Epidural saline given	No neurological sequelae
Weigert <i>et al.</i> , 2000 ⁽⁸⁾ UK	Thiopentone 6 ml 2.5% (150 mg) Epidural L3-L4	46/F Sigmoid colectomy	Epidural test dose 4 ml given. Before the incident, 9 ml 0.5% bupivacaine (from a 20 ml syringe) was given. For GA induction, 14 ml (from a 20-ml syringe) of thiopentone 2.5% was used At the start of surgery, an error occurred during top-up dose administration via the epidural catheter The patient's cardiovascular status was stable, and surgery continued. No complaints in recovery	None reported	Immediate aspiration via the epidural catheter was attempted; 1 ml aspirated Bacterial filter discarded Soon after the error (intraoperatively), 80 ml of NS was drawn from a filter needle injected over 30 min into the epidural space Epidural kept, but not used. The next morning, epidural catheter was removed	No neurological sequelae
Huang <i>et al.</i> , 2006 ⁽¹⁰⁾ Taiwan	Thiopentone 10 ml 2.5% (250 mg) Epidural L2-L3 In place of 10 ml solution containing 1% lidocaine and morphine 2 mg	76/M Colorectal	After the 2-ml lidocaine test dose, an error occurred. No pain or discomfort. Ten minutes later, GA was administered with propofol, fentanyl and rocuronium BP decreased to 60/40 mmHg from 160/90 mmHg. Hypotension did not respond to fluid bolus and ephedrine. Arterial line and central lines inserted. Hypotension persisted Forty minutes later, the error was realised The patient was awake and had no complaints after 4 h of surgery	None reported	Fluid bolus, ephedrine. Dopamine and norepinephrine infusions for severe hypotension Aspiration from the epidural catheter – no fluid Surgery proceeded and was completed Epidural catheter removed Post-op analgesia with morphine patient controlled analgesia.	Follow-up during hospitalisation

Contd...

Supplemental Table: Contd..

Author, year Country	Drug Dose Route	Age/sex Surgery	Clinical features	Investigations	Management	Outcome
Abedini <i>et al.</i> , 2015 ^[1] Iran	Thiopentone Dose unknown Intrathecal In place of 0.5% bupivacaine	Unknown age/M Ortho (elective tibial surgery)	The patient was initially comfortable and had no haemodynamic instability or sensory or motor block Cauda equina syndrome Within a few hours – low back pain, leg and buttock numbness, bladder and bowel incontinence. By 1 month, bladder tonicity	MRI was normal EMG and nerve conduction study showed axonal lesions at L4, L5–S1 roots	Methylprednisolone (unknown dose) IV and 20% MgSO4 (unknown dose) were administered IV for neuroprotection	No mention of follow-up
Touhy <i>et al.</i> , 1982 ^[1,2] Australia	Thiopentone 15 ml 2.5% (375 mg) Axillary sheath (during brachial plexus block) In place of 1% lignocaine with adrenaline 1:200,000	17/M Orthopaedic	Complained of mild pain at the site during the early part of the injection. Pain persisted. Error realised 40 ml of intended LA injected Successful motor, sensory and sympathetic blockades occurred Four hours later, the patient had some paraesthesia in the fingers and the motor function returned to normal Moderate pain and tenderness in the axilla for 2 days There was no sensory or motor abnormality on examination, and readmission for surgery 2 days later	None reported	Forty millilitres of the prepared local anaesthetic solution was injected, and the needle was withdrawn from the sheath Five minutes later, 40 ml of NS was injected into the axillary sheath to dilute thiopentone A left stellate ganglion block was also performed using 0.25% bupivacaine 15 ml injected by a paratracheal approach Surgery postponed Dexamethasone 8 mg administered IV Elevation of the arm	The patient was discharged on the same day The patient was readmitted 2 days later for surgery under GA Follow-up at 4 weeks No neurological sequelae
Burbridge <i>et al.</i> , 2021 ^[1,3] USA	Propofol 329.88 mg (32.9 ml) Intrathecal (via lumbar drain) Infusion for 56 min With remifentanyl 3.84 ml (193.13 µg)	51/F Neurosurgery (endoscopic posterior fossa tumour resection)	Once realised, the infusion was disconnected Surgery did not proceed (an error occurred before the start of surgery) No neurological or haemodynamic, or respiratory problems	None reported	GA was maintained with sevoflurane 30 ml of white opaque fluid drained from the lumbar drain. Tracheal extubation. The patient was shifted to ICU Following 2 days, CSF was drained via <i>in situ</i> lumbar drain, with a maximum of 5 ml/h On day 2 after the incident, CSF became clear After that, surgery was performed uneventfully	No neurological sequelae No mention of follow-up

Contd...

Supplemental Table: Contd..

