Review Article

Pharmacology related to paediatric anaesthesia

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ABSTRACT

A child is not a mini adult. They differ from adults in terms of weight, shape, anatomical size and major body systems such as cardiovascular and respiratory as well as psychologically. Each organ system is immature in paediatric age group and their growth and development can dramatically affect the pharmacokinetics of different drugs. Children differ in every way from an adult thus mandating to have a basic knowledge of the pharmacokinetic and pharmacodynamic principles in paediatric population to prevent under dosing or toxicity of drugs. This review article aims to simplify the basic principles of pharmacokinetics and pharmacodynamics in paediatric population. It also highlights physiological and pharmacological differences between adults and paediatric age. We performed a PUBMED search for English language articles using keywords including pharmacology, child, paediatric anaesthesia. We also hand searched references from relevant review articles and text book chapters. We have also discussed drug interaction in anaesthesia, pharmacology pertaining to neuromuscular junction and effects of anaesthesia over the developing brain.

Key words: Anaesthesia and developing brain, neuromuscular junction pharmacology, paediatric anaesthesia, paediatric pharmacokinetics, paediatric pharmacology

INTRODUCTION

The pharmacokinetic (PK), pharmacodynamic (PD) and side effect profile of medications differ among adults and children. PK is affected by maturity of organ function and body composition as well.[1] The PD effects differ in children depending upon the capacity of end organs like brain, heart, liver, skeletal muscle, etc. To achieve the desired clinical response and avoid toxicity in children dose modification is required, which is based on knowledge of PK and PD.[2] The proportion of fat, protein and body water changes constantly during infancy and childhood. Also, major organ systems mature in size and function during childhood. Therefore, it is of utmost importance to have a thorough knowledge of PK and PD principles in paediatric patients to prevent mishaps in drug dosing. For this narrative review, we performed a PUBMED search for English language articles using keywords including pharmacology, child, and paediatric anaesthesia. We also hand searched references from relevant review articles and text book chapters.

PHYSIOLOGICAL AND PHARMACOLOGICAL DIFFERENCES

Physiological differences between children and adults are important determinants while planning anaesthetic management in paediatric patients. The salient features of paediatric physiology are:

i. Oxygen consumption of neonates is more than 6 ml/kg which is about twice that of adults on a weight basis. Therefore alveolar ventilation is twice that of adults
ii. Infants revert from the adult circulation to foetal type of circulation (transitional circulation) following triggering factors. During this period pulmonary artery pressure increases to systemic

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levels, blood is shunted past the lungs through patent foramen ovale and the ductus arteriosus may reopen, allowing blood to shunt at the ductal level. Therefore hypoxemic events in infants are often prolonged despite adequate pulmonary ventilation with 100% oxygen

iii. The sympathetic nervous system and baroreceptor reflexes of infants are not fully mature. The cardiac output of neonates and infants is dependent on heart rate. The infant's cardiovascular system maintains lower catecholamine stores and displays a blunted response to exogenous catecholamines

iv. Hypotension without tachycardia is characteristic of intravascular fluid depletion in neonates and infants

v. Cardiac calcium stores are reduced because of immaturity of the sarcoplasmic reticulum. Therefore, neonates have greater dependence on exogenous calcium and probably increased susceptibility to myocardial depression by potent inhaled drugs that have calcium channel blocking activity[3,4]

vi. Total body water at birth constitutes 80% of body weight, but falls dramatically to around 60% by the end of the first year.[5] By 18 to 24 month of age, the proportion of extracellular fluid volume relative to body weight is similar to that in adults

vii. Renal function is diminished in neonates because of low perfusion pressure and immature glomerular and tubular function. Complete maturation of renal function occurs by about 2 years of age[6,7]

viii. By 1 month of age, the blood volume varies between 70 and 80 ml/kg as in adult. The oxyhaemoglobin dissociation curve approximates that of adult by 4 to 6 months of age

ix. The infant compensates for heat loss by means of shivering and non-shivering (cellular) thermogenesis. The minimal ability to shiver during the first 3 months of life makes cellular thermogenesis (metabolism of brown fat) the principle method of heat production.[8] Anaesthetic agents can alter many thermoregulatory mechanisms, particularly non shivering thermogenesis in neonates[9,10]

x. Functional maturity of the liver is incomplete at term. Most enzyme systems for drug metabolism are developed but not yet stimulated by the drugs that they metabolise

xi. At birth, gastric pH is alkalotic; by the second day of life, pH is in the normal physiologic range

xii. Neonates have low glycogen stores that predispose them to hypoglycaemia.

