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Adverse Effects of Regional Anaesthesia in Children

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Abstract

True complications of regional block procedures pertain to the performance of the block technique and the local anaesthetic. Such complications include lesions caused by the device used, and many of these complications can be avoided by using specifically designed devices.

Complications related to the local anaesthetic solution mainly consist of local and systemic complications. Local toxicity has mainly been reported in adults following spinal administration of 5% lidocaine (lignocaine), a drug that is not usually used in children. Systemic toxicity consists of CNS and cardiovascular complications, methaemoglobinaemia and allergic reactions. Systemic toxicity has special features in children, especially in those <1 year old. Infants have a much higher free serum concentration of local anaesthetics than older children and adults, and are more prone to the deleterious effects of local anaesthetics. Additionally, as regional blocks are usually performed under general anaesthesia in children, signs of CNS toxicity may be concealed.

Because of their higher heart rate, newborns and infants are thought to be more prone to the phasic block produced by tertiary amine agents such as bupivacaine than are adults. Serum concentrations at which bupivacaine (and etidocaine) exert cardiac toxicity seem to be similar to those producing CNS toxicity. As there is an increased threshold for CNS toxicity in infants plus an increased (or equal) sensitivity to bupivacaine cardiotoxicity, cardiac signs may not be preceded by any sign of CNS toxicity. Cardiac complications include: (i) arrhythmias with high degree conduction block, major QRS widening, torsade de pointes, and ventricular tachycardia related to re-entry phenomena; and (ii) major vascular collapse favoured by a concomitant decrease in the myocardial contractile force.

Other complications of regional block procedures result from poor selection of agent, and inadequate safety precautions and monitoring of the patient, especially during the postoperative period. There are 2 other groups of disorders often reported as complications of regional anaesthetics: (i) effects that were not anticipated by the anaesthetist because of a lack of knowledge of all the consequences of the technique used; and (ii) complications attributed to a concomitant regional block procedure but with no established, sometimes even improbable, causal link with the regional technique.

The overall morbidity of regional anaesthesia in children is low. Sound selection of local anaesthetics, insertion routes and block procedures, together with appropriate and careful monitoring, should prevent any major undesirable effects and enable regional anaesthesia to be a well tolerated and effective tool to overcome pain associated with minimal morbidity.

The use of regional blocks has increased in children in recent years with a subsequent increase in reports of complications. From 1985 to 1992, the Committee on Professional Liability of the American Society of Anaesthesiologists (ASA) evaluated 2400 closed malpractice claims; 238 involved children, of whom only 7 had received a regional anaesthetic.[1] This low morbidity rate is not significant because of the small proportion of children given conduction anaesthesia in the US during the evaluation period. Currently, there is a need to evaluate precisely the morbidity associated with the different techniques in use, with the aim of reassessing their indications and the conditions required to perform them safely.

1. Complications Related to the Devices Used

1.1 Type of Block Needle Used

The block needle used in paediatric block procedures can damage nerve trunks, especially when the wrong needle is used or when it is imprudently inserted.[2-9] Lesions of blood vessels, especially at

spinal levels, may result in compressive haematoma and definitive paraplegia. In adults, the risk of spinal haematoma ranges from 0.00055% (with spinal block procedures) to 0.0007% (with epidural block procedures).[10] Emergency surgery is requested after an urgent magnetic resonance imaging (MRI) or computed tomography (CT) scan has established the diagnosis.

Arteries can be damaged during peripheral blocks[11,12] and presenting symptoms may be delayed by several hours.[13] Tissue damage and pneumothorax may occur, especially following interpleural,[14] intercostal, stellate ganglion, interscalene and paravertebral blocks.[15,16] As introduction of epidermal cells into the spine may lead to the (possibly delayed) development of an intraspinal dermoid cyst,[17] only styletted needles must be used, at least for central blocks.

1.2 Technique of Nerve/Space Localisation

These complications include electrical damage to nerve fibres (inappropriate nerve stimulator), dilution and increase in the injected volume of local anaesthetic (fluid detection of epidural space), and nerve damage while seeking for paraesthesia.[2,7,8] The loss of resistance technique (LORT) with air, used for identifying the epidural space, may produce minor adverse effects such as transitory headache[18] or patchy anaesthesia due to epidural bubbles,[19,20] but major complications, such as lumbar compression,[21,22] multiradicular syndrome,[23] subcutaneous cervical emphysema[24] and venous air embolism, may also occur.[25,26] Several paediatric cases have been reported[27-29] and some authors have advocated abandonment of the technique,[29,30] which is acceptable for older children but not for infants (because of dilution and increase in the volume of the local anaesthetic and difficult diagnosis of inadvertent dural penetration). In the very young, LORT should be performed using an appropriate technique,[31] i.e. using small volumes of air (1 to 2ml) or carbon dioxide instead of air.[32]

