Spinal Anesthetic Block Failure due to the Hyperbaric Nature of 2% Chloroprocaine Local Anesthetic

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Introduction

Spinal anesthesia is not a 100% certain successful technique. Failure rates of 0.72%% to 16.0% have been reported. [1,2,3] The cause of some failures may be due to technical inability to identify the subarachnoid space and that is obvious at the moment and understandable. The explanation for spinal block failure that occurs despite apparent technically correct injection of the correct drug can be mystifying.

The under reporting of specific cases with block failure and mechanisms of failure may reflect a general attitude that a regional anesthetic failure is although unfortunate, is "normal" and not a complication deserving investigation. A repeat spinal block as a remedy for a failed spinal block may be contraindicated depending on the first drug used due to the risk of neurotoxicity.

The following case report is of a failed spinal block that mystified the anesthesiologist at first but simple assessment provided a clear probable explanation. A following discussion will highlight causes and remedies. The patient gave telephonic consent to present this case on the day after his discharge from hospital.

Case Report

A 58-year-old male arrived for outpatient ambulatory surgery in the early afternoon, to undergo removal of two screws from the lateral side of his right ankle that had been inserted for fractures incurred seven months prior. He was allergic to sulfa drugs. He was a non-smoker. He was using oral opioids for ankle pain, metoclopramide for intermittent nausea, and loperamide for irritable bowel syndrome. He had undergone several uncomplicated general anesthetics for a variety of small surgeries (hernia repair, tonsillectomy), and was otherwise healthy.

However, previous regional and local anesthetic blocks had only been occasionally successful. At the time of the initial injury seven months earlier, emergency room physicians administered a sciatic nerve block that failed. The patient subsequently had a successful 0.75% hyperbaric bupivacaine spinal anesthesia for the surgery, administered by anesthesiologists. The patient reported that when past dentists administered lidocaine to him it often resulted in partial analgesia. He did note though that his current dentist's tooth nerve injections were consistently effective.

For the spinal anesthetic being reported here, anesthesia was induced via a 25 G Whitacre point needle inserted at the L4-5 interspinous space. The patient was in an upright sitting position. The subarachnoid space was at a depth of six centimeters from the skin, and it was identified by clear fluid considered to be cerebrospinal fluid dripping from the needle. Two milliliters of 2% Chloroprocaine was injected. After injection of one milliliter of drug, a half-milliliter of cerebrospinal fluid was aspirated into the needle and then re-injected with the remaining chloroprocaine. After completion of the injection, clear fluid considered to be cerebrospinal fluid still dripped from the back of the needle.

The anesthesiologist made a point of keeping the patient sitting for two additional minutes as per advice from a peer anesthesiologist who had recommended this technique and drug. The clinical goal was to have a short acting spinal anesthetic for foot surgery. The patient was returned to the supine position. After fifteen minutes had passed there was no evidence of sensory anesthesia. Ice applied to the mid-anterior thigh bilaterally produced the same cold sensation as that applying the ice to the upper chest and neck region. The toes were equally able to sense cold. The patient was thought to have slight reduced foot plantar flexion strength, but this was not compared to pre-spinal block strength. In addition the patient could not flex or extend toes bilaterally suggesting a degree of motor block was present. The chloroprocaine ampule of drug used was inspected and it was verified to be the intended drug to be used and corresponding amount of drug had been removed from the ampule. All other drugs in the anesthesiologist's possession had appropriate syringe labels and the expected content volumes. There was nothing to suggest a wrong spinal drug had been injected, as cause of the failed block.

It was decided to induce general anesthesia with mask inhalational anesthesia using sevoflurane vapor and then place a laryngeal mask airway.

The surgery proceeded uneventfully. On emergence the patient was pain free. His spinal block was assessed again about an hour after block insertion. He still had intact sensation for ice induced coldness on the toes and in the mid anterior thigh region. He could move both sides' toes and foot. He however had no sensation at all about his anus and posterior aspect of the scrotum. No other areas were tested.