PHARMACOKINETICS

Absorption

Oral

The efficacy of orally administered drug depends on the rate and extent of absorption from the gastrointestinal tract (pH of gastric secretions, gastric emptying time, gut blood flow) and physiochemical nature of the drug.[11] The gastric pH, at birth is 6 to 8, and then within first 24 hours it reduces to 1 to 2, finally reaching adult level between 6 months to 3 years of age. Decreased bile acid secretion in neonates decrease the absorption of lipid soluble drugs. Long chain fatty acids (found in neonatal formula) delay gastric emptying, and thus are important while determining the NPO status of neonates before surgery. Vomiting, drug destruction by digestive enzymes, cause irregularities in absorption.[12]

Transmucosal

This route bypasses the first pass hepatic effect and causes a rapid onset of drug action e.g., sublingual nitro-glycerine, nasal midazolam, ketamine as premedicants[13] and desmopressin in children with enuresis.[14]

Transdermal

This route is hazardous in neonates as their stratum corneum is very thin and a well hydrated epidermis leads to enhanced drug absorption and toxicity,[15] as seen with percutaneous administration of lidocaine and corticosteroids.[1] Any factor causing increased vascularity of skin, e.g., fever will increase drug uptake. Such as, percutaneous theophylline gel for treatment of apnoea in newborns.[16]

Parenteral

After IM administration, systemic absorption of drug is more rapid and predictable than oral or rectal administration because of high density of skeletal muscle capillaries in infants.[11] Drugs injected intravenously act immediately.

Rectal

Drugs given rectally avoid few disadvantages of orally administered drugs. This route should be avoided in immunosuppressed patients or those undergoing

chemotherapy.[11] Drugs administered below the dentate line bypass the liver after absorption, while drugs inserted above dentate line are absorbed via the superior rectal vein to undergo first pass hepatic metabolism. Absorption of drugs is slow and irregular and also depends on the drug form (suppositories, rectal capsules or enemas).

Intrapulmonary

This mode is commonly being used in infants and children e.g., surfactant and adrenaline. Developmental changes in the architecture of the lung and its ventilatory capacity (e.g., minute ventilation, vital capacity and respiratory rate) can alter patterns of drug deposition and hence systemic absorption after intrapulmonary administration of drug.[1]

Sometimes non-traditional routes need to be practiced like the intraosseous route (dose same as that for IV route) for difficult intravenous access and endotracheal route for administering atropine, epinephrine, naloxone or lignocaine with proper dose adjustments (usually two to three times the IV route).

Distribution

The drug distribution is directly related to the lipid solubility and inversely related to the protein binding. Neonates have greater proportion of body water (approx. 75%) and are called as "little bags of water". Therefore, the volume of distribution of water-soluble drugs is higher in neonates. Neuromuscular blocking drugs (NMBDs) and aminoglycosides distribute rapidly into the extracellular fluid (ECF), but enter cells more slowly. The requirement of initial dose of such drugs is therefore higher in the neonate compared to the infant, older child or adult.

Neonates lack in muscle and fat content; resulting in prolonged clinical effect of the drugs like thiopentone which redistribute to muscle and fat. The concentration of albumin and alpha1 acid glycoprotein which bind to the acidic and basic drugs respectively is decreased in neonates thereby requiring great caution when administering drugs like phenytoin, theophylline and certain antibiotics which are highly protein bound.[17] Serum albumin concentrations approximate adult values by 5 months of age, and binding capacity approaches adult values by 1 year of age. Immaturity of blood brain barrier in neonates also increases the risk of toxicity of otherwise lipid insoluble drugs like morphine.

Metabolism

Liver is the principle site of drug metabolizing enzymes. Liver function is deficient in neonates reaching adult values by one year of age and manifesting as slower rate of drug metabolism. As an infant grows, the ability to metabolise medications increases rapidly for two reasons (a) Hepatic blood flow increases and more drug is delivered to the liver (b) The enzyme systems develop.[18]

The plasma levels of albumin and other proteins necessary for binding of drugs are lower in term newborn (and are even lower in premature infants) than in older infants. This has implications in neonatal coagulopathy (e.g., the need for vitamin K at birth), as well as for drug binding and pharmacodynamics; lower the albumin value; less is the protein binding and greater the levels of free drug. Drug binding to albumin may be altered in the presence of hyperbilirubinaemia for some medications in the neonatal period.[19]

Drug metabolism can be divided into Phase I and Phase II metabolism. Phase I metabolism involves small structural alterations to the drug molecule. It decreases lipophilicity and enhances renal excretion of the molecule. Drugs undergoing phase I metabolism include: paracetamol, codeine, ropivacaine, omeprazole and phenothiazines (oxidation); prednisone, warfarin, halothane (reduction); amide local anaesthetic agents, remifentanil (hydrolysis). Phase II metabolism involves the conjugation of a functional group on the parent drug or Phase I metabolites with hydrophilic endogenous substrates like glucuronidation, sulfation, acetylation.

