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Review Article

Total spinal anaesthesia following obstetric neuraxial blockade: a narrative review

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ABSTRACT

Background: Total spinal anaesthesia (TSA) is an emergency caused by high neuraxial blockade. It is a recognised complication of all neuraxial techniques in obstetric anaesthesia. Its incidence and outcomes have not been evaluated. There is compelling evidence that TSA continues to be a problem in contemporary practice, having the capacity to cause significant morbidity and mortality if not recognised early and promptly treated. This review based on a literature search aims to clarify the epidemiology of TSA, summarise its pathophysiology, and identify risk factors and effective treatments.

Methods: We performed a literature search using PubMed, Web of Science and Google Scholar databases using specified search terms for materials published using search terms. For each case, the type of block, the difficulty of the procedure, the dose of local anaesthetic, positivity of aspiration before and after the event, maternal outcome, Apgar score, onset of symptoms, cardiorespiratory and neurological manifestations, cardiorespiratory support employed, admission to an intensive care unit, cardiac arrest events and duration of mechanical ventilation were extracted.

Results: A total of 605 cases were identified, of which 51 were sufficiently detailed for analysis. Although TSA is described after all neuraxial techniques, spinal after epidural was a particular concern in recent reports. Respiratory distress was universal but apnoea was not. The onset of apnoea was variable, ranging from 1 to 180 min. Hypotension was not invariable and occurred in approximately half of cases. Multiple fatalities and neurological injuries were reported, often in under-resourced areas when providers were not skilled in airway management or when recognition and intervention were delayed. In the most recent reports good outcomes were achieved when effective treatments were rapidly provided.

Conclusions: The available literature confirms that TSA remains an active clinical problem and that with prompt recognition and treatment good outcomes can be achieved. This requires anticipation and preparedness in all clinical areas where neuraxial techniques are performed.

Introduction

Total spinal anaesthesia (TSA) is a recognised complication of all neuraxial local anaesthetic (LA) techniques. It refers to a high neuraxial block causing respiratory failure and/or loss of consciousness, usually requiring airway intervention.[1–7] In contrast to other emergencies, there are few evidence-based guidelines for its prevention and treatment. We have performed a narrative review which aims to describe the epidemiology, pathophysiology and management of TSA.

Methodology

Following an OVID MEDLINE search, we analysed 20 abstracts using a deep learning algorithm known as bidirectional encoder representations from transformers. This is a family of language models that helps artificial intelligence programs understand the context of words in text. This generated further search terms which we used to search PubMed, Web of Science and Google Scholar. We also searched abstracts from the Obstetric Anaesthesia Association meetings from

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2000 to 2022. All United Kingdom (UK) Confidential Enquiry into Maternal Death Reports (CEMD) from inception were read and relevant cases extracted. After removing duplicate publications, the list of 1483 publications was manually searched (Fig. 1). Case reports, cases series, observational studies and insurance claim reviews were included. From filtered publications, two independent reviewers identified relevant information. For each relevant case a full text report was obtained and the following information was extracted: publication date, type of block, procedural difficulty, dose and volume of LA, cerebrospinal fluid (CSF) aspiration before and after the event, maternal outcome, Apgar score, the onset of symptoms, cardiorespiratory and neurological manifestations, cardiorespiratory support, admission to the Intensive Care Unit (ICU), cardiac arrest events and duration of mechanical ventilation. For data entry and statistical analysis, Microsoft Excel and the R programming language were used. Two reviewers (MR, CMC) screened and retrieved reports.

Epidemiology

We identified 605 cases of TSA in obstetric practice of which 51 were case reports and the remainder case series and within databases. The incidence from 1953 to 2003 ranged from 1 in 2383 to 1 in 54 000.[4–11] The highest incidence was reported in the 1950s when LA was injected directly through epidural needles without preceding test doses.[6]

A survey carried out by the Society for Obstetric Anesthesia and Perinatology in the United States (US) in 2014 reported the incidence of high neuraxial block necessitating intubation or conversion to general anaesthesia was 1 in 4336.[9] Among the 58 reported cases, the most common cause of TSA according to this definition was an unrecognised intrathecal catheter in 14 cases, 40% of which were spinals and 60% epidurals. The incidence of TSA in labour epidurals was 1 in 12 297. Analysis of the UK National Obstetric Anaesthesia (NOAD) database in 2020 reported the rate of high neuraxial block resulting in loss of consciousness to be 1 in 6667.[10] In 2022 the UK Obstetric Surveillance System group reported 89 cases in which women needed ventilatory support or cardiopulmonary resuscitation as a consequence of high neuraxial blockade. Eighty-two patients required intubation, giving an estimated incidence of 1 in 6230 for all neuraxial blocks: of these, 48% arose following a single-shot spinal after an epidural technique.[11] The incidence for spinal anaesthesia was 1 in 4366 which was double that of the 1 in 10 869 associated with epidural anaesthesia. In the 7th National Audit Project in the UK, high neuraxial block was among the most common causes of cardiac arrest in obstetric anaesthesia care, along with haemorrhage and bradyarrhythmia.[12]

