Continuous peripheral nerve catheters and regional analgesia in pregnancy – a brief review of safety

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Abstract

Continuous regional anesthetic (CRA) techniques are becoming increasingly more common, as the safety and efficacy of the technique, and the lower cost associated with more rapid hospital discharge, become drivers of healthcare change. This is particularly applicable to ambulatory CRA techniques, in which patients are discharged from the hospital with regional anesthesia indwelling catheters and continuous local anesthetic infusion pumps. Because these techniques may be used in clinical settings in which little, if any, safety research has been performed to support such use, data compiled from previous studies have been applied to settings such as pregnancy, which pose particular safety concerns to both mother and fetus.

Keywords: continuous regional anesthesia; local anesthetic toxicity; pregnancy

Introduction

Continuous regional analgesia (CRA), initially practiced in only a few academic centers, is enjoying increased utilization, as evidence of increased superiority over traditional analgesic techniques is reported [1]. Procedures previously requiring hospitalization for anticipated severe pain such as major shoulder surgery are now commonly performed as ambulatory or 23-hour procedures due to the improved analgesia accorded by CRA techniques. As the frequency of ambulatory procedures (and CRA) has increased, guidelines for patient eligibility for ambulatory discharge have been published [2]. These guidelines, however, have not addressed the safety of CRA during pregnancy. While it may seem that pregnancy may be an attractive consideration for CRA by avoiding general anesthesia and the administration of systemic opioids, pharmacologic considerations suggest caution against indiscriminate use of CRA during pregnancy. Pregnancy presents a unique circumstance of ongoing dynamic physiologic changes affecting both mother and fetus. It is important that the practitioner be aware of these changes and their implications for the safe practice of regional anesthetic procedures. It is understood that elective surgery is rarely recommended during pregnancy and that concerns regarding CRA apply to emergency situations such as major fractures and other trauma.

Risk of LA toxicity during pregnancy

Central neuraxial infusions of local anesthetic (LA) used during pregnancy are usually combined with opioids, allowing significant reduction in LA dose, and thus such infusions are not usually associated with LA toxicity. Unlike central neuraxial infusions, chronic peripheral neural infusions usually contain only LA, and therefore require higher doses, which may enhance the potential for LA toxicity.

There have been case reports of single-injection (“single-shot”) femoral, sciatic, supraclavicular, and stellate ganglion blocks performed in parturients without significant complication to either mother or
protein that plays a greater role in supratherapeutic albumin represents a high-capacity, low-affinity binding property of AGP, possibility of LA systemic toxicity. In contrast to the binding of AGP to buffer the LA is exceeded, free fractioning the safety margin of LA infusions. If the capacity of AGP levels are reduced significantly, thereby decreasing LA toxicity from chronic LA infusions. In pregnancy, is considered one of the primary buffers to prevent them, AGP has a high affinity for binding LA, and thus neutral lipophilic drugs, have been described. Among the activities of possible physiological significance, such as the ability to bind and carry numerous basic and neutral lipophilic drugs, have been described. Among them, AGP has a high affinity for binding LA, and thus is considered one of the primary buffers to prevent LA toxicity from chronic LA infusions. In pregnancy, AGP levels are reduced significantly, thereby decreasing the safety margin of LA infusions. If the capacity of AGP to buffer the LA is exceeded, free fraction levels of LA increase dramatically, creating the possibility of LA systemic toxicity. In contrast to the high-affinity, low-capacity binding properties of AGP, albumin represents a high-capacity, low-affinity binding protein that plays a greater role in supratherapeutic plasma concentrations of LA. Additionally, protein binding of LA, particularly bupivacaine, is significantly decreased in pregnancy, with implications of possible enhanced toxicity. For highly protein-bound drugs such as ropivacaine and bupivacaine, small changes in protein binding will have significant effects on the unbound concentration. There are many pathological conditions associated with pregnancy that may affect renal and hepatic function, thereby altering the metabolism of LA. The beta half-life (elimination) of bupivacaine in parturients at term is up to 9 hours, compared with a value of 3.5 hours in non-pregnancy.

The placental transfer of bupivacaine and ropivacaine has been demonstrated to be similar using a dual-perfused, single cotyledon human placental model. When fetal pH perfusate was adjusted to simulate fetal acidemia, maternal-to-fetal transfer of ropivacaine increased. This is consistent with what was observed previously with bupivacaine. In this model, it was shown that the increase in ropivacaine transfer was due to enhanced transfer, rather than accumulation. This occurred despite ropivacaine’s lower lipid solubility. Both ropivacaine and bupivacaine appear to be sequestered in the placenta, and this may represent a source of continued fetal exposure, even after maternal concentration of local anesthetic decreases.