Excretion

Excretion is the domain of kidneys which attain maturity by 2 years of age. Renal function is decreased in neonates and preterm babies due to low perfusion pressure and immature glomerular and tubular function. The ability to handle free water and soluble loads may be impaired in neonates, thus half-life of drugs excreted by kidneys will be prolonged[18] e.g., aminoglycoside, cephalosporin.

Neonates are obligate sodium losers and cannot concentrate urine. Therefore, adequate exogenous sodium and water must be provided during the perioperative period. Conversely, neonates are likely to excrete volume loads more slowly and are therefore more susceptible to fluid overload. Premature neonates often possess multiple renal defects, like decreased

creatinine clearance, impaired sodium retention, glucose excretion and bicarbonate reabsorption; and poor diluting and concentrating ability. These abnormalities increase the importance of meticulous attention to fluid administration in the early days of life.[20]

Pharmacodynamics

Pharmacodynamics deals with the reactions between drugs and living systems. The child's response to drugs is affected by maturity of the targeted receptor, immature transduction of drug-receptor interaction into intracellular messages as well as by the incapability of the immature tissue or the organ to respond to the message. These pharmacodynamic alterations influence not only the therapeutic action but also the adverse reactions. An example is the presence of immature gamma-aminobutyric acid (GABA) receptors which exhibit excitatory rather than inhibitory response with benzodiazepines like midazolam in preterm and newborn infants manifesting as paradoxical seizures.[21]

PHARMACOKINETIC AND PHARMACODYNAMIC INTERACTIONS IN ANAESTHESIA

Drug interactions can occur on a PK or PD level, or both. PK drug interactions will generally also result in an altered PD effect. When a combination of drugs is administered, it may result in an alteration of dose–response relationship.

After anaesthesia with halothane and diazepam, peak plasma concentrations of paracetamol administered 1 hour after surgery were delayed and decreased, compared to concentrations without anaesthesia, as a result of delay in gastric emptying and slower absorption.[22] Therefore, higher doses of orally administered drugs may be required to guarantee equivalent plasma concentrations.

Volume of distribution is the apparent volume in which an administered dose would need to be dissolved in order to yield some particular plasma concentration. When a drug has a higher affinity for tissues other than plasma, the volume of distribution may be large. This is the case with propofol, which is characterised by considerable redistribution to adipose tissue, resulting in a large volume of distribution of ~300 litres.[23]

Simultaneously administered drugs affect the volume of distribution through many ways. First, drugs may compete for binding sites on plasma proteins (albumin and α1acid glycoprotein), thus increasing the unbound fraction and resulting in a higher volume of distribution.[14] Second, drugs that decrease cardiac output may decrease the perfusion of tissues involved in redistribution of drugs, thereby altering their volume of distribution.[24] A decrease in propofol requirements has been found in the presence of esmolol, probably as a result of distribution alterations.[25] As described in an animal model by Ludbrook and colleagues,[26] drugs that alter cardiac output also alter liver blood flow and influence clearance. In a sheep model, cardiac output is found to be inversely related to arterial and brain propofol concentrations.[26] Lange and colleagues[27] described how propofol decreases liver perfusion and decreases its own excretion. In a recent study, it was shown that a decreased cardiac output, induced by a remifentanil infusion, led to a higher propofol concentration due to decreased hepatic and renal blood flow.[28] Activation of liver enzymes by anti-epileptic drugs lead to decreased plasma concentrations of fentanyl, methadone, pethidine, paracetamol, pancuronium, rocuronium and vecuronium.[29]

Volatile anaesthetics and opioids exhibit strong supra-additive interactions. Even small doses of opioids reduce the MAC of volatile anaesthetics. The interaction between opioids and the i.v. anaesthetic agents is also supra-additive. Interaction between propofol and alfentanil on laryngoscopy and surgical stimuli in patients undergoing elective surgery showed supra-additive interactions.[30] However, alfentanil also amplifies the depressant effect of propofol on blood pressure and therefore does not contribute to haemodynamic stability during induction.[30] The interaction between propofol and remifentanil has been found supra-additive for noxious stimuli, laryngoscopy, intubation, intra-abdominal surgery and postoperative pain.[31]

