Background and Objectives: Some topics in the clinical management of regional anesthesia in children remain controversial. To evaluate and come to a consensus regarding some of these topics, The European Society of Regional Anaesthesia and Pain Therapy (ESRA) and the American Society of Regional Anaesthesia and Pain Medicine (ASRA) developed a joint committee practice advisory on pediatric regional anesthesia (PRA).

Methods: Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Evidence-based recommendations were based on a systematic search of the literature. In cases where no literature was available, expert opinion was elicited. Experts selected controversial topics in PRA.

Results: The performance of PRA under general anesthesia or deep sedation is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3). Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary (Evidence B4). The use of either air-loss of resistance or saline-loss of resistance techniques is supported by expert opinion, but the literature supporting one technique over the other is sparse and controversial; when used appropriately, each technique may be safely used in children. There are no current evidence-based data that the use of RA increases the risk for acute compartment syndrome or delays its diagnosis in children.

Conclusions: High-level evidence is not yet available for the topics evaluated, and most recommendations are based on Evidence B studies. The ESRA/ASRA recommendations intend to provide guidance for the safe practice of regional anesthesia in children.

METHODS

Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Committee members met in workgroups, and decisions on topics to be addressed were made through consensus. The committee used similar methodology on the generation of practice advisories previously described by the American and European anesthesiology societies. In brief, an evaluation of availability and strength of the evidence was systematically performed. Scientific evidence was obtained by performing a systematic search of literature. All committee members participated in the expert opinion decisions because all involved have had extensive experience (>20 years) on the topic. No other clinician outside of the committee was consulted.

Published reports evaluating the practice of RA for pediatric patients were searched using the National Library of Medicine’s...
In response to those concerns, thought leaders in pediatric anesthesiology opined that it was safe and consistently stated that it was acceptable care to perform PRA under GA/DS in children. Nevertheless, objective data were lacking, and the discussion about the safety of PRA during GA/DS was largely based on opinion and anecdote. A 2008 ASRA practice advisory guideline acknowledged the need for performance of regional blockade under GA or DS in children.

Current Evidence Base for the Safety of PRA Performed During GA/DS

Apart from reports of single-center experiences with regard to PRA, there are currently 4 major large-scale (>10,000 patients per study) multicenter studies available that specifically have focused on the incidence of complications after PRA. A summary of these seminal studies is provided below. None of the studies reported any cases of paralysis after the use of neuraxial anesthesia/analgesia, leading to an incidence (95% confidence interval [95% CI]) of 0 (0%-0.004%) for paralysis.

The first large-scale effort focused on the complications associated with the use of PRA was published by the French-Language Society of Paediatric Anaesthesiologists (ADARPEF) in 1996. At the 38 participating centers, all use of regional anesthesia was prospectively registered during 1 year (May 1993–April 1994), with a special focus on safety issues. There were 24,409 regional anesthetics included in the study, of which 89% were performed under GA. Neuromuscular blocks were the most common; caudal blockade was by far the most common individual block performed. Peripheral blocks and local anesthesia techniques were used in only 38% of the registered cases. The overall complication rate was found to be very low (0.9 per 1000 blocks), but neuraxial blocks were found to have a higher complication rate compared with peripheral techniques (1.5 and 0 per 1000 blocks, respectively). None of the observed complications resulted in long-term disability or medicolegal action (follow-up period of 12 months) (Evidence B2).

The second large-scale effort focused on the complications associated with the use of PRA was conducted by the 2007 UK Prospective National Pediatric Epidural Audit. To quantify the risk associated with the use of pediatric epidural analgesia, the Association of Paediatric Anaesthetists of Great Britain & Ireland undertook a prospective audit within its membership, with the aim to include 10,000 epidural infusions. The audit was performed from 2001 to 2005. If an individual patient complication was recorded, a more detailed 12-month follow-up was undertaken. An expert panel adjudicated complications and graded the severity. A total of 10,633 epidurals in all pediatric age groups were included in the study. All but one were placed under GA. Overall, 96 incidents were reported, with the large majority being classified as minor (1:189). Only 5 incidents were recorded as serious (1 of 2000) and an additional 9 as major (1:1100). One child, who had a drug infusion error, experienced persistent paresthesia still present at the 12-month follow-up (1:10,000). Four patients developed compartment syndrome, but the expert panel judged that there was no delay in diagnosis because of the epidural infusion (Evidence B3).