It was diagnosed that he had a saddle block of the sacral dermatomes.

This is compatible with use of a hyperbaric local anesthetic drug (2% Chloroprocaine) in a patient where subarachnoid injection was made in the sitting position and where the patient was kept in the sitting position for few minutes after injection before reclining to the supine position.

Discussion

Horlocker and Wedel Human reported the density of many local anesthetics adjusted for temperature to match human normal temperature. [30] Increasing the drug temperature from room temperature to 37 degrees centigrade decreases the drug's density. Human cerebrospinal fluid (CSF) has a specific gravity of 1.00063 to 1.00075 at 37 degree centigrade generally, and 1.00030 gram per milliliter in term pregnant woman *a*. [4,5] Preservative free chloroprocaine 2% and 3% solutions have specific gravities of 1.00123 and 1.00257 gm per milliliter respectively, which makes them hyperbaric without any added dextrose. Kopacz investigated the effect of added dextrose to 2% chloroprocaine in volunteers with a crossover spinal blocks protocol . With their technique of patient positioning during and immediately after administration of spinal anesthesia they found adding dextrose to 2% chloroprocaine did not increase the thoracic block extent of T4 seen when using dextrose free 2% chloroprocaine. The group who received the dextrose-enhanced 2% chloroprocaine group however had longer duration sacral block, on the basis of indirect evidence with delayed normalization of bladder function. Accordingly addition of 10% dextrose did not alter the pre-existing hyperbaric characteristics of 2% chloroprocaine significantly.

In this case report the anesthesiologist intentionally kept the patient sitting for a period after injection of the spinal chloroprocaine, on wrong advice. The chloroprocaine shifted to the most dependant part of the subarachnoid sack to only effectively block the lowest sacral spinal nerves supplying the perineum leaving the lumbar nerve roots supplying the legs unblocked. This is called a saddle block. No dextrose had been added to the chloroprocaine. This confirms the known hyperbaric nature of 2% chloroprocaine solution. [29,30]

This patient's substantial history of failed regional anesthesia in the hands of dentists and emergency room physicians may raise the question of resistance to local anesthetic drugs. Sebrechts in 1934 noted apparent differences in resistance to spinal anesthesia between Italians and Anglo-Saxons and proposed the term 'rachi-resistance". [7] A pharmacogenetic mutation of sodium channels associated with reduced lidocaine sensitivity has been described but the frequency or relevance of genetic based local anesthesia resistance in the large population is unknown. [8] In this case report the patient's history of other failed regional anesthesia blocks more likely reflects technical failures of the practitioners involved with the failed nerve blocks, as another different dentist and anesthesiologist produced successful blocks on other occasions.

A failed nerve block is not widely considered a "complication". Regardless a failed block can force a change in anesthesia care plan that can be suboptimal or detrimental to the patient. Textbooks neglect failed spinal anesthesia as a topic or do not consider it a complication. *Spinal And Epidural Anesthesia* by Wong (McGrawhill 2007) offers no discussion or listing of failed spinal anesthesia at all. In the book *Complications In Regional Anesthesia And Pain Medicine* by editors Neal and Rathmell (Saunders 2007), block failure is not regarded as a complication. The only mention made of spinal block failure is incidental in the context of spinal drug maldistribution (to the cauda equina) and the use of repeat doses of chloroprocaine as potential cause of neurotoxicity. The book references work by A Gissen and K Drasner. A Gissen's 1984 editorial speculated on the possible causes of the neural complications then recently observed during chloroprocaine epidural blocks including consideration of inherent drug neurotoxicity. [11] Drasner studied how baricity of various local anesthetic drugs affected the propensity and potential of the drug to pool in the dependant parts of the subarachnoid space such as the cauda equina. [9] In 1991 Drasner recommended NOT repeating a chloroprocaine dose for failed spinal block in case the first dose was in fact administered subarachnoid and the total of the two doses would then exceed safe total dose limits for avoiding neurotoxicity. [10]