Author, year Country	Drug Dose Route	Age/sex Surgery	Clinical features	Investigations	Management	Outcome
Tiefenthaler <i>et al.</i> , 2006 ^[14] Austria	Propofol 1% 10 ml (100 mg) Intracerebroventricular With remifentanyl 3.84 ml (150 µg)	51/M Implantation of an intrathecal infusion system for chronic upper limb neuropathic pain	The error occurred via an intracerebroventricular totally implantable access port placed in the right infralacravicular region. Within seconds, the patient complained of severe neck pain Sedation	CSF examination on the next day normal Blood reports normal, except for a mild increase in c-reactive protein	Bag mask ventilation Neck pain disappeared following the withdrawal of approximately 20 ml of a mixture of propofol, remifentanyl and CSF Peripheral IV line established GA was administered, and the airway was secured. Surgery was done as planned. Tracheal extubation	No neurological sequelae
Howell <i>et al.</i> , 2008 ^[15] USA	Etomidate 20 mg (10 ml) (with rocuronium 100 mg- 10 ml) Intracerebroventricular (ventriculostomy catheter)	61/M Neurosurgery (Aneurysm clipping)	Post-op intracranial aneurysm clipping. Reintubation was required due to increased oxygen requirements, waxing and waning mental status. An error occurred during rapid sequence induction and intubation. The patient lost consciousness and became apnoeic Endotracheal intubation was immediately performed. Excellent intubating conditions Over 10 min, CSF became progressively more blood tinged The patient did not improve neurologically and developed multiorgan failure. Developed cerebral infarction	CT scan demonstrated some effacement of the right lateral ventricle, a new finding of uncertain significance Cerebral angiography – vasospasm	20 ml of CSF was aspirated from the ventriculostomy catheter, and the catheter was left open to drain Family informed Management for vasospasm and other complications (renal failure, atrial fibrillation)	The management was withdrawn after consultation with the family a few weeks later The patient died after a few weeks
Ahmadi <i>et al.</i> , 2023 ^[16] Iran	Etomidate Intrathecal Dose? In place of ropivacaine 0.5%	73/F Surgery?	No neurological or haemodynamic symptoms or signs	None reported	Surgery was postponed The patient was monitored for 2 days Surgery was performed after 2 days	Follow-up at 5 days The patient was discharged
Wells <i>et al.</i> , 1987 ^[17] USA	Methohexital 5 ml 1% (50 mg) Epidural L1–L2 In place of lidocaine 2%	25/F 63 kg Gynaecology (laparotomy for ovarian tumour)	Epidural test dose (0.5% bupivacaine with epinephrine) and bolus dose (10 ml 2% lignocaine) were administered. GA was administered with methohexital An error occurred intraoperatively during 'top-up' dose administration The surgery lasted for 2 h. Tracheal extubation was done During transfer to the recovery room – somnolent, drowsy and shallow respirations. Sleep in the recovery room for half an hour One hour after, the patient was fully awake and complained of pain at the surgical site	None reported	After the error, epidural NS 10 ml followed by 10 ml NS with 40 mg methylprednisolone was administered. Also, 10 ml NS with 300 units of hyaluronidase was administered via epidural catheter intraoperatively Fentanyl 75 µg and morphine 4 mg were administered via the epidural catheter for pain management The next day, epidural 5 mg morphine was administered before removing the epidural catheter	No neurological sequelae Neurological examination every day till the fifth day of discharge The patient was discharged on day 5

Contd...

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Author, year Country	Drug Dose Route	Age/sex Surgery	Clinical features	Investigations	Management	Outcome
Fukuda <i>et al.</i> , 1994 ^[16] Japan	Thiamylal IV 3 ml 2.5% (75 mg) Epidural L2-L3 In place of 3 ml lidocaine 1.5% with epinephrine 15 µg	36/F Gynaecology (for bicornuate uterus)	Epidural procedure completed. An error occurred during test dose administration via the epidural catheter Burning back pain L1 area. No motor or sensory changes Back pain resolved 15 min after injection of lidocaine, saline and steroid. Sensory analgesia up to T6 Neurological examination 1 day following the incident was normal	None reported	Aspiration of the epidural catheter was unsuccessful After 5 min, 10 ml 2% lidocaine and 10 ml NS containing hydrocortisone 100 mg were administered via the epidural catheter GA was administered, and surgery was completed	No neurological sequelae The patient was discharged on day 14 Follow-up 2 weeks after surgery

BP=blood pressure, CSF=cerebrospinal fluid, CT=computerised tomography, F=female, GA=general anaesthesia, ICU=intensive care unit, IV=intravenous, LA=local anaesthetic, LSCS=lower segment caesarean section, M=male, MRI=magnetic resonance imaging, NS=normal saline