It also has been determined that preterm neonates have 50% less alpha-1 acid glycoprotein than term neonates, who in turn have significantly less AGP than infants. The concentration of AGP in a term neonate is 37% of maternal values. The implications of these findings are that the fetus, in varying levels of development, has less protein buffer to protect against potential LA toxicity. Serum proteins also differ qualitatively with age. It has been reported that protein binding in neonates is qualitatively less than in infants. These findings have implications for potential LA toxicity in the developing fetus. The beta half-life of bupivacaine in neonates ranges from 2.5 to 18 hours, with implications in the fetus of possible LA accumulation.

Pathological conditions associated with pregnancy can result in varying degrees of uteroplacental insufficiency resulting in fetal asphyxia. Animal models of fetal asphyxia have determined that significantly less LA is required to induce central nervous and cardiac toxicity, due in part to enhance cerebral and coronary blood flow during asphyxia. Intracellular accumulation of LA due to ion trapping also occurs during asphyxia. Additionally, acidosis results in decreased serum protein binding of LA.

Clinically acceptable doses of bupivacaine during chronic paravertebral infusions in nonpregnant patients have resulted in LA toxicity. In military trauma patients receiving perineural infusions, serum ropiva-
caine concentrations were found to be in the toxic range in 2 of the 15 patients studied [24].

There are no data documenting blood levels during chronic infusions of LA following peripheral blocks in pregnant patients. The previously discussed hormonal effects, which result in decreased protein binding and alpha-1 acid glycoprotein (AGP) levels, suggest necessary dose reduction if any chronic LA infusion is to be entertained.

Treatment of LA toxicity. The effect of lipid emulsion infusion

Whenever LA toxicity is suspected in either mother or infant, administration of intravenous lipid emulsion should begin as soon as possible, concurrent with supportive therapy. A bolus of 1.5 mL/kg of 20% lipid emulsion should be administered over 1 minute followed by an infusion of 0.25 mL/kg/min for at least 10 minutes after attaining circulatory stability [25, 26]. If there is no clinical improvement after 5 minutes, a second bolus should be given followed by a doubled infusion rate of 0.5 mL/kg/min. Additionally, preparation for an expeditious Cesarean delivery should be considered. There is only one case report of lipid resuscitation during pregnancy, involving an 18-year-old parturient who developed bupivacaine toxicity; a favorable outcome was reported for both mother and infant after initiating lipid therapy prior to Cesarean section [27]. The mother regained consciousness within 30 seconds of the lipid administration. Whether or not the lipid infusion crosses the placenta in significant amounts is currently unknown. In a study of 20 pregnant patients receiving total parenteral nutrition (TPN) with lipid emulsion, there were no untoward fetal effects. Normal-appearing placentae were observed in these patients after delivery. However, there is a single report of a 31-year-old woman who, after receiving TPN for 8 weeks, suffered an intrauterine death [28]. In this patient, placental fat deposits, which may have been implicated in the fetal demise, were observed. It appears that in the acute setting, lipid emulsion is relatively safe to both mother and infant, and possible placental lipid transfer should not be a detractor at the time of emergent resuscitation from LA toxicity.

Conclusion

The possible deleterious effect of chronic maternal LA infusion on the fetus cannot be understated. Decreased alpha-1 acid glycoprotein (AGP) levels, decreased protein binding, and less physiological adaptation to stress place the fetus at an increased risk of LA toxicity. Until data are available that document the safety of chronic LA infusions in pregnancy, it is recommended that single-injection blocks or very short-term infusions of LA with peripheral nerve catheters be utilized, particularly in an unmonitored environment.

Conflict of interest

Nothing to declare

References

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Cateterle perineurale periferice și analgezia regională continuă în cursul sarcinii – despre siguranța pacientului

Rezumat

Tehnicile anesteziei regionale continue (CRA) devin din ce în ce mai frecvent utilizate, în condițiile în care siguranța și eficiența acestea, costul mai redus și externarea mai rapidă a pacienților au devenit factori determinanți în transformările ce au loc în sistemele de sănătate.
Aceste avantaje sunt evidente în cazul tehnicilor CRA efectuate în chirurgia ambulatorie, în care pacienții sunt externați cu catetere de analgezie regională și cu pompe de perfuzie continuă a anestezicului local. Chiar dacă aceste tehnici regionale continue utilizate în condiții clinice, la pacienți internați, nu au generat studii numeroase privind siguranța pacientului, datele preluate din studii anterioare au fost aplicate și în situații clinice particulare, cum ar fi graviditatea, și au ridicat serioase îndoieli privind siguranța mamei și a fătului.
Cuvinte cheie: anestezie regională continuă, toxicitatea anestezicului local, sarcină