1.3 Catheter-Related Complications

Mechanical complications of epidural catheters[33-37] are positively correlated with the length inserted and negatively correlated with the size.[38] Misplacement, kinking, knotting, and, if attempts are made to withdraw it through the epidural needle, breaking are commonly reported; the retained tip may cause lumbar stenosis.[39] The catheter has also been suspected of secondarily migrating into: (i) the subarachnoid space[40-42]; (ii) a blood vessel;[43-45] (iii) the subdural space;[46-50] and (iv) the paravertebral space.[51,52]

2. Complications Related to the Performance of the Block Procedure and the Management of the Patient

2.1 Bacterial Contamination

Severe bacterial contamination including epidural abscess,[35] meningitis, arachnoiditis,[53,54] radiculopathies,[55] discitis and vertebral osteitis have been reported following central blocks. Interposition of a bacterial filter have proved to be effective.[56] The overall risk of epidural infection has recently been evaluated as low in children;[57,58] however, presenting symptoms may be delayed by months and thus escape inclusion. In our opinion, the caudal route appears to be unsuitable for placement of re-injection catheters because of the potential infectious hazard.[59] However, skin abscess may also occur when other routes are used.[60]

2.2 Unsafe Technique of Injection

The wrong technique of injection may produce, by itself, severe complications. Fast epidural injections[61] quickly move the cerebrospinal fluid, which can produce intense headache, loss of consciousness, intra-cranial hypertension and coma. Rapid injection close to a nerve trunk can result in nerve compression.

2.3 Injection in the Wrong Space

2.3.1 Subcutaneous or Intramuscular Injection

Failure of the block is usually the only consequence of subcutaneous or intramuscular injection; however, there is a danger of toxicity if another block is performed without considering the dose already injected.

2.3.2 Total Spinal Anaesthesia

If dural puncture goes undetected, an epidural dose of local anaesthetic may enter the subarachnoid space and produce extensive spinal anaesthesia.[62-65] This results in almost immediate respiratory arrest and, in adolescents, cardiovascular collapse requiring immediate controlled ventilation and use of sympathomimetics. This complication is rarely encountered if proper precautions are taken during the procedure.

2.3.3 Subdural Anaesthesia

Subdural anaesthesia can follow an apparently uneventful epidural approach and injection. The sensory block is delayed (20 minutes), is extensive (involving cranial nerves up to the fifth pair) but with minimal motor and sympathetic block (which makes the difference with a total spinal block), and is short in duration (60 minutes). The incidence of subdural blocks[47,66-68] has increased in recent years and a causal link with the increasing use of rather blunted spinal and epidural needles such as Whitacre and Sprotte needles[10] may be suspected.

2.4 Undesired or Excessive Spread of Local Anaesthetic

2.4.1 Undesired Nerve Block

Excessive spread of the local anaesthetic may lead to undesired nerve blocks.[38,69-72] Compartment blocks, either deliberately attempted or not, may result in apparently unexpected nerve blocks such as a femoral block following an ilio-inguinal nerve block.[73-76]

2.4.2 Respiratory Failure

Intercostal muscle paralysis due to high epidurals (above T4) can impair breathing[77] in a child with previous respiratory impairment. In a normal child, respiratory failure occurs only when the diaphragm is paralysed (cervical epidural above C4);[64,78,79] interscalene, lumbar plexus and intercostal nerve blocks can be involved. The same respiratory and haemodynamic assistance as for total spinal anaesthesia is requested.

2.4.3 Horner Syndrome

Horner syndrome is commonly seen after supraclavicular blocks.[80-82] A bilateral syndrome is the consequence of an excessively high epidural or spinal anaesthesia.[83,84]

2.5 Post-Dural Puncture Headache

The incidence of post-dural puncture headache varies from 1% (with use of thin spinal needles) to more than 30% (accidental dural punctures during attempted epidural anaesthesia) in adults.[85] The design, size and deflection of the needle play an important role,[86,87] and repeated dural punctures seem to increase the incidence of this complication.[88] Hearing loss is a frequently associated symptom. The treatment consists of dorsal decubitus, hyperhydration, then epidural blood patch,[89-91] which is not free of complications.[88,92,93] Post-dural puncture headache seems to be infrequent in paediatric patients.[94-96]

3. Complications Due to the Local Anaesthetic Solution

3.1 Injection of Wrong Solutions

Use of wrong solutions[97,98] or additives[99-101] can be detrimental. This complication is easily avoidable by paying attention to the vials and syringes used. A very effective way to avoid syringe mismatch consists of using a specific cart for regional block procedures.