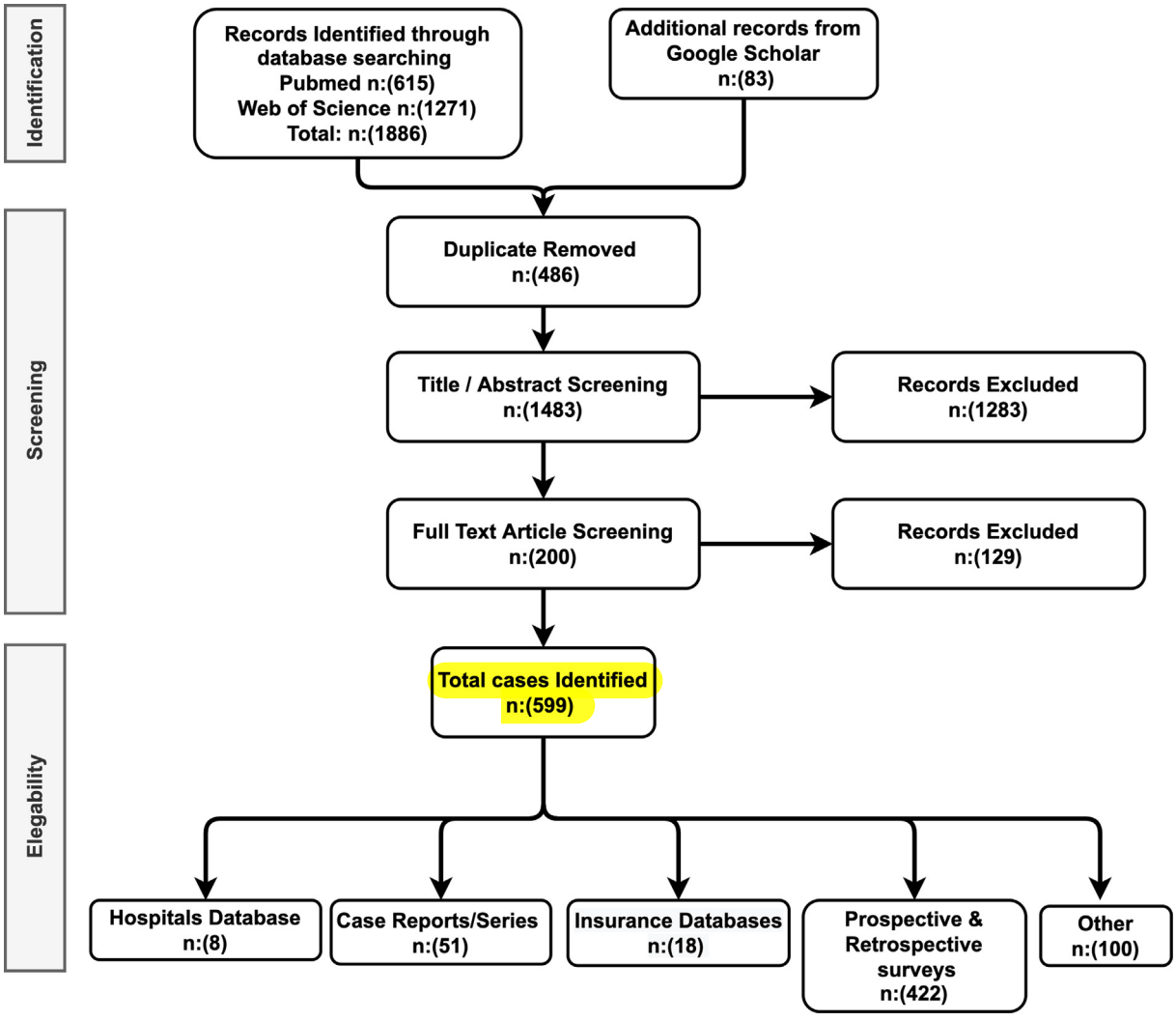

Fig. 1. Flow diagram

Mortality and morbidity

Deaths and serious morbidities, including permanent neurological injuries, are potential consequences of TSA.[13–23] Psychological distress and awareness during emergency tracheal intubation has also been reported. Our analysis identifies a number of risk factors that contributed to poor outcomes. In many cases the person designated to monitor the patient was not skilled in airway management or resuscitation. In other cases there were failures to monitor and delays in recognising clinical deterioration. In other deaths, inadequate resuscitation equipment on the labour ward and unnecessary transfers to the operating room were factors.[23] Medical error also contributed, specifically when doctors failed to interpret obvious signs of intrathecal LA administration while using epidural analgesia for labour. In some cases, large doses of LA were administered through catheters known to be intrathecal.

In an analysis of an insurance database in the US (1998–2006), Lofsky described multiple cases of cardiorespiratory arrest after neuraxial blockade.[23] Although limited clinical data were provided, it was evident that more than 50% of cases were the result of an undetected intrathecal epidural catheter location. Most of these women died and there was only one neurologically intact survivor, as the remainder suffered permanent brain injuries. In that report, all infants delivered prior to or following maternal arrest were developmentally normal.[23]

In the obstetric closed-claims analysis from 1999 to 2003 in the US, high neuraxial block was responsible for 22% of claims in which anaesthesia contributed to maternal death or brain injury.[16] Of these, most were caused by accidental intrathecal injection during epidural analgesia. The UK CEMD contains 10 cases in which death was fully or partially attributable to TSA. In the UK Cardiac Arrest in Pregnancy Study, the single most common cause of cardiac arrest was neuraxial anaesthesia, most commonly following de novo spinal injection.[24] Interestingly, the majority of patients were obese and all survived, this being attributed to rapid intervention by anaesthetists. Neurological outcomes were not stated. A recent survey of obstetric anaesthetists in the UK found that a quarter of respondents had experience of critical events in relation to epidural top ups, including high blocks progressing to cardiac and respiratory arrest.[25] A UK study did not identify either maternal or neonatal mortality but described six cardiorespiratory arrests and 16 intensive care unit (ICU) admissions related to TSA. In that study, at least seven women reported awareness or psychological distress at the time of intubation during high neuraxial blockade.

In low- and middle-income countries, Sobhy et al. reported that high blockade after spinal anaesthesia was responsible for 6% of the 987 anaesthesia-attributable maternal deaths.[19] In contrast airway difficulties were responsible for 45% of deaths.[19] There is strong evidence from the South African National CEMD which has been operational since 1999 that TSA has been a factor in many of the deaths associated with neuraxial anaesthesia.[26]

In addition to complications of neuraxial anaesthesia in obstetrics, TSA has been described in association with other LA nerve blocks, during early prophylactic epidural blood patch and during epidural saline infusion.[27,28]

Lessons from case reports

Precipitating events

Total spinal anaesthesia was reported after de novo spinal anaesthesia in nine case reports (Table 1).[28–36] The median dose of bupivacaine was 12.75 mg (range 10–15 mg). In the single case in which lidocaine was used, the dose was 75 mg.[30] A similar clinical pattern in terms of onset and recovery was observed in the 14 cases where single-shot spinal anaesthesia was used after an epidural bolus had been inadequate for surgery.[37–46] The lowest reported dose was 8 mg bupivacaine (median 11.25, range 8.0–15.0 mg) suggesting that even though doses are often deliberately reduced by practitioners, TSA may still occur.[45] It is noteworthy that TSA was reported after an epidural test dose in four cases containing sufficient detail for analysis, indicating that tests doses may not be benign.[47–50] Lidocaine was used in all four cases at a median dose of 45 mg (40–80 mg). Total spinal anaesthesia was reported after labour epidural analgesia loading and top up doses in 12 cases,[7,9,15,51–57] the median dose for bupivacaine being 25 mg (range 10.0–50.0 mg).

