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A fatal accidental subarachnoid injection of lidocaine and levobupivacaine during a lumbar paravertebral block

Francesco Paolo Busardò [a,*], Luigi Tritapepe [b], Angelo Montana [c], Francesca Indorato [c], Simona Zaami [a], Guido Romano [c]

[a] Department of Anatomical, Histological, Forensic and Orthopaedic Sciences, Sapienza University of Rome, Viale Regina Elena 336, 00161 Rome, Italy
[b] Department of Anesthesiology and Intensive Care, Sapienza University, Rome, Italy
[c] Department "G.F. Ingrassia", Laboratory of Forensic Toxicology, University of Catania, Italy

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ABSTRACT

Paravertebral block (PVB) is the technique of injecting a local anesthetic solution alongside the vertebral column, close to where the spinal nerves emerge, resulting in unilateral somatic and sympathetic nerve blockade. Here is reported a fatal case involving a 60-year-old woman with spondylitis arthropathy, who developed cardiac and respiratory arrest 40 min after receiving an accidental subarachnoid injection (L5-S1 bilaterally) of depomedrol lidocaine and levobupivacaine. A complete autopsy including histological and toxicological analyses was performed in order to establish the cause of death. Liquid/liquid extraction (LLE) and GC–MS analysis were performed according to a previously published method. Lidocaine and bupivacaine were detected both in blood, at concentrations of 14.8 mg/L and 13.3 mg/L respectively, and in cerebrospinal fluid (CSF) at concentrations of 287.1 mg/L and 464.2 mg/L respectively. Both lidocaine and bupivacaine were also detected in the urine. The toxicological findings along with the autopsy allowed us to establish that the accidental subarachnoid injection of lidocaine and levobupivacaine had led to a progressive hypotension and normovolaemic shock caused by a severe ganglionic block, determining the patient's death.

1. Introduction

Paravertebral block (PVB) – performed by Hugo Sellheim in 1905 – is the technique of injecting a local anesthetic solution alongside the vertebral column, close to where the spinal nerves emerge, resulting in unilateral somatic and sympathetic nerve blockade [1].

This method was successively adopted in order to obtain surgical anesthesia. Lumbar PVB was confirmed to be a reliable, easy to perform method of analgesia in chronic, intractable bone pain of neuropathic origin. PVB has also been used to facilitate outpatient surgery and provide an analgesic option in patients where general anesthesia could have adverse effects and where epidural anesthesia may be contraindicated [2].

Here is reported a fatal case involving a 60-year-old woman with spondylitis arthropathy, who developed cardiac and respiratory arrest 40 min after receiving an accidental subarachnoid injection (L5-S1bilaterally) of depomedrol 40 mg, lidocaine 10 mg and levobupivacaine 10 mg.

2. The case

A 60-year old female went to a private clinic to have pain relief treatment for spondylitis arthropathy. Paravertebral block (PVB) was discussed and the patient gave her consent. The physician unintentionally performed a subarachnoid injection (L5-S1 bilaterally) of depomedrol lidocaine and levobupivacaine. After the injection, the patient complained of pain and a burning sensation in the lower limbs, then hypotension and nausea started causing her death 40 min later, despite resuscitation efforts.

PVB was performed with a bilateral paravertebral penetration at the level of L5-S1 space. The needle used was a 25 G Quinke needle and most likely the site of injection was the foraminal space instead of the paravertebral space with subsequent penetration into the intrathecal space. This complication seems to be related to the blinded technique and the main surgical errors were not having immediately recognized the symptoms (pain caused by irritation from intrathecal dexamethasone and motor symptoms of local

* Corresponding author at: Department of Anatomical, Histological, Forensic and Orthopaedic Sciences, Sapienza University of Rome, Viale Regina Elena 336 (00185), Rome, Italy. Tel.: +39 06 49912622; fax: +39 64455335.
E-mail address: fra.busardo@libero.it (F.P. Busardò).

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anesthetic), not having aspirated CSF before injecting and in particular not having prepared an immediate vasopressor therapy to prevent normovolaemic shock.

3. Materials and methods

A complete autopsy including histological and toxicological analyses was performed in order to establish the cause of death.

3.1. Reagents

Mepivacaine, bupivacaine and lidocaine were purchased from Molteni (Milan, Italy); sulphuric acid (98%) and 1-chlorobutane were purchased from Merck (Milan, Italy).

3.2. Extraction and analysis

A liquid/liquid extraction (LLE) was performed according to the procedure for the extraction pathway for strong bases by Moffat et al. [3]. Sample preparation was performed as follows: to 1 mL blood sample, 100 μL internal standard (mepivacaine 10 μg/mL) and 2 mL of saturated sodium borate (pH to 12) were added, mixed, 8 mL 1-chlorobutane were added, then centrifuged (3000 rpm for 10 min). The organic layer was collected and transferred to second tube and 3 mL of sulfuric acid (0.1 mol/L) was added. After centrifugation, the aqueous layer was removed and 0.4 mL sodium hydroxide (2 mol/L) and 3 mL 1-chlorobutane were added. The aliquot was mixed and centrifuged, then the aqueous layer was discarded and the organic layer was transferred to a 3 mL conical tube and evaporated to dryness under nitrogen at 60 °C. The residue was reconstituted in 50 μL 1-chlorobutane and transferred into autosampler vial and 1 μL were injected into the GC–MS system.