3.2 Local Toxicity

Local toxicity resulting in cauda equina syndrome has been reported in adults following (continuous) subarachnoidal administration of 5% lidocaine (lignocaine) and 0.5% tetracaine.[102,103] Transient neurological damage can occur with even less concentrated intrathecal solutions.[104] The paediatric

prevalence of this local toxicity is not known, but as children are thought to be more sensitive to the blocking effects of local anaesthetics, as experimentally established on young rabbit nerve fibres,[105] still greater care should be taken in selecting the spinal anaesthetic solution. Local anaesthetics seem to be well tolerated when correctly administered into the subarachnoidal space, but have a potential for neurotoxicity which is aggravated by additives, concomitant ischaemia, high local drug concentration or long exposure.[106] Preservatives (such as metabisulfites), epinephrine (adrenaline) and/or antioxidants increase the potential for direct neural toxicity as well as for allergy.[107,108] The US Food and Drug Administration recently recommended that 5% hyperbaric lidocaine be diluted with either cerebrospinal fluid or normal saline on a 1 to 1 basis prior to subarachnoidal injection.[10,109] In infants, lidocaine is avoided due to its short duration of action and either 0.5% tetracaine or, preferably because it is less toxic in human, and in animal models,[102,103,110] 0.5% bupivacaine are commonly used for spinal anaesthesia.[111,112] For virtually all other block procedures, diluted solutions of lidocaine (1% or less) and bupivacaine (0.25% and less) are recommended, and etidocaine, which results in long lasting motor blockade, should be avoided.

3.3 Systemic Toxicity

Systemic toxicity of local anaesthetics has special features in children, especially in infants >1-year-old, and can lead to CNS and cardiovascular complications and methaemoglobinaemia; allergic reactions are rare. The systemic concentrations attained are never high enough to block other ganglia or affect neuromuscular transmission.

3.3.1 CNS Toxicity

Lidocaine has anticonvulsant properties at low to moderate serum concentrations (1 to 5 μg/L).[113] At concentrations higher than 8 to 10 μg/L, convulsions occur which are followed by hypotension, respiratory arrest and profound circulatory collapse. Bupivacaine has the same effects on the CNS at serum concentrations higher than 2 to 2.5 μg/L in adults,[114] i.e. bupivacaine is 4 times more toxic than lidocaine. Since the first signs of toxicity are subjective, i.e. they are only perceived by the person undergoing the anaesthesia, they are not observed in patients under associated general anaesthesia. Objective signs, i.e. signs that can be measured (shivering, muscular twitching, tremors initially involving the face) immediately precede the occurrence of seizures. Relative insensitivity to the convulsant effects of lidocaine and bupivacaine has been demonstrated in newborn sheep and pig, when compared with adult sheep and pigs.[115-117] but these data must be interpreted with care. In fact, infants have a much higher free serum concentration of local anaesthetics than children and adults, and are, therefore, probably more prone to the deleterious effects of local anaesthetics, both cardiac and neurological. Additionally, as regional blocks are usually performed under associated general anaesthesia in children, signs of CNS toxicity, such as convulsions, may be concealed.

In clinical practice, seizures may occur: (i) rapidly after either a massive inadvertent intravenous injection, or because of a rapid absorption process at the site of administration; and (ii) several hours (even days) after initiation of perineural infusion for postoperative analgesia, due to accumulation.[118-120] In adults, convulsions occurring intraoperatively are usually free of major consequences when treated immediately[121] but this might not be the same when seizures and respiratory depression occur on the hospital ward during a prolonged infusion.

The treatment of convulsions, respiratory depression and/or coma is basically the same in children as in adults: (i) oxygenation and airway management; and (ii) treatment of seizures if they still occur after oxygenation using small doses of benzodiazepines or thiopental sodium. Most benzodiazepines have been shown to potentially increase the cardiotoxicity of bupivacaine[122,123] but this effect does not seem to be clinically relevant and use of benzodiazepines, even in premedication, is mandatory.

3.3.2 Cardiac Toxicity

Local anaesthetics mainly act by preventing fast inward sodium channels in myocardium from opening. This block has 2 components, tonic and phasic (use-dependent or frequency-dependent). When the rate of impulse increases, the intensity of the phasic block increases too; this is responsible for the antiarrhythmic properties of lidocaine and the cardiotoxic effects of bupivacaine. Lidocaine exerts a more profound effect in that respect in newborn rodents as compared with adult rodents,[124,125] whereas bupivacaine seems to exert equal effects in fetus, newborn, infant and adult animals.[126,127] However, because of their higher heart rate, newborns and infants are thought to be more prone to the phasic block produced by tertiary amine agents such as bupivacaine than are adults. Serum concentrations at which bupivacaine (and etidocaine) exert cardiac toxicity seem to be similar to those producing CNS toxicity. In adults, cardiotoxic reactions to bupivacaine or etidocaine may occur suddenly without any prodrome, usually after massive inadvertent intravenous injection.[128,129] During continuous infusion for pain relief, subjective and objective signs of CNS toxicity usually precede cardiac manifestations, but this is not always the case in infants,[130,131] since general anaesthesia, which is most often administered with regional anaesthesia, may conceal CNS manifestations.[132] Isolated toxic cardiac manifestations have been reported in infants following bupivacaine infusion for several hours.[131] The increased threshold for CNS toxicity in infants as compared with adults and the increased (or equal) sensitivity to bupivacaine cardiotoxicity may explain why cardiac signs may not be preceded by any sign of CNS toxicity.

