

Successful but prolonged resuscitation after local anesthetic-induced cardiac arrest : is clonidine effective ?

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Abstract : Local anesthetics when injected intravascularly result in serious cardiac complications including therapy-resistant cardiac arrest.

We report a case of cardiac arrest after lumbar plexus block using a combination of 0.5% bupivacaine and 2% lidocaine with epinephrine (1:200.000). Resuscitation was performed by a combination of chest compression, repeated external countershocks and i.v.epinephrine. Clonidine had poor effect.

The whole resuscitation required 90 minutes. The patient was discharged four days later without any sequelae. Blood sampling at 10 minutes showed a concentration of 2.02 mg/l lidocaine and 0.87 mg/l bupivacaine.

Prolonged resuscitation is necessary in local anesthetic-induced cardiac arrest.

Key words : bupivacaine ; clonidine ; local anesthetic ; regional anesthesia ; cardiac toxicity ; resuscitation.

INTRODUCTION

Local anesthetics (LAs), especially bupivacaine, when injected intravascularly result in serious cardiac complications (1-3). We report a case of cardiac arrest after a lumbar plexus block using a combination of 0.5% bupivacaine and 2% lidocaine with epinephrine (1:200.000).

CASE REPORT

A 73-yr-old man, 70 kg ASA III was scheduled for left total hip replacement using the combination of lumbar plexus blockade and general anesthesia. Previously he had undergone several operations, including coronary artery by-pass graft surgery. Anamnesis did not reveal any problems caused by general anesthesia during these operations. His chronic medication consisted of 80 mg metoprolol daily. His preoperative anesthetic examination including cardiologic consultation with electrocardiogram (ECG) did not reveal any contraindication for the intended procedure. After oral premedication with 0.25 mg alprazolam he was

taken to the operating room. Standard monitors (three-lead electrocardiogram, pulse oxymeter and body pressure cuff) and an i.v. line were placed. Subsequently the patient was turned to the lateral decubitus position so that a posterior lumbar plexus blockade could be performed. For this purpose a 21 G 100 mm Uniplex needle (Pajunk, Gelsingen, Germany) was placed at the L3-L4 level under sterile conditions. The lumbar plexus was localized with use of a nerve stimulator at the first attempt using the Winnie's classical approach (4). Repeated aspiration for blood or cerebrospinal fluid was negative and a 2 ml test dose of a 30 ml mixture(1:1) of 0.5% bupivacaine (75 mg) combined with 2% lidocaine (300 mg) with epinephrine 1:200.000 was administered. Three boluses of 4 ml were infused uneventfully. After completion of the fourth dose, convulsions occurred. At that moment the patient had received 18 milliliters of the solution corresponding with 45 mg bupivacaine and 180 mg lidocaine. He was immediately turned to the supine position. Pure oxygen was administered by face-mask ventilation and 400 mg thiopental was slowly infused intravenously. Within one minute the convulsions stopped. The patient was tracheally intubated and manually ventilated with 100% oxygen. The patient's cardiac rhythm was normal at the beginning of the infusion, except for a supraventricular tachycardia (150 bpm). Three minutes later, his heart rhythm suddenly changed into ventricular tachycardia, immediately followed by ventricular fibrillation and asystoly. At the same time, his arterial pressure was not measurable noninvasively and

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no carotid pulse was perceived. After a precordial thump, chest compressions were started. At 10 min, venous blood was sampled for measurement of local anesthetic plasma concentrations. The continuous ECG showed ventricular fibrillation which was treated by three repeated external defibrillation shocks (250 J). These shocks did not enable a return to ventricular tachycardia. The intravenous administration of 150 µg of clonidine resolved the ventricular fibrillation with a return to a supraventricular rhythm but only temporarily. At that time, 5 µg/kg/min dobutamine was also infused to maintain his arterial pressure at 95/50 mmHg and oxygen saturation around 92%. Few minutes later, the ECG showed the reappearance of ectopic ventricular extrasystoles. The patient then had a second episode of ventricular fibrillation followed by complete asystoly. Repeated injections of epinephrine to reach a total dose of 2 mg were necessary to restore his circulation. The treatment of his ventricular fibrillation required 3 other external defibrillation shocks (250 J). The subsequent ventricular tachycardia was converted, as previously described, into a supraventricular rhythm with a second dose of .150 µg clonidine. A third episode of asystoly was treated with 3 mg of epinephrine completed with a continuous infusion of 1 mg per hour. The entire resuscitation, including continuous chest compression, until hemodynamic stability was restored (arterial blood pressure 105/60mmHg and oxygen saturation 96%) and without dysrhythmia, lasted 90 minutes. By this time the patient had received 1000 ml of Ringer's lactate solution and 500 ml of NaCl 0.9%. He was sedated with midazolam (10 mg/h). One hour after resuscitation his arterial blood gas was normal when he was admitted into the intensive care unit and tracheally extubated a few hours later. Troponin levels remained within normal limits. Venous blood sampling performed at 10 minutes after the start of resuscitation showed a local anesthetic concentration of 2.02 mg/l lidocaine and 0.87 mg/l bupivacaine. The patient was discharged four days later without any cardiac or neurologic sequelae. He was operated uneventfully, three months later, under general anesthesia combined with a postoperative femoral catheter. The preoperative check-up did not show any evidence of cardiac sequelae.