The third large-scale effort focused on the complications associated with the use of PRA was the 2010 ADARPEF study. In this prospective 1-year study (November 2005–October 2006) including 47 different institutions, a total of 29,870 regional blocks were performed under GA and 1262 regional blocks without concomitant GA. Compared with the earlier ADARPEF study, peripheral nerve blocks were used with increasing frequency (66% peripheral vs 34% neuraxial). However, in children younger than...
3 years, the use of neuraxial and peripheral blocks was similar, whereas, in older children, peripheral nerve blocks were performed 4 times more frequently than neuraxial blocks. The authors did not analyze differences in complications under GA/DS. Only 41 complications were recorded in this study (1.2:1000), and none resulted in long-term sequelae. Similar to the 1996 ADARPEF study, neuraxial blocks were associated with a 6-fold higher incidence of complications (Evidence B3).

The fourth large-scale effort focused on the complications associated with the use of PRA was the 2014 Pediatric Regional Anesthesia Network (PRAN) report.19 To allow for prospective and continuous audit of practice trends as well as the incidence of complications, 6 academic centers in the United States pioneered an Internet-based PRAN database in 2006.20 They reported on 53,564 cases of PRA prospectively collected between 2007 and 2012.19 They were able to demonstrate that performing PRA under GA (with or without neuromuscular blockade [NB]) did not increase the risk of immediate or late complications. The incidence of neurological complications (all of which were minor with 1 exception that resolved) in patients under GA without NB was lower than that seen in any other group: 0.62 of 1000 (CI 0.4–0.92) compared with 2.4 of 1000 (CI 1.6–3.6) in patients under GA with NB, 8.3 of 1000 (4.9–13.3) in sedated and 3.4 of 1000 (CI 0.7–10.0) in awake patients (Evidence B2). Pediatric regional anesthesia was performed in awake patients most commonly in neonates and infants younger than 6 months (n = 290) and teenagers (n = 515); those in which sedation was used included mainly teenagers (n = 2060).

Cautionary Case Reports

A strong evidence base exists supporting the safety of PRA performed under GA/DS. However, this does not ensure that serious complications cannot occur under certain circumstances. Thus, if PRA is performed with the wrong type of equipment or without basic safety precautions, if the operator has insufficient training and/or skills, or if PRA is used in particularly vulnerable patient categories, serious complications may still occur, a fact that may be especially true in association with the use of epidural placement20 (Evidence B3). There were no positive test doses in children; 5) the LA used; and 6) the GA technique used.32

Possible Interfering Factors Specific to Efficacy of the Test Dose in Children

One of the main problems is interpreting the hemodynamic response induced by an IV injection of LA mixed with a small dose of epinephrine.31,32 The following factors have been demonstrated or theorized to alter the reliability of a test dose: 1) the general anesthetic agent used and its dose at the time of injection of the test dose; 2) a higher basal heart rate in infants and small children; 3) a possible age-dependent variation of the reactivity of the cardiovascular system to epinephrine; 4) the premedication received; 5) the LA used; and 6) the GA technique used.32–36

In children under sevoflurane anesthesia, the IV injection of 0.1 mL/kg of an LA solution containing 5 or 2.5 μg/mL epinephrine produces (Evidence B3):

Evidence-Based Conclusions and Clinical Advice

• The performance of PRA under GA/DS is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3).

• The overall risk for complications is 0.66% (95% CI, 0.6%–0.7%), whereas the risk of paralysis is estimated at 0 (95% CI, 0%–0.004%) (Evidence B2 and Evidence B3).

• Despite the reassuring safety of PRA performed under GA/DS, serious complications may still occur. In the event of an unexpected clinical outcome, especially unanticipated motor blockade during continuous postoperative regional block after the use of PRA, a high index of suspicion for neurological injury is warranted and appropriate diagnostic and therapeutic measures must be performed without delay (Evidence B4).

Test Dose and Intravascular Injection

Because differences exist in both the physiological and clinical conditions under which regional anesthetics are administered in children compared with adults, there is considerable controversy and disparity of practice regarding the use of local anesthetic (LA) test doses in children. The epinephrine-containing test dose initially was designed to be used in awake adults who were not receiving β-blocking agents to detect accidental intravascular injection during epidural anesthesia.20 In an awake adult, the injection of 3 mL of an LA solution containing 15 μg epinephrine produces hemodynamic effects (mainly tachycardia) if injected intravascularly. Most children, however, have their regional blocks placed while under GA/DS, making the recognition of accidental intravascular injection of LA with epinephrine more difficult.