Cardiac manifestations of bupivacaine and etidocaine toxicity consist of: (i) arrhythmias including high degree conduction block, major QRS widening, torsade de pointes, ventricular tachycardias that are related to re-entry phenomena;[133] and (ii) major collapse favoured by a concomitant decrease in the myocardial contractile force. After massive intravenous injection these direct cardiac signs may be accompanied by additional manifestations such as a sudden paleness[132] and, in non-anaesthetised patients, convulsions. Cardiac complications require urgent and appropriate therapeutic measures including oxygenation, ventilation and cardiac massage if appropriate. In infants, cardiac output almost exclusively depends on heart rate and increasing the rate might be essential, especially in the presence of high degree atrioventricular block (and also during episodes of torsade de pointes). However, it must be remembered that increasing the heart rate also increases the use-dependent block[133] and some authors do not recommend the use of epinephrine in this case.[134] Life-threatening arrhythmias and/or collapse require prolonged cardiac massage at first.[135] In fact, bupivacaine wash-out from the heart seems to be relatively rapid when coronary perfusion is maintained.[136] Phenytoin has been recommended;[119,131] it mainly acts by blocking sodium channels[137] and is supposed to competitively bind to the same receptor as bupivacaine.[131] However, sufficient data are not available to recommend using phenytoin. Despite its arrhythmogenic potential, epinephrine appears to be the only useful drug, which requires careful titration using boluses of 0.01 μg/kg,[138] in order to avoid ventricular tachycardia or fibrillation.

3.3.3 Methaemoglobinaemia

Methaemoglobinaemia may develop several hours following the administration of prilocaine,[139] benzocaine and, occasionally, lidocaine.[140-144] The patient develops cyanosis when the methaemoglobin level exceeds 20 to 30% of the total haemoglobin level. When the level exceeds 70%, dyspnoea, tachycardia, headache, vertigo, hypoxia and death, though rare, can occur. Infants are very sensitive to prilocaine and doses exceeding 5 mg/kg should be avoided.[141] In the absence of predisposing factors such as haemoglobinopathies, glucose-6-phosphate dehydrogenase deficiency, exposure to aniline dyes and oxidants (sulphonamides, nitrites, nitrates, antimalarials), the use of eutectic lidocaine-prilocaine cream ('EMLA') in normal amounts (2.5g, i.e. half a small tube) is well

tolerated, even in neonates. Treatment of methaemoglobinaemia consists of injecting methylene blue (1 to 5 mg/kg) intravenously to convert methaemoglobin to haemoglobin.

3.3.4 Prevention of Systemic Toxicity

Most adverse effects of local anaesthetics observed in paediatric patients are related to pharmacokinetic misunderstanding. Indeed, neonates and infants present some substantial pharmacokinetic peculiarities which must be kept in mind.[145]

Pharmacokinetic Specificity of Paediatric Patients

A more rapid absorption process by the airway, a larger volume of distribution, a decreased hepatic clearance and lower plasma levels of albumin and α_1-acid glycoprotein (AAG) are the 4 factors in paediatric patients that may have wide-ranging effects on pharmacokinetic parameters.

Topical Anaesthesia of the Airway

Local disposition of lidocaine after topical anaesthesia of the airway is enhanced in infants >1-year-old.[146] Because of fast absorption, peak plasma concentrations above toxic levels are reached 1 minute following application (by spray) of 4 mg/kg of 4% plain lidocaine.[146] Safe topical anaesthesia requires: (i) decreasing the dose; and (ii) using a calibrated device delivering a precise (and low) dose.[147]

Disposition and Elimination

Amide local anaesthetics are metabolised in the liver by the cytochrome P450 enzymes, which are not fully developed at birth.[148] A first degree of maturation occurs within the first 2 to 3 weeks of life. Clearance of local anaesthetics is low at birth and increases during the first months of life to reach adult values at the age of 6 to 9 months.[149-151] A parallel inverse evolution occurs for the volume of distribution, which is much larger in infants than in older children and in adults.[150,152] Therefore, after a single injection, peak plasma concentrations measured in infants are similar to those in adults (with greater variability). However, following reinjections, accumulation of bupivacaine can rapidly occur and result in systemic toxicity, especially because the free drug concentration is markedly higher before the sixth month of life (see figures 1 and 2) due to lower serum protein levels. Amide local anaesthetics (particularly bupivacaine) bind to AAG and to serum albumin, the plasma concentration of which is very low in young infants.[153,154] Consequently, toxic concentrations are rapidly attained in infants since the toxic fraction of the drug is the free fraction, with an expected toxic threshold of 0.2 μg/L for bupivacaine.[155]