Propofol–remifentanil combinations for upper gastrointestinal endoscopy revealed that this combination is associated not only with better conditions for oesophageal instrumentation, but also with rapid return of responsiveness, compared with propofol-only regimens.[32]

Propofol–sevoflurane interaction was of simple additivity for response to laryngeal mask insertion, laryngoscopy, loss of consciousness (LOC) and movement in response to skin incision.[33] In conclusion, information about pharmacokinetic and

pharmacodynamic drug interactions can optimise anaesthetic drug dose.

PHARMACOLOGY OF NEUROMUSCULAR JUNCTION

Acetylcholine receptors (AChRs) appear over human muscle fibres at about 8 weeks of gestational age. Between 9 and16 weeks, AChRs join to form primitive motor-end plates on one side of the muscle fibres. From 16 to 24 weeks the number of nerve terminals decrease (poly to mononeuronal innervation). Between 24 and 31 weeks, the neuromuscular junctions attain a mature appearance and continue to grow until the first year of life.[34] The nicotinic AChR in mammalian muscles exists in foetal and adult forms. The foetal form is composed of five subunits designated 2α, β, γ, and δ. In the adult form, the γ subunit is replaced by a subunit designated ε.[35] Foetal AChRs are not normally detected on human muscle fibres after 31 weeks of gestational age, but they may reappear in pathological states associated with prolonged inactivity (e.g., burns, denervation injury, prolonged muscle paralysis). They appear within 18–24 h of injury and have a shorter half-life of <24 h. These receptors are sensitive to succinylcholine and a reduced response to non-depolarising NMBDs. When stimulated, these channels have a 2 to10 fold longer mean channel open time, promoting greater efflux of potassium ions with the risk of hyperkalaemia. The increased sensitivity of the neuromuscular junction of the human neonate and infant to non-depolarising neuromuscular blocking agents is the result of reduced release of acetylcholine from immature motor nerves.[36] The relatively high volume of extracellular fluid in infants and children correspond to an increase in the volume of distribution of Neuromuscular blocking drugs (NMBDs) and influence dose requirements.

NMBDs are quaternary ammonium compounds, mimicking the quaternary nitrogen radical of acetylcholine. NMBDs are the most common cause of anaphylaxis under general anaesthesia, with succinylcholine being topmost reason. Atracurium and rocuronium are the next most commonly implicated agents.

MUSCLE RELAXANTS IN CHILDREN

Recent developments like laryngeal mask airways in clinical practice have eliminated the need for muscle relaxants in paediatric anaesthesia. Muscle relaxants are required for intubation and procedures requiring profound muscle relaxation. Specific relaxants and doses can be administered as per need.[37]

On a weight basis neonates and young infants are resistant to both depolarising and non-depolarising NMBDs; when dose is calculated according to surface area; neonates and young infants are not resistant to succinylcholine, but appear sensitive to non-depolarizing relaxants probably due to variation in extracellular fluid volume. Dose-response studies suggest that infants and children require at least 3 mg/kg and 2 mg/kg of succinylcholine to produce reliable conditions for intubation respectively.[38] The duration of action of these doses is about same or less than that of the standard 1 mg/kg intubating dose in adults (6–8 min). The increased dose requirement of succinylcholine in younger patients is result of its rapid distribution into extracellular fluid rather than an altered response to the action of the drug at post-junctional AChRs.

During nitrous-oxide narcotic anaesthesia, the effective dose of atracurium was found to be significantly lower in neonates and infants than in children.[39]

The effective dose of cisatracurium is similar to adults. Increased potency is associated with greater specificity of drug action and fewer side effects; cisatracurium has fewer propensities for histamine release and provides greater cardiovascular stability than atracurium. The main disadvantage of increased potency is a slower onset of action which necessitates a relative high dose to achieve reliable intubating conditions at 2 min.[40] After a dose of 0.15 mg/kg onset of maximum block occurred more rapidly in infants than in children (2.0 min vs. 3.0 min). Onset and recovery times following cisatracurium 0.15 mg/kg appeared to be somewhat shorter in infants and children than in adults.