High neuraxial block with dyspnoea was reported following a combined spinal-epidural (CSE) technique in a single case for which programmed intermittent epidural bolusing (PIEB) was used. The event occurred after the fifth PIEB dose and intubation was not required.[58]

Importantly, TSA may occur after negative epidural catheter aspiration for CSF, as was reported for 13 cases. [7,9,50,52–54,56–62] In seven of these cases, positive aspiration was reported after the event, having been negative beforehand.[7,52–54,56,58] In two cases, catheter aspiration remained negative after the event and in both cases the catheter was identified in the subdural space.[59,62] In total there were 10 clinically proven (by aspiration or post mortem examination) intrathecal catheters in the epidural group.[7,9,15,42,47,49,51,52,54,58] There is no clear explanation for the mechanism. Speculative explanations include initial unrecognised subdural placement with subsequent arachnoid rupture during drug administration.[59] It has also been suggested that false negative aspiration is more likely if the filter is left in place or large syringes are used, leading to the recommendation that aspiration should be performed with small syringes with the filter removed.

There were seven reported possible cases of TSA after full or partial subdural placement, of which four were radiologically confirmed.[32,37,57,59,61,62] The median onset of TSA was slower (10 min) than when associated with single-shot spinal anaesthesia or an epidural top-up. The mean duration of ventilation required was 1.5 h (range 0.3–3.0 h). Two cases of possible subdural spread after single-shot spinal were reported.[31,35]

There is one reported case of TSA which occurred two hours after commencement of an epidural saline infusion provided as a prophylactic treatment after a recognised dural puncture and subsequent epidural top for caesarean section (CS).[28] The catheter was radiologically confirmed to lie in the subarachnoid space, but 23 mL of bupivacaine 0.5% had been administered through it earlier for the CS, without high block developing at the time.

Respiratory effects and interventions

The onset of respiratory distress after TSA was variable (range 30 s to 15 min), with a mean of 8.1 min (Fig. 2). When larger doses of LA were given for surgical anaesthesia, the onset of respiratory distress was often extremely rapid, with a median time of 1 min (Fig. 2).[53,55,59–63] While respiratory distress was universal, apnoea was reported in 15 cases and its onset was variable, occurring as quickly as 2 min after injection (median 7.0 min, maximum 10.0 min).

Tracheal intubation was performed in 40 of 51 (78%) case reports and facemask ventilation in 7 of 51 (14%).[30,31,35,37,40,52,64] Intubation failed in three patients, of whom two did not receive neuromuscular blocking drugs.[30,31,59] In some cases airway management was initiated once a high block had been recognised prior to the onset of apnoea or hypoxaemia. The duration of mechanical ventilation was shortest after spinal LA injections (0.5 h) and longest after epidural top ups (median 2.0, range 0.6–24 h), indicating that larger quantities of intrathecal LA have longer effects. Consequently, mechanical ventilation in the operating theatre may be adequate as initial management in some cases, with a longer duration of ventilation in an ICU only required for TSA associated with large volume epidural top ups.

Table 1
Case reports

Author	Year	Local Anaesthetic	Respiratory Distress Onset (min)	Respiratory Intervention	Ventilation Duration (h)	Haemodynamic Instability	Circulatory Support	Maternal Outcome
Single Shot Spinal								
Anand[32]	2003	13 mg bupivacaine	6	ETT	0.30	Yes	Mephenteramine 6 mg Fluids	Good
Ashfaw[29]	2020	15 mg bupivacaine	16	ETT	24.00	Yes	Epinephrine	Good
Bari[36]	2006	10 mg bupivacaine	0	ETT	NS	Cardiac arrest	Ephedrine Epinephrine CPR	Good
Bhati[30]	2004	75 mg lidocaine	12	Failed intubation Facemask	0.40	No	None	Good
Chan[31]	2000	10 mg bupivacaine	20	Failed intubation Facemask	NS	Yes	Ephedrine 5 mg	Good
Kayaalti[35]	2019	9.5 mg bupivacaine	10	FMV	NS	Yes	IV Fluids	Good
Pantha[34]	2011	12.5 mg bupivacaine	5	ETT	0.25	Yes	Atropine Mefenteramine	Good
Russell[33]	1985	15 mg bupivacaine	5	ETT	0.50	NS	NS	Good
Wagner[28]	1994	11.25 mg bupivacaine	2	ETT	2.00	No	None	Good
Epidural Test Dose								
Al Fahel[47]	2017	45 mg lidocaine	NS	ETT	NS	No	None	Good
Caliskan[48]	2005	40 mg lidocaine	NS	ETT	24	Yes	Ephedrine 10 mg, IV Fluids	Good
Moir[49]	1965	80 mg lidocaine	1.0	NS	NS	Yes	NS	NS
Palkar[50]	1992	45 mg lidocaine	2.0	FMV	NS	Yes	IV Fluids	Good
Epidural Loading Dose for Surgical Anaesthesia								
Abouleish[62]	1986	420 mg chloroprocaine	25	ETT	1.25	Yes	None	Good
Aly[60]	2002	60 mg levobupivacaine	17	ETT	0.60	Yes	Ephedrine 12 mg Atropine 0.6 mg Methoxamine 2 mg	NS
Forrester[59]	1999	300 mg lidocaine	10	Failed intubation Fibre-optic intubation	1.50	No	None	Good
Hodgkinson[63]	1981	127.5 mg bupivacaine	8	ETT	NS	Yes	Ephedrine 20 mg	Good
Hodgkinson[63]	1981	127.5 mg bupivacaine	2	ETT	6.50	Yes	Ephedrine 5 mg	Good
Hodgkinson[63]	1981	120 mg bupivacaine 200 mg chloroprocaine	2	ETT	6.50	Yes	Ephedrine 5 mg	Good
Kar[7]	2001	75 mg bupivacaine	NS	ETT	2.50	Yes	Ephedrine, IV fluid	Good
Kim[53]	1975	62.5 mg chloroprocaine	0.5	ETT	NS	No	No	Good
Scott[55]	1995	NS	NS	NS	NS	No	None	Good
Shaw[61]	2001	NS	15	ETT	3.00	No	Ephedrine 18 mg	Good
Programmed Intermittent Bolus in Labour								
Betti[58]	2017	NS	180	NS	NS	Yes	Ephedrine 10 mg, phenylephrine, IV Fluid	Good
Epidural Loading Doses and Top Ups for Labour Analgesia								
Crawford[9]	1985	50 mg bupivacaine	10	ETT	2.00	Cardiac Arrest	Ephedrine Adrenaline	Good
Crawford[9]	1985	25 mg bupivacaine	NS	FM	NS	No	None	Good
Denison Davies[51]	2008	15 mg levobupivacaine	7	ETT	24.00	Cardiac Arrest	CPR Adrenaline	NS
Guterres[52]	2010	50 mg bupivacaine	15	NIV	0.60	No	NS	Good
Kar[7]	2001	20 mg bupivacaine	2	ETT	NS	Cardiac Arrest	Adrenaline	Good
Kim[53]	1975	40 mg chloroprocaine	0.5	ETT	NS	No	No	Good
Philip[54]	1976	35 mg bupivacaine	15	ETT	1.25	No	None	Good
Pitkanen[15]	2012	10 mg ropivacaine	10	ETT	NS	NS	CPR	Death
Scott[55]	1995	NS	NS	ETT	NS	Cardiac Arrest	CPR	Good
Skowronski[56]	1981	10 mg bupivacaine	10	ETT	2.00	No	None	Good
Wills[57]	2005	12.5 mg bupivacaine	1	ETT	NS	Cardiac Arrest	Ephedrine	NS
Spinal Following Epidural								
Barada[37]	2021	10 mg bupivacaine	10.0	FMV	0.70	No	None	Good
Beck[38]	1992	10 mg bupivacaine	5.0	ETT	0.80	Yes	Ephedrine 15 mg	Good
Beck[38]	1992	12.5 mg bupivacaine	10.0	ETT	0.90	Yes	Ephedrine 60 mg	Good