Evolution of Clearance with Time

The decrease in hepatic clearance of local anaesthetics with time may contribute to toxicity during prolonged administration. Three factors appear to be involved in this phenomenon. The first is the fact that the clearance measured after a single injection may not reflect the true elimination clearance because of complex distribution processes, lack of precision of the assay and the unreliability of the pharmacokinetic models used. This problem of what truly represents a pharmacokinetic parameter at a precise time has led to the concept of 'context-sensitive half-life' in other circumstances.[156] The second factor, in the postoperative period, is the decrease in free drug concentration in the serum due to the rapid increase in plasma concentration of the stress proteins, especially AAG, which

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Fig. 1. Bupivacaine free fraction *vs* age in 11 infants after the administration of 0.5% plain bupivacaine 2.5 mg/kg by the caudal route, showing a strong negative correlation between age and free fraction (normal value for free fraction in adults is 0.05%) [reproduced from Mazoit et al.,[150] with permission].

leads to a parallel decrease in hepatic clearance of drugs with low to moderate hepatic extraction ratios. The magnitude of this phenomenon is believed to compensate exactly the decrease in clearance of local anaesthetics previously mentioned. The third mechanism is a true decrease in intrinsic hepatic clearance, likely due to the inhibition of hepatic microsomes by the products of metabolism, as is well established for lidocaine.[157] These mechanisms seem to apply also to bupivacaine, at least in the dog.[158]

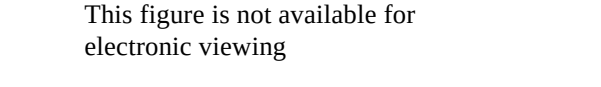

Fig. 2. α_1-Acid glycoprotein (AAG) and serum albumin (SA) levels in 11 infants aged 1 to 6 months. AAG level is low at birth and significantly increases with age. There was a close relationship between AAG level and bupivacaine free fraction in the same infants (see fig. 1) [reproduced from Mazoit et al.,[150] with permission].

Recommendations for Dosage

In infants aged 10 days to 6 months, bupivacaine 2.5 mg/ml with epinephrine 5 μg/L (i.e. 1/200 000) is the most commonly used agent for single shot injections. The maximum recommended dose is 2.5 mg/kg, i.e. 1 ml/kg of 0.25% solution for the caudal route.[145] As the free drug concentration is increased before the age of 6 months, re-injections must be performed with care, preferably via the lumbar instead of the caudal route. Lumbar epidural injection of 1.25 to 1.75 mg/kg bupivacaine (0.5 to 0.7 ml/kg of 2.5% bupivacaine with epinephrine 1/200 000) provides adequate anaesthesia in infants.[159] Re-injections (0.75 to 1 mg/kg i.e. 0.3 to 0.4 ml/kg of 2.5% bupivacaine with epinephrine 1/200 000) may then be performed with improved safety. After the age of 6 month, the problem of the free fraction is less crucial.

At any age, the maximum dose of lidocaine or mepivacaine is 10 mg/kg. In grown up children (with a bodyweight <30kg) the doses should be decreased and in no case should a child be given a dose exceeding the maximum dose for an adult, i.e. bupivacaine 150mg, lidocaine 600mg or mepivacaine 600mg. If mixtures of local anaesthetics are used it is also important to remember that their toxicity is additive[160] and that adding lidocaine to bupivacaine does increase the potential toxic hazard of bupivacaine.

Local Anaesthetics in the Postoperative Period

Long term infusions of bupivacaine in infants require accurate dosage calculation.[145,161] In a patient with a clearance of 2 ml/min/kg and a free fraction of 10%, an infusion of 0.24 mg/kg/h of bupivacaine leads to a steady-state total concentration of 2 mg/L with a free drug concentration of 200 μg/L, which is close to the toxic threshold.[155]

Thus, the maximum infusion dose of bupivacaine is 0.2 to 0.25 mg/kg/h in infants <1 year old, 0.3 to 0.35 mg/kg/h in children aged from 1 to 4 years and 0.4 mg/kg/h in children >4 years old.[162] As usual, these recommendations safely apply to the majority of the population but they may lead to systemic toxicity in some individuals with very low intrinsic hepatic clearance. As infants are at greater risk of complications for the above-mentioned reasons (pharmacokinetics, high heart rate, relative increased threshold for CNS toxicity compared with cardiac toxicity), they need both close clinical surveillance (consciousness, global haemodynamics, survey of motor blockade) and careful monitoring (electroencephalogram, percutaneous oxygen saturation). Injection of top-up doses in addition to continuous perineural infusion must be avoided to prevent temporary toxic peak plasma concentration: if analgesia is insufficient, it is safer to temporarily increase the infusion rate.