The dose of chloroprocaine above which the drug may be neurotoxic in spinal doses is quoted as 60 mg. [11–16] *Complications of Regional Anesthesia* by Finucane (Churchill Livingston 1999) says "it seems unnecessary to list failure (of neuraxial blocks) as a complication . . ." The book however does cover the topic of failed spinal anesthesia in one paragraph, mentioning drug maldistribution and arachnoid cysts as causes of block failure. The book *Regional Anesthesia and Analgesia* by Brown (Saunders 1996) has a chapter on regional anesthesia complications that presents Drasner's recommendations for managing failed spinal anesthesia (see below). More recently in 2009 the subject of failed spinal anesthesia enjoyed its first large review *Failed spinal anaesthesia: mechanisms, management, and prevention* by Fettes. [17] A recent case report by Hoppe of four failed obstetric spinal blocks gives a good summary of anatomical reasons and ligamentous cysts that can cause technical failure. [18] The Fettes' review and Hoppe's case report are recommended reading.

Causes of failed spinal anesthesia can be classified as

1. Successfully injected drugs that are maldistributed relative to the needs of the planned surgery.
2. Unrecognized failed injection of drug, partial or total.
3. Technical failure to enter the subarachnoid space, with no drug injection.
4. Drug errors, as wrong drugs and inappropriate additives.
5. Local anesthetic resistance.
6. Pseudo block failure, due to excessive expectations for speed of block onset.
7. Subdural injection of a spinal dose is conceptually a possible cause of spinal block failure, but has never been reported, recognized or studied in this context of small volume injections.

The evidence that 2% chloroprocaine is potentially neurotoxic comes from anecdotal human case reports, animal studies, and cell studies. Evidence of clinical toxicity is not clear cut. Laboratory evidence of toxicity is indirect and dependant upon study methodologies far removed from replication of clinical practice. Human cases reports associating cauda equina syndrome with use of chloroprocaine epidural anesthesia accumulated in the 80s. [19] One theory was that in these cauda equina syndrome cases large doses of chloroprocaine had transferred to the subarachnoid space. Some research attributed the cauda equina syndrome cases to the additive Sodium bisulphite. Sodium Bisulfite in laboratory studies was shown to have neurotoxicity potential. [20] Research by RS Ravindran in dogs suggested chloroprocaine was neurotoxic itself in the subarachnoid space in a dose related fashion. [21] A similar study in rats by DF Li also suggested 2-chloroprocaine had a dose related neurotoxicity. [22] A study in cats by DJ Ford assessing peripheral nerve toxicity of 2-chloroprocaine and bisulfite suggested that pH of the drug solution as well as bisulfite concentration was critical

in the addition of bisulfite to chloroprocaine to cause evidence of neurotoxicity. Evidence in this last study even suggested that the combination of 2-chloroprocaine with bisulfite could reduce the magnitude of bisulfite's neurotoxicity when administered alone. Masahiko Taniguchi conversely in 2004 clearly showed bisulfite could actually reduce the neurotoxicity of 2-chloroprocaine when used in combination .Taniguchi suggested chloroprocaine was the more neurotoxic single substance, of the two substances, namely sodium bisulfite and chlorprocaine, and that unexpectedly they were least neurotoxic when used as combination. In 2005 the resurgent new popularity of 2-chloroprocaine as replacement for lidocaine in spinal anesthesia evidenced by four human spinal 2-chloroprocaine studies was reviewed and discussed in an editorial by Kenneth Drasner . He stated "there is little doubt that large doses of subarachnoid chloroprocaine . . . can induce permanent neurological injury". We note that comment, and accordingly concur with the recommendation of Drasner from 1991 to limit the maximum dose of chlorprocaine to 60 mg [10]. An apparently clinically failed chloroprocaine spinal block, as in our case reported here, does not exclude the possibility of the drug having been injected subarachnoid and the addition of second full subarachnoid dose could result in a potentially neurotoxic dose of chloroprocaine being administered.