Table 1 (*continued*)

Author	Year	Local Anaesthetic	Respiratory Distress Onset (min)	Respiratory Intervention	Ventilation Duration (h)	Haemodynamic Instability	Circulatory Support	Maternal Outcome
Dell[39]	1993	12.5 mg bupivacaine	2.0	ETT	2.00	NS	NS	Good
Furst[40]	1995	12 mg bupivacaine	5.0	ETT	0.80	No	NS	NS
Furst[40]	1995	9 mg bupivacaine	NS	FMV	NS	Yes	Ephedrine 15 mg	NS
Goldstein[41]	1994	40 mg lidocaine	1.0	ETT	1.00	NS	NS	NS
Gupta[42]	1994	12.5 mg bupivacaine	5.0	ETT	NS	Yes	Ephedrine 30 mg	Good
Gupta[42]	1994	15 mg bupivacaine	2.0	ETT	NS	Yes	Ephedrine	Good
Gupta[42]	1994	10 mg bupivacaine	2.0	ETT	NS	Yes	Ephedrine 25 mg	Good
Mets[43]	1993	11.25 mg bupivacaine	0.5	ETT	0.75	Yes	Ephedrine	Good
Siddik-Kayyid[44]	2011	10.5 mg bupivacaine	10.0	ETT	1.30	No	Phenylephrine infusion	Good
Stone[45]	1989	8 mg bupivacaine	3.0	ETT	2.80	Yes	Ephedrine 6 mg, IV Fluid	NS
Virgin[46]	2016	13 mg Bupivacaine	1.0	ETT	NS	No	None	Good
Epidural Top Up For Surgical Anaesthesia Through Known Spinal Catheter								
Thomas[65]	2002	10 mg bupivacaine	NS	ETT	NA	Cardiac Arrest	Ephedrine Atropine Epinephrine CPR	Death
Yuan[64]	2014	40 mg ropivacaine	5	FMV	NS	Yes	Phenylephrine, IV Fluid	Good

CPR: Cardiopulmonary resuscitation; ETT: Endotracheal intubation; FMV: Face mask ventilation; IV: Intravenous; LSCS: Lower segment Caesarean Section; NIV: Non-invasive ventilation; NS: Not stated.

Cardiovascular effects and interventions

Cardiac arrest was reported in eight cases, of whom two died.[7,9,15,36,51,55,57,65] In one of these deaths, causation was multifactorial. In addition to a high neuraxial block, massive bleeding also occurred and oxytocin was thought to have contributed to haemodynamic instability.[67] In this case there was uncertainty regarding the amount of LA administered because a 20 mL syringe had been used to deliver 2 mL of injectate. The second death was caused by epidural dosing of an unrecognised intrathecal catheter inserted at the T12-L1 level.[15]

Hypotension did not always occur but was reported in 24 of 51 (47%) cases. In 20 of 51 (39%) patients, haemodynamic instability was evident and required both intravenous fluids and vasopressors. Ephedrine was the most commonly used drug for haemodynamic support, being given in 19 of 51 (37%) cases at a mean dose of 18 mg (range 5–75 mg). None of the events in the cases that could be analysed occurred in patients on prophylactic vasopressor infusions.

Central nervous system effects

Observed central nervous system (CNS) effects included upper limb weakness, diaphragmatic paralysis, cranial nerve dysfunction (ptosis, nystagmus, trigeminal nerve dysfunction), pupillary dilatation, loss of consciousness and apnoea.

Mode of delivery and fetal outcomes

Caesarean section was performed in 41 cases, of which 10 were unscheduled and precipitated by TSA. Four of the 16 (25%) women who had TSA as a complication of labour epidural analgesia delivered vaginally during or after a period of mechanical ventilation.[9,53,54,56] The neonatal outcome was reported in only 55% of cases. There were no reported neonatal deaths. The median Apgar at 1 min was 8 (range 2–9) and at 5 min 9 (range 8–10).

Historical perspectives: deliberate total spinal anaesthesia

High spinal anaesthesia was a deliberate anaesthetic technique first described by Morton in 1901.[66] The majority of its proponents used lumbar access sites with large quantities of LA and barbotage. Koster described his experience of 3500 cases across a broad population including neonates and elderly adults, for a range of surgeries including sub-diaphragmatic and later head and neck procedures.[67] Hypotension was common, with impalpable pulse or unmeasurable blood pressure in 5% and attributed to 'vascular collapse', with the primary treatment being Trendelenberg positioning. The popularity of the high spinal anaesthesia waned in parallel with advances in other anaesthetic techniques.[68] Later, anaesthetists used the technique to create bloodless fields via hypotension but used artificial airways and supplementary oxygen and artificial ventilation when required. These techniques are no longer in use owing to their inherent danger.