3.4 Adverse Effects of Adjuvants and Additives

3.4.1 Opioids

Opioids produce adverse effects in 50% of patients.[32,163-165] Some of these adverse effects are merely unpleasant, whereas others are serious[37,166,167] and require specific therapy. Vomiting occurs in 30% of patients, even at low doses[168] and is effectively treated using small doses of droperidol (bolus of 20 μg/kg) or ondansetron. Urinary retention is common and can be treated with intravenous naloxone; however, bladder catheterisation is frequently necessary to avoid abolition of the analgesic effects. The most serious complication is respiratory depression, which may appear 3 to 12 hours after injection and become severe within 2 to 3 hours. Severe generalised pruritus and increasing somnolence[168] should be considered as warning symptoms for respiratory depression. Treatment consists of intravenous naloxone 10 μg/kg (which can be repeated if this is insufficient) followed by a continuous infusion of 10 μg/kg/h for 24 hours.

3.4.2 Adjuvants

Epinephrine 1/200 000 is usually added to lidocaine and bupivacaine for caudal or epidural anaesthesia. Epinephrine is expected to decrease the peak plasma concentration of local anaesthetics[155] and increase the duration of postoperative analgesia.[169] However, it might have a deleterious effect on spinal cord vascularisation.[170] These authors recommend the use of epinephrine 1/400 000, i.e. 2.5 μg/L.

Clonidine (1.5 to 2 μg/kg) is frequently added to prolong the effects of local anaesthetics during caudal or epidural anaesthesia.[171] No deleterious effect (such as respiratory depression) has been reported.

3.5 Consequences of Sympathetic Blockade

3.5.1 Hypotension

Hypotension caused by sympathetic blockade is common in adults, but is uncommon before 8 years of age and is only moderate in severity when it occurs in adolescents.[172,173] This is probably due to immaturity of the autonomic nervous system[174,175] in conjunction with the small proportion of blood sequestered in the lower limbs,[176,177] decreased threshold of peripheral vascular resistance[178] and decrease in parasympathetic tone (which counteracts the low physiological orthosympathetic tone of young children).[179]

3.5.2 Hypoglycaemia

A high level epidural/spinal blockade abolishes the hyperglycaemic response to surgery.[180,181] The increase in plasma glucose levels due to the stress response to surgery has been shown to be lower in children receiving an epidural than in children receiving opioid analgesia.[182] However, children with diabetes mellitus or who are malnourished may then experience hypoglycaemia.[183]

3.6 Other Adverse Effects

3.6.1 Anterior Spinal Artery Syndrome

The ventral part of the low thoracic and high lumbar spine is often supplied by a single artery, the artery of Adamkiewicz, which may be impaired

intra-operatively, either because of the surgical procedure or, hypothetically, because of vasoconstriction resulting from the administration of local anaesthetics with epinephrine.[166] Interruption of blood supply by this artery results in definitive loss of motor function with, at least partially, intact sensory function.

3.6.2 Flaring of Latent Infection

Epidural anaesthesia has been implicated in reactivating viral infections such as herpes and acutely evolving neuro-immunological diseases such Guillain-Barré syndrome.[184] Of greater concern is the risk of unmasking latent neurological diseases such as spinal cord compression, cerebral tumour, angioma or an epidural abscess.

3.6.3 Allergic Reactions

Allergy to amino-amides is rare[185-187] and most adverse reactions are related to epinephrine.[188] Amino-esters may induce allergic reactions related to metabolic products of para-aminobenzoic acid derivatives.[189] Preservatives such as metabisulfite may be involved in allergic reactions.[190]

4. Complications Related to Inadequate Selection or Management of Patients

Some complications of regional anaesthesia in children are related not to the block procedure itself but are related to the fact that the procedure was performed in the wrong patient or under inappropriate environmental conditions. For example, patients with bacteraemia are at risk of meningitis[191] and those presenting with stenosis of the spinal canal may develop neurological complications after epidural anaesthesia.[53,192,193] Inappropriate positioning of the patient, either for the intended block or surgery, may result in nerve damage and eschars at pressure points. The performance of the block under general anaesthesia conditions may worsen some complications (e.g. intraneural injection) and delay their recognition. Inappropriate monitoring may also delay the diagnosis of otherwise easily predictable complications such as respiratory depression due to epidural opioids. Compression and compartment syndromes[194-197] can go unrecognised in patients with a plaster cast if the haemodynamic status of the limb is not carefully and regularly checked, since the usual first alerting symptom, pain, is suppressed. However, regional blockade, *per se*, does not preclude the diagnosis[198,199] if appropriate management is guaranteed.