In the initial assessment of failed chloroprocaine spinal block we recommend Drasner's 1991 guideline's with modification. [16] Namely;

1. Visualize Cerebro Spinal Fluid (CSF) before and after injecting spinal drugs. This may be done by observation of spontaneous CSF like clear fluid dripping from the needle or by aspiration of CSF like clear fluid into the syringe.
2. Examine sacral dermatomes as well when assessing any failed spinal block,
3. If a spinal block has failed despite pre- and post-injection visualization of CSF, regard the drugs as actually administered into CSF. This may modify the dose of a repeat spinal block depending in the drug first used. There is no way to assess the fraction of the injected amount of drug actually delivered into the subarachnoid space, in this circumstance, and it should be assumed, for safety purposes, to be the full dose.
4. If chloroprocaine is being used, and repeat injection is considered in the presence of suggestive evidence of correctly injected spinal drugs (CSF observed or saddle block present), reduce the second chloroprocaine dose to stay under a total dose of 60mg. Alternatively switch to using an entirely different drug administered at its own full dose. There are two case reports where a repeated spinal injection of dibucaine local anesthetic likely caused neurotoxicity by exceeding that drug's recommended subarachnoid safe dose , .
5. If CSF was not seen after the spinal drug injection and the spinal block fails, repeat a "full spinal dose" if a saddle block has been excluded. Absence of a saddle block suggests the spinal drug never reach the subarachnoid space at all. Alternatively switch to using an entirely different drug at its own full dose.

A failed spinal block may be an apparent complete failure or only a partial failure. Management of a failed spinal anesthetic could include (i) abandonment of the procedure, (ii) repeat spinal anesthetic, (iii) use of supplementary sedation and analgesia, (iv) conversion to general anesthesia, or (v) addition of distal peripheral nerve blocks. Specific circumstance and patient considerations would determine the wisest course to follow.

A failed spinal block has previously been reported related to use of dextrose enhanced bupivacaine and the sitting position. [27] One series analysis has shown difference in failure rates of 19.4% when using hyperbaric solutions and 2.9% when using isobaric solution within one institution. [28] This suggests isobaric solutions are inherently more reliable. The lowest reported spinal block failure rate of 0.72% was in urological surgery series where intentional saddle blocks using hyperbaric solutions were done for perineal urological procedures. These all suggest that the *unintentional* saddle block is the largest cause of failure after successful intrathecal drug injection, and that avoidance of hyperbaric solutions and sitting position would favor higher success rates with spinal block for non-perineal surgery, for example orthopedic surgery as in this case report. Spinal anesthesia for Caesarean section on the other hand enjoys high success rates with hyperbaric local anesthetic solutions that are gravitationally directed, in a controlled fashion, to the thoracic dermatomes.

In conclusion, it is important to remember that 2-chloroprocaine is hyperbaric relative to human cerebrospinal fluid even without added dextrose, especially since 2-chloroprocaine is being widely promoted currently as a short acting spinal anesthesia drug in ambulatory surgery. [29, 30] Secondly we wish to caution against a second chloroprocaine spinal dose as a means to correct a failed first chloroprocaine spinal anesthetic lest the cauda equina nerve be exposed to a double dose of a potential neurotoxic drug. We however find no reason to discourage use of chloroprocaine spinal anesthesia as a short acting anesthetic, if the above considerations are kept in mind.

Lastly we would argue that any failed nerve block deserves to be considered a "complication" of an intervention. A complication has consequences that can force alternate interventions or therapies to be utilized which may be less favorable for the patient. In addition any outcome (such as failed spinal block) treated as a complication will receive more attention for analysis, discussion, prevention and education, all of which should benefit patients ultimately.

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SUPPLEMENTARY INFORMATION: Time line.
Monitoring initiated 13H45.
Midazolam 2mg administered 13H50.
Spinal block inserted 13H55.
Ketamine 10 mg administered 14H00
Ketamine 15mg administered 14H05
Gas induction at 14H15 due to absence of loss of sensation to cold on both anterior mid thighs compared to cold sensation on chest.
Re-examination in PACU 15H00

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