To detect accidental intravascular injection of an LA solution in children, some practitioners add epinephrine to the LA solution at a concentration of 2.5 or 5 μg/mL, a concentration of 1/400,000 or 1/200,000, respectively. However, a small child’s increased resting heart rate, combined with the fact that most regional blocks are performed under GA/DS, makes that the utility and accuracy of test dosing remain a matter of controversy among pediatric anesthesiologists. The volume of a pediatric test dose was empirically defined as a volume of 0.1 mL/kg of an LA solution containing 5 μg/mL of epinephrine, that is, a dose of 0.5 μg/kg epinephrine.22 This was thought to be sufficient to induce an easily detectable hemodynamic change but also small enough to avoid complications and is supported by a dose-response study.28

Incidence of Accidental Intravenous Injection of LA During Regional Anesthesia in Children

In the first prospective study of ADARPEF, 6 of the 25 complications observed were caused by the accidental intravascular injection of the LA25 (Evidence B3). The second ADARPEF study reported 15 cases of LA toxicity, of which 6 had a negative test dose18 (Evidence B3). In a prospective study of 1100 caudal blocks, the incidence of unintentional vascular puncture was 6.9% and 8 (0.7%) accidental intravascular (IV) injections, all occurring in infants weighing less than 10 kg, were observed23 (Evidence B4).

In another prospective study including 742 epidural caudal or lumbar blocks, a 5.6% incidence of unintentional vascular injections was observed. In addition, in 12 cases out of 36, aspiration for blood had been negative before the injection of the epinephrine-containing LA24 (Evidence B3). In an audited cohort from the PRAN database composed of a total of 26,949 blocks using a test dose, there was a 0.21% incidence of positive test doses, almost all of which occurred during caudal or epidural placement (Evidence B3). There were no positive test doses in other blocks, with the exception of 1 single-injection truncal block, although test doses were less frequently used in non-neuraxial blocks when ultrasound guidance was used.

All the aforementioned studies attested to the importance of dose calculation and staying below the maximum recommended LA dose to avoid complications related to LA toxicity.

Possible Interfering Factors Specific to Efficacy of the Test Dose in Children

One of the main problems is interpreting the hemodynamic response induced by an IV injection of LA mixed with a small dose of epinephrine.31,32 The following factors have been demonstrated or theorized to alter the reliability of a test dose: 1) the general anesthetic agent used and its dose at the time of injection of the test dose; 2) a higher basal heart rate in infants and small children; 3) a possible age-dependent variation of the reactivity of the cardiovascular system to epinephrine; 4) the premedication received; 5) the LA used; and 6) the GA technique used.32–36

In children under sevoflurane anesthesia, the IV injection of 0.1 mL/kg of an LA solution containing 5 or 2.5 μg/mL epinephrine produces (Evidence B3):
1) An early modification (within 20–40 seconds) of the T wave morphology on the electrocardiogram (ECG): the increase in T wave amplitude is more pronounced in younger children. This modification is best observed in leads I, II, III, or V5 on the ECG. The pathophysiology of this modification of the T wave is unknown: it can be observed after the accidental IV injection of a large dose of a mixture of lidocaine and bupivacaine without epinephrine but also when a small dose of epinephrine is injected IV without any LA. 

2) A change in heart rate: this is most often manifested as a heart rate increase of more than 10 beats/min observed somewhat later than the T wave changes. However, bradycardia or other dysrhythmias may be observed, too, and about 25% of patients may not demonstrate any change in rate.

3) A transient increase in systolic blood pressure: this can be missed during intermittent noninvasive measurement of blood pressure, as is usually the case in routine pediatric anesthesia cases.

4) In children receiving GA with propofol and remifentanil-based total intravenous anesthesia, the T wave amplitude changes are highly inconsistent—elevation is seen in only 25% of cases, whereas no change or depression is seen equally in the remainder. Other hemodynamic criteria need thus to be defined in this context. Diastolic blood pressure elevation, measured between 1 and 2 minutes after injection, was reported to be a highly sensitive indicator and was observed in all cases studied.

Evidence-Based Conclusions and Clinical Advice

- Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary. In clinical practice, if a test dose is used, there may be false-negative results, especially when the test dose is only partially administered intravascularly or when the general anesthetic agents can blunt the hemodynamic effects of epinephrine. A negative result after the injection of a test dose therefore is reassuring but does not rule out vascular placement of needle or catheter. Any injection of an LA solution should be performed slowly, in small aliquots (0.1–0.2 mL/kg) and with intermittent aspiration and observation of the ECG tracing (Evidence B4).