5. Complications Attributed to a Concomitant Regional Block Procedure

Discovery of a neurological symptom in a patient previously given a regional block is immediately causally related to the block procedure,[200] whereas on closer analysis very few such causal links can be verified.[201] In patient number 22 in the study of Dahlgren et al.[202] a block procedure was assumed to be the causative factor of neurological symptoms simply because the operation was supposedly performed under combined general and regional anaesthesia but, in reality, the patient was only given a general anaesthesia. Surgical manipulations, blood loss, hypotension and positioning of the patient[203] may, *per se*, cause neurological lesions. Cauda equina syndrome has been reported in 6 patients operated on under only general anaesthesia in a hyperlordotic position.[204] Similarly, operations performed in the lithotomy position result in persistent neuropathies due to stretching of the cauda equina and not to regional anaesthetic techniques, the incidence of which has been estimated to be 1:3608.[205] Laraki at el.[206] reported the case of a female adolescent who, following surgery under combined general and lumbar epidural anaesthesia, presented with paraplegia; however, the condition resolved spontaneously within 6 days and was attributed to hysteria.[206]

Patients with sickle cell disease are prone to experiencing vaso-occlusive crises and thromboses of small vessels, especially in case the presence of hypoxaemia; ischaemic neuropathies[207] and spontaneous epidural haematomas[208] have also been reported to occur during sickle cell crises. Sudden infant death may be erroneously attributed to a previously performed caudal block for inguinal

Table I. Complications and morbidity rate associated with regional anaesthetic block procedures in children [data were obtained from the 24 409 paediatric regional anaesthesias covered by the French-Language Society of Paediatric Anaesthesiologists' (ADARPEF's) prospective survey][3]

Complications	Spinal anaesthesia (n = 506)	Caudal anaesthesia (n = 15 013)	Lumbar epidural anaesthesia (n = 2396)	Sacral epidural anaesthesia (n = 293)	Thoracic epidural anaesthesia (n = 135)	Peripheral blocks and local anaesthesia (n = 9396)	Total (n = 24 409)
Dural penetration	0	4	2	2	0	0	8
Uncomplicated	0	0	1	1	0		2
Post-dural headaches	0	0	1	1	0		2
Extensive spinal anaesthesia	0	4	0	0	0		4
Intravascular injection	1	2	3	0	0	0	6
Uncomplicated	1	0	1	0	0		2
Convulsions	0	1	1	0	0		2
Cardiac arrhythmia	0	1	1	0	0		2
Technical problem	0	2	1	0	0	0	3
Delayed block	0	1	0	0	0		1
Rectal penetration	0	1	0	0	0		1
Catheter knotting	0	0	1	0	0		1
Overdosage with cardiac arrhythmia	0	1	1	0	0	0	2
Transient paraesthesias	0	0	2	0	0	0	2
Post-morphine apnoea	0	1	0	0	0	0	1
Skin lesion	0	1	0	0	0	0	1
Morbidity rate	1 (2.0 per 1000)	11 (0.7 per 1000)	9 (3.7 per 1000)	2 (6.8 per 1000)	0 (0.0 per 1000)	0 (0.0 per 1000)	23 (0.9 per 1000)

repair rather than to sickle cell disease. The problem is similar with evolving neurological diseases: no data suggest that local anaesthetics could worsen the course of the disease but no data either have established that local anaesthetics can be safely used in patients with neurological diseases.

6. Incidence of Complications Related to Regional Blocks in Paediatric Patients

Very little data on the morbidity associated with regional anaesthesia in children is available. The 1-year prospective French-Language Society of Paediatric Anaesthesiologists' (ADARPEF's) survey, involving 38 institutions from 3 countries,[3] collected data from 85 412 paediatric anaesthesia cases including 24 409 regional anaesthesias, of which 15 013 were central blocks and 9396 peripheral blocks. A total of 23 incidents were reported, all occurring during central block (table I). This study established the overall safety of regional anaesthesia in the paediatric population. It also showed that central blocks, especially caudal blocks, are not as safe as is commonly believed, whereas peripheral nerve blocks were extremely safe (0 complications). Two additional findings were important: (i) half the complications were directly related to a faulty technique, i.e. they could have been entirely avoided; and (ii) adverse effects occurred during very common techniques performed in healthy patients not during more hazardous techniques (e.g. thoracic epidurals, spinal anaesthesia in ex-premature infants, etc). These findings mean that when great care is taken complications can be virtually avoided.