Following the more widespread use of epidural analgesia in labour, C.J. Massey Dawkins presented a paper at the World Congress of Anaesthesiology in 1968 which summarised 25 years of published outcomes and their own experience of 4000 blocks.[69] He drew attention to the concept of 'total spinal anaesthesia' and separately, the 'massive extradural' which occurred 20 min after epidural drug administration. There was no satisfactory explanation for this at the time. In the last large series, published in 1974, Evans describes the deliberate use of TSA in general surgical patients by lumbar injection of 30–40 ml of 1% lidocaine in conjunction with controlled ventilation.[70] The effect was variable and TSA was not reliably produced, with failure in 17 or 100 cases and higher doses necessary for a consistent effect. In one case TSA occurred after 10 mL of injectate. In many cases, the onset was within minutes but in others it was delayed for up to 45 min. Metaraminol was used for haemodynamic support in the majority of patients and apnoea occurred in most cases, lasting between one and two hours. There was no awareness despite the absence of maintenance agents. During recovery temporary deafness was common. Evan's observations have direct relevance to under-

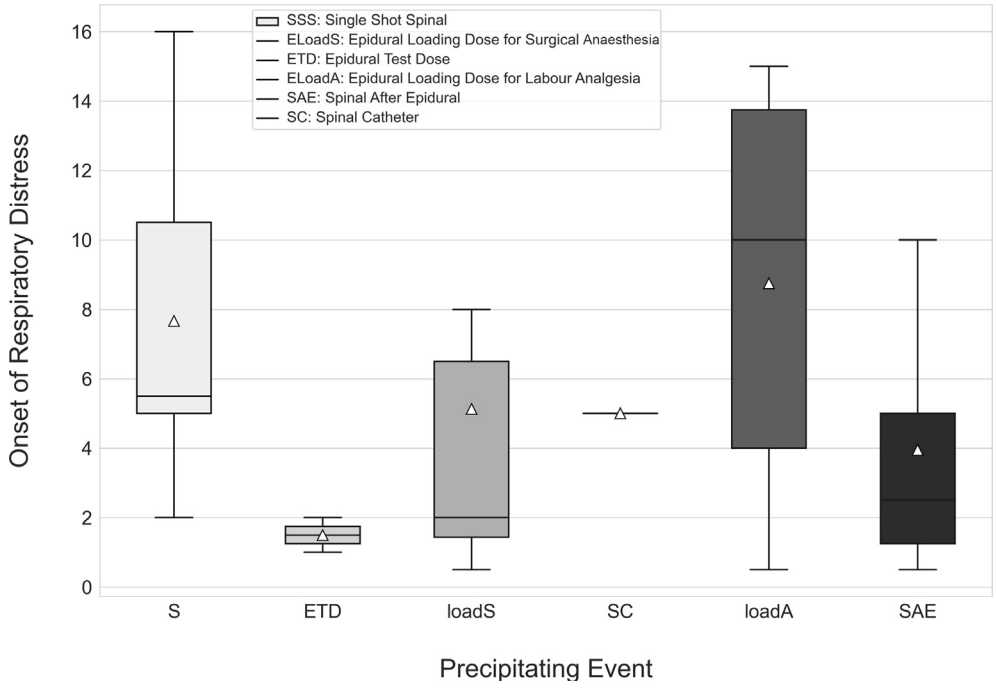

Fig. 2. Onset of respiratory distress based on data from case reports. Data are median, interquartile range and 95% confidence interval. SSS: Single shot spinal. ELoadS: Epidural Loading Dose for Surgical Anaesthesia. ETD: Epidural Test Dose. ELoadA: Epidural Loading Dose for Labour Analgesia. SAE: Spinal After Epidural. SC: Spinal Catheter

standing the variability of TSA and its management. The variability in onset and occasional absence of hypotension potentially explains why negative test doses and the absence of adverse effects within five minutes do not guarantee exclusion of accidental intrathecal injection.

Pathophysiology

Mechanisms

In the context of labour ward epidural analgesia, most reported cases of TSA followed accidental injection of LA directly into the CSF through an unrecognised intrathecal catheter; or indirectly via the subdural space with subsequent subarachnoid spread via a breach in the arachnoid membrane. In the operating room, some cases occur after intentional subarachnoid injection of conventional LA doses subsequent to an epidural bolus. This is thought to be a result of dural compression and distortion of the thecal sac leading to greater cephalad spread of LA. A very small number of cases are attributed to subdural injection of LA where no breach of the arachnoid layer was demonstrated. Fewer cases still are thought to be solely due to cephalad spread within the epidural space itself, despite the physiological changes known to occur in pregnancy that diminish the volume of the epidural space and promote cephalad spread. It is thought that large volumes of the injectate are required to reach the cervical epidural space as much of the injectate exits through intervertebral foramina and is absorbed by epidural fat.[71] The onset of blockade would be slower than after intrathecal injection and this is reflected by the typical 20–40 min onset time of respiratory impairment after direct cervical epidural LA injection.[72]

Respiratory system effects

Total spinal anaesthesia causes respiratory failure through a combination of peripheral nerve blockade and central effects. Impairment of respiratory function is proportionate to the height of the block.[73] The intercostal nerves control the motor function of both the internal and external intercostal muscles, these having both inspiratory and expiratory functions. Intercostal nerve blockade is common in neuraxial anaesthesia and is generally well tolerated due to diaphragmatic function being maintained.[74] Acute phrenic nerve dysfunction caused by cephalad movement of LA, even if unilateral, causes marked impairment of respiratory function through diaphragmatic paralysis.[75] Cervical level blockade also impairs function of the accessory muscles of respiration.[76] Apnoea can also be caused by high concentration of LA in the intracranial CSF, although this seems an unlikely cause of apnoea in the absence of extremely large drug dose administration.[77] Apnoea and bradypnea can also be caused by severe hypoxaemia, and with concomitant hypotension are usually a consequence of delayed recognition and intervention. The duration of apnoea seen in the clinical series is variable and was longest after larger quantities of LA had been injected. The most common clinical presentation is a patient complaining of difficulty breathing.