- In all experimental studies using the deliberate IV injection of an LA solution containing epinephrine to model accidental IV injection, no false-positive results were observed: any modification of the T wave or of the heart rate within 30 to 90 seconds after the injection of a test dose should thus be interpreted as an accidental IV injection until disproven (Evidence B3).

- Imaging modalities (ultrasound, fluoroscopy) may help to avoid or visualize accidental intravascular needle placement in peripheral blocks, but data are lacking in PRA to determine the value of these techniques (expert opinion).

Loss of Resistance

Despite the introduction of ultrasound guidance as a complement to regular LOR, the traditional LOR techniques using air or saline still remain the most widely used techniques for detecting needle placement in the epidural space. In 1995, a case series was published reporting a serious complication after the use of air-LOR in children, which immediately triggered an intense discussion regarding whether saline-LOR is a safer option and therefore should be the only recommended technique (Evidence B4). This discussion has since been ongoing and has divided the pediatric anesthesia community into 2 camps, those in favor of saline-LOR and those who prefer to use air-LOR. Recently, a third option has been advocated as a “compromise”—use of a combination of air and saline.

Air-LOR

Several complications related to the air-LOR technique have been published (nerve root compression, pneumocephalus, incomplete analgesia, and venous air embolism) (Evidence B4). However, all these complications were associated with the total amount of air injected (eg, multiple attempts, large injection volume). Thus, expert consensus is that the amount of air in the syringe should be limited to a maximum of 0.5 to 1 mL and used only to detect the change of resistance, releasing the pressure on the plunger immediately on entry into the epidural space. Restricting the volume of air that is/can be injected will on theoretical grounds substantially limit the risk for any air-related complications. The use of air-LOR is currently the preferred choice in some countries.

Other gases have been tried as alternatives to air for LOR. From a theoretical point of view, CO₂ may offer some theoretical advantages. Carbon dioxide is extremely soluble in blood and therefore will mitigate the risk of air embolism; in addition, CO₂ may possess bactericidal properties. However, the availability of CO₂ is limited in most operating rooms and may therefore be an impractical alternative as compared with either air or saline.

Saline-LOR

The use of saline avoids most of the issues related to the use of air. However, as with air, it is essential to limit the volume of the injectate because excessive amounts of saline may dilute subsequently injected LA, may make the identification of unintentional dural puncture more difficult, and can together with the volume of LAs cause transient reduction in cerebral blood flow in small infants. Despite these issues associated with the use of saline-LOR, the exclusive use of saline has been recommended by some experts and has become the general practice in some countries.

Air/Saline-LOR

One publication involving 500 pediatric epidural blocks described the use of saline with a bubble of air in the syringe (Evidence B3). This was reported to permit easy detection of the epidural space with a lower incidence of dural puncture (0.5%) than what has been reported for exclusive use of air or saline.

Evidence-Based Conclusions and Clinical Advice

- The use of either air-LOR and saline-LOR techniques are supported by different international experts, and the literature supporting 1 technique over the other is sparse; as long as either technique is used appropriately, each may be safely used in infants and children. The combination of air and saline may represent a better alternative that will minimize the risk of injecting air and reduce the volume of saline injected. This method is also associated with a low risk for unintentional dural puncture (expert opinion).

- There are insufficient data in children to determine if using LOR to air or saline to detect needle entry into the epidural space will result in clinically significant differences regarding safety, accuracy, and subsequent efficacy of the injected LA (Evidence B3 and Evidence B4). Thus, both the aforementioned alternatives are acceptable if care is taken to keep the injected volume at a minimum.
In neonates and infants, the volume of air contained in the syringe should be limited to less than 1 mL, and air injections should not be repeated if multiple attempts are made to enter the epidural space (expert opinion).

Although the committee recognizes that an air embolism with hemodynamic consequences is rare when LOR-air is used, enough evidence is lacking regarding the brain safety even for small amounts of air in the presence of a right-to-left cardiac shunt.

Compartment Syndrome

Acute compartment syndrome (ACS) of a limb is caused by high pressure in the closed noncompliant muscle compartment, which leads to compromised circulation, ischemia, and, if unrecognized, to motor and sensory impairment, neuronal death, and myonecrosis. Therefore, the time to diagnosis of ACS is essential because a delay in treatment of more than 4 hours can lead to irreversible limb damage and possible limb loss.