DISCUSSION

The risk of accidental intravascular injection and consequent acute toxicity is ever present with

most neural blockade techniques (2). The severity of cardiovascular and central nervous system (CNS) toxicity is directly related to LA potency, dose, and rate of administration. LAs block the propagation of impulses along nerve fibers due to the inactivation of voltage-gated sodium channels which initiate the action potential. They are blocked by different toxins such as tetrodotoxin on the outside of the cell and by LAs at the cytosolic side of the phospholipidic membrane (3, 5). More precisely, LAs cross the membrane in their unionised free base form, and then diffuse in the cytoplasm in their ionized form to mechanically block the pore of the channel by binding to a specific amino-acid inside the pore. LAs bind differently to the sodium channel depending of the state of the channel. A phasic block also called frequency-dependent or rate-dependent block is superimposed to a basal block (tonic block). When the frequency of stimulation increases, the molecule cannot unbind from the channel and the intensity of the block increases. LAs also block potassium and calcium channels at concentrations slightly higher than those required to block sodium channels (7).

Intravascular administration of bupivacaine may result in cardiac arrest, because it binds rapidly to the sodium channel in a "fast in - slow out" manner. This relates to depression of the conduction system of the heart leading to decreased cardiac output, heart block, hypotension, bradycardia and sometimes ventricular arrhythmias e.g. ventricular fibrillation, ventricular tachycardia and cardiac arrest. These cardiac effects will normally accompany severe CNS effects but sometimes cardiac arrest can occur without accompanying CNS effects. Thus, cardiac resuscitation is extremely difficult and may become successful only after the bupivacaine has dissociated from the sodium channel and is metabolized (7-9). Beta-adrenergic blockers, as in our patient, may enhance bupivacaine cardiotoxicity (10), but in patients with a previous history of coronary disease, many arguments support to maintain these until anesthetic induction. On the other hand, lidocaine in combination with bupivacaine may also have enhanced the toxicity even if the plasmatic concentration of lidocaine was below the theoretical toxic 3 mg/L and the one of bupivacaine below 1.6 mg/L : such a synergistic effect has to be considered (11).

Treatment of local anesthetic-induced cardiac arrest includes resuscitation measures i.e. oxygenation, cardiac massage, and epinephrine. Epinephrine should be injected in small incremental boluses starting with 2-4 µg/kg. If ventricular

fibrillation persists, defibrillation (2-4 Joule/kg) must be performed. In the case of bupivacaine-induced toxicity, final success may occur after a prolonged resuscitation.

It has been suggested in a preclinical study that clonidine (0.01 mg/kg IV) and dobutamine (5 µg·kg⁻¹·min⁻¹) could correct bupivacaine-induced cardiac arrest (12). Clonidine reverses the slowing of ventricular conduction velocities induced by bupivacaine, and the combination of clonidine and dobutamine may correct the cardiac disturbances induced by bupivacaine in anesthetized dogs. A nearly similar case with a transitory effect of the first dose and a definitively successful second dose was reported by PHAM DANG *et al.* (13). Their patient scheduled for total hip arthroplasty was still anesthetised and under controlled ventilation at the time of bupivacaine administration during a lumbar plexus block performed via the posterior approach. Ventricular dysrhythmia and seizures occurred five minutes after the injection of 30 mL of 0.5% bupivacaine with 1:200.000 epinephrine. Normal cardiac activity and stable hemodynamic conditions were restored after one hour of resuscitation including 15 defibrillation shocks and administration of epinephrine up to 40 mg and two doses of 150 µg of clonidine (13).

In another case report, a patient with pre-existing heart failure undergoing an orthopedic surgical procedure, a mixture of 75 mg bupivacaine and 15 µg clonidine was administered accidentally by the intravenous route. He immediately developed nodal rhythm with extreme bradycardia, severe shock and convulsions. Following 75 µg clonidine iv, arterial pressure rose to 90/70 and heart rate to 90 min. Cardiac rhythm was converted to a sinus rhythm with first degree atrio-ventricular block. Epinephrine and dobutamine were effective to treat myocardial depression (14).

In another preclinical study, pre-treatment with clonidine protected the effects of ropivacaine cardiotoxicity and increased the success rate of resuscitation, though it did not affect bupivacaine toxicity (15). In our patient, however repeated administration of clonidine converted ventricular fibrillation into a supraventricular rhythm, but this effect remained transitory, and was not enhanced by dobutamine. Nevertheless no ventricular fibrillation occurred again after the second dose of clonidine.

One report stated that cardiopulmonary bypass was initiated to aid in the patient's recovery (16). Several recent reports of successful infusion of lipidic solution (Intralipid®) to treat severe local anesthetic-induced toxicity may open new horizons

to reduce these complications (17-20) but such a solution was not used in this case because it was not available in the orthopedic unit. Lipidic therapy acts by challenging with bupivacaine at the sodium channels: 150 ml of the solution is infused intravenously after which a further 350 ml are infused till the restoration of the normal cardiac rhythm.

It is noteworthy that in a previous large-scale French survey dedicated to regional anesthesia, posterior lumbar plexus blockade was associated with frequent and serious complications (2). As bupivacaine may be associated with more difficult resuscitation than recently developed LAs (21-23) this may be an argument to dissuade the further use of bupivacaine in peripheral single-shot blockade.

In conclusion, prolonged resuscitation may be necessary when intravascular bupivacaine injection occurs because of the "fast-in slow-out" effect of bupivacaine. On the other hand, during a regional anesthetic procedure, prolonging the speed of administration of LA from 1 to 3 minutes is necessary and may decrease the maximal concentration obtained. In addition, giving fractionated doses may be advantageous because this enables the anesthesiologist to timely interrupt the administration of the drug if signs or symptoms of toxicity occur. The use of ultrasound guidance may be solution to avoid such problems.

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