Central nervous system effects

The function of the CNS is altered by severe hypoxia-induced neuronal depression. Consciousness is impaired at partial pressures of oxygen of < 30 mmHg in the presence of hypotension and progresses to loss of brainstem reflexes and motor function.[78] Total spinal anaesthesia has direct effects on brainstem function which cause cranial nerve dysfunction, apnoea and loss of the gag reflex. When direct intracranial LA injections are performed in rodent experiments, brain stem evoked potentials and peripheral motor function return to baseline in 135 min.[76] The effect of TSA on level of consciousness is variable. In patients undergoing deliberate total spinal blockade for treatment of chronic pain with intrathecal injection at C1–C2, 0.3 mL/kg of 1% lidocaine induced an unconscious state for 40 min.[79] Evans, in a series of 100 deliberate spinal anaesthetics for adults undergoing general surgery, used 30–40 mL of lidocaine or mepivacaine injected at lumbar levels but did not always achieve TSA.[70] When TSA did occur, unconsciousness was universal and no patient had recollection of surgery despite the absence of general anaesthetic maintenance agents. However, very few of the patients in the cases described had LA doses close to those used for TSA and it

should be anticipated that if unconsciousness occurs it may be brief. To reduce the risk of awareness, anaesthetic drugs should be administered, particularly if the airway has been instrumented or the patient has received neuromuscular blocking drugs to improve intubating conditions. Depth of anaesthesia monitoring should be used in these circumstances if available. Typical neurological symptoms are ascending weakness of the upper limbs and facial numbness.

Cardiovascular effects

Neuraxial anaesthesia causes hypotension in proportion to the level of sympathectomy and is caused by arteriolar and venous dilation.[80,81] As the block ascends, cardiac accelerator fibres are inhibited and there is vagal predominance resulting in bradycardia. The bradycardia facilitates cardiac filling and increases stroke volume and cardiac output. With progressively higher blockade to the brain stem level vagal inhibition occurs and the heart functions as a denervated heart with minimal heart rate variability. Blood is redistributed to the viscera. Total spinal anaesthesia has no direct effect on cardiac inotropy but cardiac function is impaired secondary to hypoxaemia and hypercarbia as a consequence of hypoventilation or apnoea. Hypoxia causes rapid onset of acute systolic and diastolic myocardial dysfunction which worsens with the severity and duration of hypoxia.[82] Hypotension most commonly manifests initially as nausea.

Cardiovascular instability under spinal anaesthesia may also be attributable to reflex bradycardia, triggered by hypovolaemia and a sudden drop in venous return. This requires a different therapeutic approach.[83] Among the mechanisms of bradycardia is activation of low pressure baroceptors in the atria and vena cava, stretch receptors in the myocardium and the Bezold-Jarish reflex in which a paradoxical bradycardia occurs in response to stimulation of mechano-receptors in the left ventricle.[84] These events are more likely in the presence of hypovolaemia. These pathways require a therapeutic approach which requires intravascular volume replacement and anticholinergic drugs.

In experimental TSA in dogs, the haemodynamics were improved by the synergistic effects of administration of oxygen and ventilation.[85] Hypoxia and hypercarbia are normally potent stimuli of catecholamine release which, based on an anaesthetised canine model exposed to n inspired oxygen fraction of 0.9%, is partially attenuated by neuraxial anaesthesia thereby impairing the normal physiological response of tachycardia and hypertension.[86] A similar experimental model indicates that vasopressin contributes to maintenance of blood pressure during neuraxial anaesthesia and its release during concomitant severe hypoxia is not impaired.[87]

Preventative strategies

There are several methods that are proposed to reduce the risk of TSA. Alternative techniques or adjunctive technologies to the conventional loss of resistance technique for epidural space identification have not been shown to reduce the incidence of intrathecal or subdural placement or TSA. Following catheter placement, the first evidence of intrathecal location is positive CSF aspiration either using a syringe or by observation of gravity-dependent flow. The estimated risk of unintentional intrathecal catheter placement after negative aspiration is 1 in 1750 to 1 in 26 490.[88] Saline is difficult to visually distinguish from CSF in the context of a loss of resistance to saline epidural technique. Test papers can be used to check pH and determine the fluid type as the pH of CSF (7.317–7.324) is higher than that of saline (7.0).[89] Bedside glucometry can also be used as CSF contains glucose 2.9 (1.3–5.1) mmol/L.[90] However, glucose concentration progressively rises within epidural injectate, even in the absence of accidental dural puncture, rendering it difficult to distinguish between CSF and epidural injectate after delayed sampling.[91] Pharmacological test dosing with LA is widely used but practice varies considerably.[92] Test doses using large quantities of LA can themselves cause TSA which has led to the use of a loading dose of low concentration LA in lieu of high concentration test doses.[93] Total spinal anaesthesia from high volumes of low concentration injectate was described in NAP 7: two patients had cardiac arrests having received 15–20 mg of bupivacaine.[3] Not all intrathecal placements will be detected using test doses as hypotension is not universal and block onset can be slow.[88] There are no societal guidelines on the composition of an ideal test dose so whatever test dose is chosen, careful observation of the clinical response is essential. This includes a combination of haemodynamic responses, speed of block onset, extent of sensory and motor block and temperature change in the feet. While hypotension is often a manifestation of accidental intrathecal LA administration, it is not inevitable and its absence is not a guarantee of correct epidural catheter positioning as TSA is mainly a respiratory event. As intrathecal medication typically causes early temperature changes in the feet of 6–7°F, an early temperature rise is a sign of intrathecal injection of LA.[94] Thermography offers the potential for objective measurement of temperature change.[95,96]

Catheter aspiration is recommended before all top-ups.[97] When converting labour epidural analgesia to an anaesthetic block for surgery, appropriate monitoring is mandatory. Once anaesthetic doses of LA have been administered, the anaesthetist should remain with the patient, monitor during transport and be prepared to deal with potential complications including TSA.[98] The earliest manifestation of TSA is usually the symptom of difficulty breathing and this symptom generally precedes monitoring changes. Clinical practice is extremely variable in this area.[25,99–101] Recommended precautions include epidural catheter inspection to rule out migration and test dosing, commonly administered in the delivery suite prior to operating room transfer, with the remaining dose given in the operating room.[99,102] A minority of practitioners administer the full dose in the delivery suite.