These data (0 deaths in 24 409 patients) compare favourably with surveys of pure general anaesthesia in paediatric patients. The British Na-

tional Confidential Enquiry into Post-Operative Deaths (NCEPOD)[209,210] reported the following mortality rates: 0.054 to 0.9 per 10 000 anaesthetic procedures for mortality exclusively related to anaesthesia and 7 per 10 000 anaesthetic procedures for deaths partly related to anaesthesia. Several deaths occurred in infants undergoing minor surgery. In Italy, the Italian Society of Paediatric Anaesthesia (SIAARTI) group,[211] reported that out of 9289 paediatric anaesthetic procedures the incidence of complications was 3.4%, of which 21 were severe and 7 resulted in death, a result comparable to that of the British NCEPOD. In a recent survey,[212] the incidence of minor sequelae following general anaesthesia in children was found to be higher than previously reported.

Comparing the outcome of different anaesthetic regimens is difficult because patient selection differs considerably and some surgical procedures cannot be performed under regional anaesthesia alone. However, the morbidity and mortality rates of deep general anaesthesia, especially in infants, are still high. Thus, when applicable, use of regional anaesthetic techniques, even when combined with a light general anaesthesia, can reduce the incidence of respiratory failure, which is the main cause of severe complications associated with deep general anaesthesia.[213] Also, since circulatory failure is an the primary cause of anaesthetic-related complications in children, the virtually zero incidence of haemodynamic disturbances caused by central blocks in children up to 8 years of age should be borne in mind when choosing a procedure.[98,213]

7. Prevention of Complications: Safety Precautions and Recommendations

7.1 Selection of Patients

Regional techniques are mainly performed to provide analgesia and, thus, have to be compared with other analgesic techniques. For each individual patient, the suitability of the proposed procedure must be investigated.[214] Axial blocks are contraindicated in patients with bacteraemia.[191] Conversely, regional procedures should be preferred in patients who are prone to anaesthesia-related complications; for example, in ex-premature neonates,[215] patients with metabolic disorders or muscular dystrophy,[216] and patients requiring emergency surgery with a full stomach.

7.2 Selection of the Techniques

Selection of the techniques depends on the distribution of anaesthesia and overall safety of the procedure. Surgery involving the patient's extremities and lower part of abdomen are excellent indications for an axial block.[167] When a continuous technique is planned, the size of the catheter, its site of insertion, and the distance to which it should reasonably be introduced has to be decided. Catheters can only be maintained in place if sterility can be guaranteed.[35]

Basically, when appropriate, a local anaesthesia is preferable to a regional anaesthesia and a peripheral block to an axial block.[3] The total dose and the number of punctures have to be considered, as the morbidity associated with a single proximal block is often lower than that associated with use of several combined distal blocks. When several insertion routes are available, the safest technique has to be selected. The selection of an appropriate block needle is essential. Too often the anaesthetist who carefully selects a tracheal tube is not concerned in selecting an appropriate block needle: half the complications of the ADARPEF's study[3] involved the wrong device and could have been avoided by using an appropriate needle.

7.3 Medico-Legal Precautions

Medico-legal concerns vary from one country to the next. Therefore, specific recommendations may vary significantly from place to place. However, general guidelines can be suggested and apply everywhere in the world. As regional anaesthesia generates an aura of suspicion and mistrust even amongst anaesthetists, it is important to follow strict safety precautions measures when paediatric patients are involved.[216]

The following guidelines should be followed.

- *Select the safest technique*: when several approaches are available, it is recommended that the technique associated with the lowest morbidity is selected.
- *Obtain informed consent from the parents*: even in case of an emergency, it is mandatory that the anaesthetist takes a few minutes to explain the procedure that will be used along with its risks and advantages, and obtain a consent. The family should also be warned about a possible failure of the block and the alternatives that can then be used.
- *Select patients carefully*: preoperative examination is necessary, and detailed medical records and family history should be obtained. Depending on the patient's age, history and clinical findings and the type of operation, laboratory examinations or x-rays might be obtained.
- *Maintain a detailed anaesthetic record*: as for any anaesthetic procedure, a detailed chart including vital signs, techniques and drugs used and any relevant information must be completed.
- *Maintain a detailed postoperative record*: regional blocks must be evaluated and monitored postoperatively, preferably using a standardised chart. Adverse effects and their treatments have to be recorded.
- *Monitoring of respiration*: respiration parameters have to be monitored, preferably in specialised units, for 24 hours if the patient has received an epidural or intrathecal opioid. In this case, monitoring should include measurement of continuous pulse oximetry.

8. Conclusion

Regional anaesthesia is a very effective way of providing analgesia to paediatric patients. Most of the techniques available are both easy to perform and well tolerated, which allows their extensive use in children. However, they are not free from adverse effects and the potential for complications must be carefully evaluated prior to carrying out the procedure. Sound selection of local anaesthetics, insertion routes and block procedures in association with appropriate and careful monitoring should prevent any major undesirable outcomes and allow regional anaesthesia to be as it is intended to be: a well tolerated and effective tool to overcome pain that is associated with minimal morbidity.

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