Both adults and children develop this syndrome, which is generally associated with trauma, fracture with subsequent casting, prolonged malpositioning during surgery, or ischemia-reperfusion injury. External or internal compression creates excessive pressure in a closed fascial compartment and leads to excruciating pain that cannot be ascribed to the trauma or surgery. A compartment pressure greater than 30 mmHg is the commonly accepted trigger for emergency intervention.

The hypothesis that RA delays diagnosis and treatment of ACS is one that continues to generate debate. Only isolated case reports describe this event, and any evidence-based conclusion is difficult. Moreover, in children, especially in preverbal or nonverbal children, the recognition of ACS is more difficult because of its unreliable warning signs (Evidence B4). Furthermore, several case reports suggest that breakthrough pain in a patient with a previously well-functioning continuous block may be an early warning sign of ACS and enhance its detection if caregivers are vigilant (Evidence B4).

Epidural infusions and peripheral single-dose and continuous LA infusions have been stated to be responsible for delayed diagnosis in children, but without convincing evidence of causation (Evidence B4). In many cases, the main root cause was not caused by the regional anesthetic technique but because of inadequate observation or to surgical malposition of the patient. Kanj and colleagues evaluating 23 children undergoing fasciotomy for ACS of the upper limb, showed that pain and swelling were the main symptoms of excessively high compartment pressure (>30 mmHg) in all but 2 patients, and that diagnosis in children is difficult and “associated with a prolonged clinical time course” (Evidence B4).

Johnson et al reviewed 12 pediatric cases of ACS associated with epidural analgesia reported in the literature. They identified the following clinical signs for impending compartment syndrome in the lower limbs (Evidence B4): 1) increasing pain with increasing need for analgesics, 2) pain remote to the site of surgery, 3) paralysis that is not attributable to analgesia technique, 4) signs of reduced perfusion of the painful site, 5) local swelling, and 6) pain on passive movement of the limb. Mar et al correlating ACS and type of analgesia (opioids or regional anesthetics), concluded that “There is no convincing evidence that patient-controlled analgesia, opioids, or regional analgesia delays the diagnosis of compartment syndrome provided that patients are adequately monitored. Regardless of the type of analgesia used, a high index of clinical suspicion, ongoing assessment of patients, and compartment pressure measurement are essential for early diagnosis.”

Evidence-Based Conclusions and Clinical Advice

There is no current evidence that the use of regional anesthetics increases the risk for ACS or delays its diagnosis in children.

A comprehensive preoperative discussion with the patient’s family and the surgical team should be performed to inform them of this rare but serious complication.

As with many controversies linked to PRA, it is almost impossible to give unequivocal statements or recommendations. We suggest the following “best practice rules” to reduce or avoid the risk of compartment syndrome in children undergoing surgery with perioperative PRA: 1) single shot for both peripheral and neuraxial blocks: use 0.1% to 0.25% bupivacaine, levobupivacaine, or ropivacaine concentrations because they are less likely to mask ischemic pain and/or produce muscle weakness than more concentrated solutions (Evidence B4); 2) for continuous infusions, bupivacaine, levobupivacaine, or ropivacaine concentrations should be limited up to 0.1%; 3) in cases of patients having tibial compartment surgery or other high-risk surgeries for compartment syndrome, restricting both volume and concentration in sciatic catheters is advisable; 4) the use of LA additives should be with caution because they can increase the duration and/or density of the block; 5) high-risk patients should have appropriate follow-up by acute pain services to allow early detection of potential signs and symptoms; and 6) if ACS is suspected, compartment pressure measurements should be urgently assessed.

CONCLUSIONS

Notwithstanding the evidence of the value, safety, and efficacy of PRA, some aspects of it remain controversial. The ASRA and the ESRA have worked together on the main controversies and present their conclusions. High-level evidence is not yet available for these controversies, and most recommendations are based on Evidence B–level studies.

A practice advisory based on consensus should only be considered within its inherent limitations. First, it may become obsolete as new information becomes available from future studies. It is, therefore, likely that this practice advisory will need to be reviewed and updated periodically. It is possible that anesthesiologists practicing PRA may encounter system and individual barriers to implement the proposed recommendations. Nevertheless, the ESRA/ASRA joint commission hopes that barriers to implementation will be overcome with the publication of this international practice advisory.

REFERENCES


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