The recent focus on TSA as a consequence of spinal anaesthesia after an epidural bolus has prompted a number of proposals. These range from considering it to be contraindicated, to no dose modifica-

Table 2
Signs and Symptoms

Symptoms	Respiratory System	Cardiovascular System	Diagnosis
A weak cough, or early signs of dyspnoea	RR ≥ 12–15 per min SpO_2 ≥ 95% Function is atpre-operative status	Hypotension and no bradycardia	High spinal is unlikely
Progressive dyspnoea Weak hand grip strength (C_8/T_1) Can't touch nose (C_5/C_6) Ineffective cough	RR: 12–15 per min SpO_2 ≤95% Function diminished	Hypotension and no bradycardia	Early signs of high spinal anaesthesia
Unable to speak	Hypoventilation SpO_2 ≤ 90% Function poor	Hypotension ± bradycardia*	High spinal likely
Unable to speak	Apnoea	Hypotension ± bradycardia*	High/total spinal established

RR: respiratory rate, SpO_2: oxygen saturation.
From: van Rensberg et al. The management of high spinal anaesthesia in obstetrics: suggested clinical guideline in the South African context.[124]
* Bradycardia is a heart rate ≤60 beats/minute.

tion, to a 20–30% reduction of a standard dose, to the use of a titratable technique such as CSE.[43,99,100,103,104] In a recent OAA survey conducted in the UK, the majority of respondents indicated they would reduce the dose of spinal anaesthetic in the scenario of a failed epidural top up for CS.[101] The most commonly selected dose range was 50–75% of normal. The optimum dose is unknown and high block has been reported with doses as low as 7.5 mg bupivacaine, although in the majority of cases it was higher.[37–46,105] The greatest risk of TSA appears to be related to a shorter time interval between the most recent epidural top up and spinal administration.[1] It seems prudent to consider delaying anaesthesia procedures by 30 min in non-urgent cases although there is no evidence for a safer time frame. The obvious disadvantage of smaller doses is a reduction in the duration of effective anaesthesia. Additional strategies include avoidance of the use of poorly functioning labour epidurals and the elective use of general anaesthesia if an epidural top up has failed.[100] Finally, some clinicians use patient positioning after spinal injection as a means of limiting block height.[104]

Treatment

A high block should be differentiated from TSA as it may not mandate airway intervention or expedited delivery provided the mother is stable and there is no fetal distress (Table 2, Fig. 3). The priorities in