3.3. Gas chromatography–mass spectrometry

The GC–MS analyses were performed on an Agilent HP 6890N GC coupled with an Agilent MSD 5973. The gas chromatograph was fitted with a EVDX-5MS Agilent column (25 m × 0.20 mm i.d., 0.33 μm film thickness). Helium was used as the carrier gas with a head pressure of 25 p.s.i. The following settings were used for the GC–MS system: the GC column temperature program was set at 100 °C (held for 1 min), increased at 30 °C/min to 220 °C, and then ramped at 5 °C/min to 300 °C. The injection temperature was 280 °C, the interface temperature was 280 °C and the source temperature was 150 °C. The following MS conditions were used: the instrument was tuned in the electron impact (EI) mode using an electron energy of 70 eV and the data were acquired in SCAN mode; data was collected over a mass range of m/z 42–550. The method has been validated according to the guidelines of Peters et al. [4].

4. Results

4.1. Autopsy findings

Autopsy was performed 48 h after death: external examination was unremarkable. During the autopsy a tract of the spinal column (L3-S1) was removed and the CSF was collected for subsequent toxicological analysis. The autopsy revealed hyper-inflated, over-expanded, ballooned lungs occupying the whole thoracic cavity. A mark left by a needle puncture involving the arachnoid at L5-S1 level was found surrounded by a slight hemorrhagic infiltration. The spinal cord was unremarkable.

Other organs showed only an intense vascular congestion. Histological examination of the samples revealed generalized stasis.

Table 1
Lidocaine and bupivacaine concentrations found in blood, CSF and urine (mg/L).

Biological samples	Lidocaine	Bupivacaine
Blood	14.8	13.3
Cerebrospinal fluid	287.1	464.2
Urine	5.8	3.9

4.2. Toxicological findings

Lidocaine and bupivacaine were detected in the blood, CSF and urine samples. All results are shown in Table 1, whereas in Fig. 1 the chromatograms of the analysis performed on blood and cerebrospinal fluid specimens are reported. Neither other drugs nor alcohol were detected.

5. Discussion and conclusions

The high concentrations of both anesthetics in the CSF confirmed the accidental subarachnoid injection. Local anesthetics (LAs) are widely used for local or regional anesthesia techniques. Lidocaine and bupivacaine have been in use for more than 50 years and, more recently, drugs such as mepivacaine and levobupivacaine have been launched on the market [5,6]. Because of the development of regional anesthesia techniques over the past few years, the use of LAs is increasing worldwide. However, prospective studies have provided evidence of significant patient morbidity and mortality associated with the use of these drugs [7–9]. The most common adverse drug reactions (ADRs) to LAs are neurological (seizures) and cardiac (conduction disorders, cardiac arrests) [10–12].

Mixtures of lidocaine with a long-acting local anesthetic are commonly used for peripheral nerve block. Little data is available regarding the safety, efficacy, or pharmacokinetics of mixtures of local anesthetics.

Summing up, local anesthetics are all potentially neurotoxic, lidocaine seems to be more neurotoxic than levobupivacaine at clinically relevant concentrations.

Levobupivacaine reversibly blocks the transmission of action potential in sensory, motor and sympathetic nervous fibers by inhibiting the passage of sodium through voltage-sensitive ion channels in the neuronal membrane just like all local anesthetics. Whereas the inhibitory action should only be localized at the site of administration, excessive doses or accidental intravascular injections may lead to activity at the level of other ion channels in excitable tissues followed by unwanted central nervous and cardiovascular adverse effects. The current pharmacodynamics evidence from animal and human studies suggests that levobupivacaine has a potentially greater margin of safety than racemic bupivacaine [13].

Hypotension has an incidence in the elderly of between 25% and 69%. The elderly run a higher risk of developing long-term complications from hypotension together with an increased incidence of systemic disease. Hypotension during subarachnoid block results primarily from a blockade of the sympathetic nervous system, which causes a decrease in systemic vascular resistance and cardiac output [5,14,15].

Systemic vascular resistance decreases consequently to the reduction in the sympathetic tone of the arterial circulation which causes peripheral arterial vasodilatation, the extent of which depends on the number of spinal segments blocked. Changes in cardiac output are more complicated in their origin, depending on both stroke volume and heart rate. Sympathetic block also causes venodilatation with pooling of blood in the large veins of the abdomen and lower limbs, which causes a reduction in preloading the heart and a decrease in stroke volume. Furthermore, spinal anesthesia may lead to myocardial ischemia and to a reduction of