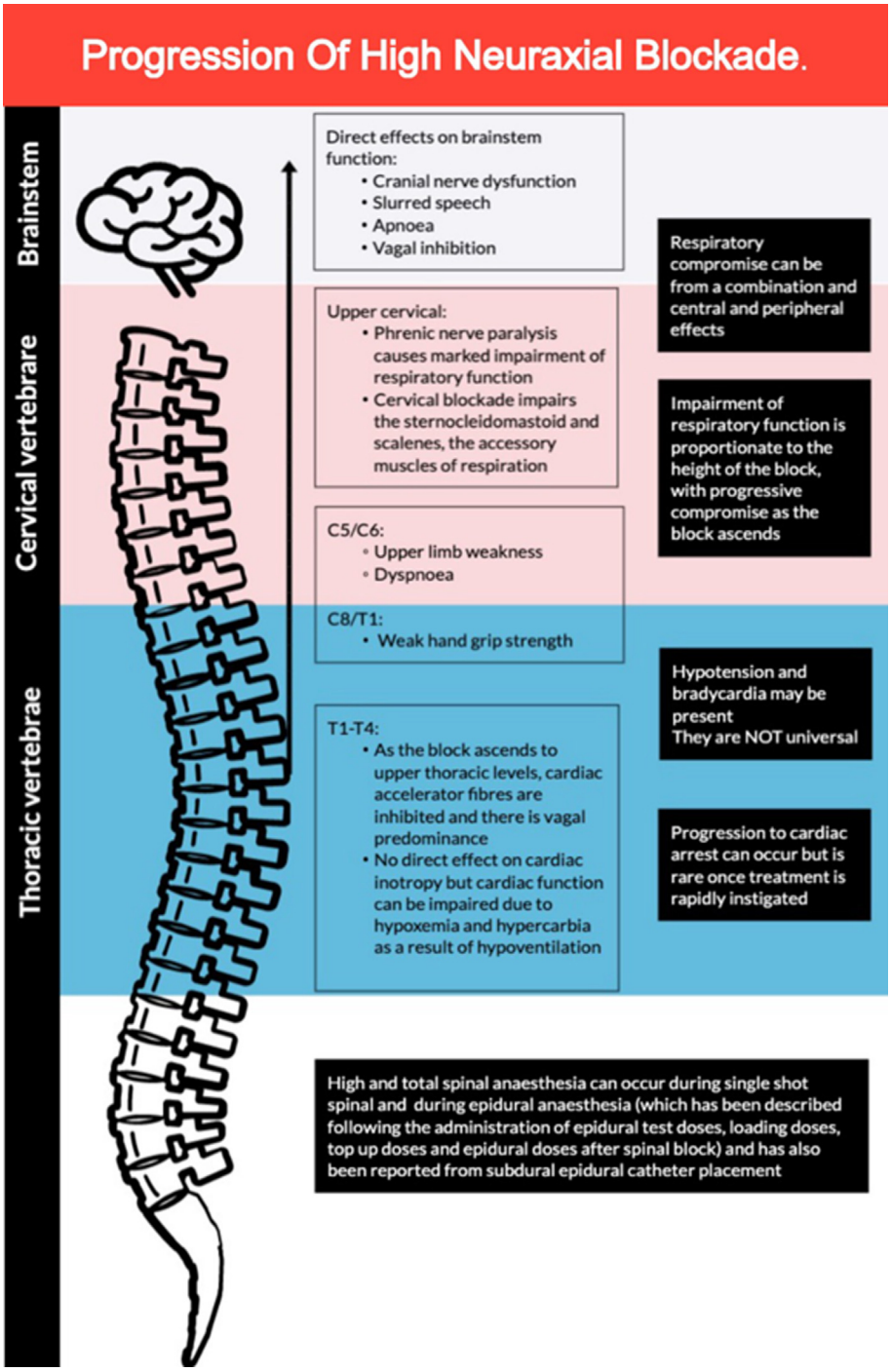

Fig. 3. Infographic

managing established or evolving TSA are restoration or maintenance of oxygenation and blood pressure. Head up positioning should be considered if hyperbaric LA has been administered. No further epidural LA should be administered. In an evolving block a patient will be conscious and symptomatic so deserves explanation and reassurance. The differential diagnosis of TSA includes severe aortocaval compression, reflex bradyarrythmia, anaphylaxis, LA toxicity, emboli (thrombotic, amniotic and air), seizures and intracranial bleeding. The delivery suite and operating room should be equipped to facilitate airway management and resuscitation.[101] Ventilation and oxygen (the highest available oxygen concentration) administration are the highest priority interventions.[85,106] Apnoeic patients should be initially managed by face mask ventilation with 100% oxygen followed by tracheal intubation. As a result of preserved upper airway reflexes, administration of neuromuscular blocking drugs may be necessary to facilitate tracheal intubation despite apparent loss of consciousness.[30] Mechanical ventilation should be maintained until recovery of neuromuscular function. This duration is variable, with longer periods of ventilation required when larger doses of medication were administered intrathecally.

Hypotension and bradycardia are common but not universal and are not generally refractory to treatment. Progression to cardiac arrest is rare once adequate oxygenation is achieved. If the patient is undelivered, in conjunction with vasopressors, aortocaval compression should be relieved by left tilting or left uterine displacement. The optimum vasopressor is not clear but ephedrine appeared to be effective in conventional doses in the published reports. In studies of healthy non-pregnant volunteers, ephedrine, methoxamine and atropine were compared to treat spinal-induced hypotension.[107] Atropine had no effect on blood pressure but the increase in heart rate was associated with a reduction in stroke volume and no increase in cardiac output, so atropine alone will not increase blood pressure in TSA.[108] Methoxamine increased blood pressure via a large increase in total peripheral resistance and a small increase in stroke volume, accompanied by a large decrease in heart rate and net reduction in cardiac output. Ephedrine increased blood pressure, peripheral resistance and cardiac output.[107] The role of phenylephrine in resuscitation during TSA is uncertain and there are no evidence-based guidelines, but it should be considered in patients who are hypotensive without bradycardia. Ephedrine increases blood pressure via increased total peripheral resistance, normalisation of stroke volume, increased heart rate and cardiac output.[107] Total spinal anaesthesia impairs the haemodynamic response to epinephrine and norepinephrine and progressive dose increases may be required to achieve normotension.[73,109] In the event of cardiac arrest, TSA has been shown to both reduce coronary artery perfusion pressure and reduce responsiveness to intravenous epinephrine during cardiopulmonary resuscitation (CPR) in a canine model and may require dose escalation. Vasopressin increases coronary perfusion pressure during CPR in a porcine model of TSA-induced cardiac arrest, with a more prolonged effect and less metabolic acidosis in the post resuscitation phase, but has no established clinical role.[115]

These experimental observations, in combination with detailed clinical descriptions, signify the importance of maintaining oxygenation during evolving high spinal anaesthesia. Airway management may be required when the airway is compromised or consciousness is impaired. This includes tracheal intubation and the use of anaesthetic drugs according to the degree of impairment of consciousness and preservation of airway reflexes. Where the airway and ventilation are supported early, hypotension may not occur and if it does, is usually responsive to ephedrine.

CSF lavage has been described in a small number of cases reports as an immediate treatment when large volume intrathecal LA administration was suspected. Ting and Tsui treated a labouring woman with a high block after an epidural top up by aspiration of a total of 40 mL of CSF in 10 mL increments via the intrathecal catheter, and replaced it with the same volume of sterile saline, and reported rapid patient recovery.[110] This technique is more frequently described after accidental intrathecal injection of chemotherapeutic agents.[111,112] Accidental injection of sodium thiopentone, propofol and tranexamic acid have also been described in anaesthetic cases.[113–115] Isolated case reports of intralipid administration for the treatment of TSA exist but are not an adequate basis to support its use at present.[116].

Resuscitation standards and societal recommendations

A consensus document written by European Obstetric Anaesthesiologists was published in 2020.[117–123] This stipulates that resuscitation equipment including airway equipment and medication should be available in delivery suites. It also states that obstetric patients should be under periodic surveillance by the anaesthesiologist, looking for signs of catheter migration (intrathecal, subdural or intravascular) and under the midwives' and/or nurses' direct and continuous surveillance. It advises that in case of a need for top-up, safety measures should be taken to avoid intravascular or intrathecal injection and that if an accidental dural puncture has occurred during labour epidural analgesia, a local protocol is advised. Local written protocols are recommended for emergencies including high neuraxial block. There are no specific recommendations for treatment of cardiac arrest due to TSA in consensus guidelines from the European Society of Anesthesiology, the European Resuscitation Council, the Perioperative Cardiac Arrest Consortium or International Consensus groups.[114,124]

Conclusion

This review identified all reported cases of TSA in the medical literature and aimed to explain the epidemiology and pathophysiology. Total spinal anaesthesia is a persisting clinical concern and can arise as a complication of all forms of neuraxial anaesthesia and analgesia with spinal anaesthesia after failed epidural anaesthesia a particular area of risk. Good clinical outcomes can be achieved with preparedness and prompt respiratory and cardiovascular support.

CRediT authorship contribution statement

M. Radwan: Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **L. O'Carroll:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **C.L. McCaul:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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Appendix

Search terms

The terms were –Anaesthesia Spinal AND Obstetric Labour Complications; Anaesthesia, Spinal/adverse effects, Mortality AND Obstetric Labor Complications: Anaesthesia, Spinal/adverse effects, Instrum, Mortality: AND Obstetric Complications Labor: Anaesthesia, Spinal, Adverse effects, Mortality: Obstetrics: Anaesthesia, Epidural, Adverse Effects, Mortality: AND Obstetric Labour Complications.

Analysis of the initial abstracts generated further search terms which we used to search PubMed, Web of Science and Google Scholar for publications. The search terms were as follows –(" Total Spinal" OR "High Spinal" AND Anaesthesia) AND (Obstetric OR Labour OR Cae-

sarean OR Subdural OR Pregnancy) AND (Respiratory OR Distress OR Dyspnoea OR Incident OR Complications OR Hemodynamic OR Apnoea OR Claim OR Maternal OR Survey).

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