Pancuronium is a potent, long-acting, aminosteroidal NMBD lacking the histamine releasing and hypotensive properties. It is mainly eliminated via the kidney; therefore, its duration of action may be prolonged in patients with renal failure. The vagolytic effect of pancuronium is an advantage in infants, in whom bradycardia is highly undesirable, or in patients undergoing anaesthesia with high-dose opioids.

Vecuronium is a long-acting neuromuscular blocking agent in newborns and infants.

Rocuronium (rapid onset-curonium) is analogue of vecuronium with a more rapid onset of action. Rapid onset is the result of reduced potency, which mandates an increase in dose. Rocuronium is longer acting in infants than in children. Rocuronium is an acceptable alternative to succinylcholine for rapid sequence induction after exclusion of possible difficult intubation.[40]

COMMONLY USED DRUGS IN ANAESTHESIA

Atropine is metabolised in the liver by N-demethylation followed by conjugation with glucuronic acid; both processes are immature in the neonate. Atropine is commonly administered to manage the muscarinic effects of neostigmine.

Glycopyrrolate is a synthetic quaternary ammonium compound with potent anticholinergic properties. It is used for antagonising the parasympathomimetic effects of neostigmine and is as effective as atropine for preventing the oculocardiac reflex.

Midazolam offers a better pharmacokinetic profile than diazepam for neonates because the active metabolite has a half-life similar to the parent compound but with minimal clinical activity. The desired clinical effects include anterograde amnesia as well as sedation and anxiolysis before induction of anaesthesia or a medical procedure.

Propofol clearance matures rapidly within 6 months of life. Induction and maintenance doses are higher in children than in adults because the volume of the central compartment is 50% larger.

Thiopentone sodium redistributes into muscle and fat terminating its effect. Dose adjustments are therefore required in undernourished child and in neonates who have reduced fat stores. In the neonate, plasma protein binding of thiopentone is reduced, so that the fraction of unbound drug is almost twice that found in older children and adults. The reduced requirement for thiopentone in neonates may be explained by decreased plasma protein binding, greater penetration of the neonatal brain or increased responsiveness of neonatal receptors. There is an increased requirement for thiopentone in infants and children compared with adults.

Ketamine is highly lipid soluble with rapid distribution, and the onset of anaesthesia after IV injection is approximately 30 seconds. The concentration–response curve for sedation is steep. This means that small serum concentration changes will have dramatic effect on the degree of sedation. In neonates the clearance is decreased but the volume of distribution is enhanced thereby increasing the doses required. Children require greater doses (mg/kg) than adults because of greater clearance. The most common side effects in children are postoperative nausea and vomiting (PONV) and postoperative hallucinations.

Fentanyl is the most commonly used opioid anaesthetic in children and has a rapid onset and shorter duration of action in children. It is metabolised by oxidative N-dealkylation into norfentanyl and hydroxylated fentanyl. Clearance in preterm neonates is markedly reduced contributing to prolonged respiratory depression.

Minimum alveolar concentration (MAC) of inhaled anaesthetics required in paediatric patients changes with age. Full-term neonates require lower concentrations of volatile anaesthetics than infants 1 to 6 months of age, e.g., the MAC is about 25% less in neonates than in infants.[41] Decreased anaesthetic requirement in neonates may be related to immaturity of the central nervous system and to increased circulating concentrations of progesterone and beta endorphins. MAC steadily increases until 2 to 3 months of age; but after 3 months, the MAC steadily declines with aging, although there is slight increase at puberty. Uptake and elimination of inhaled anaesthetics is more rapid in paediatric patients than in adults. The principle reasons for this appear to be increased respiratory rate and cardiac index and a greater proportional distribution of cardiac output to vessel rich organs.

TARGET CONTROLLED INFUSION

Adequacy of TIVA depends on the maintenance of brain propofol and remifentanil concentrations which are clinically appropriate and in equilibrium with levels in the plasma. The best way to achieve this state is by TCI from dedicated pharmacokinetic pumps. These devices solve the complex equations which describe the distribution of agents between compartments and allow for rapid adjustments in targets to achieve the desired clinical effect.[42]

Key components of a TCI infusion system

User interface to enter patient details and target blood concentration.

Software with pharmacokinetic model- validated for specific drug to control infusion rate.

Communication between 'control unit' and pump hardware.

Common TCI models available

Marsh model used for propofol

Schüttler and White-Kenny (WK) models for propofol

Schnider model for propofol

Kataria and Paedfusor model in children

Minto model for remifentanil.[43]

ANAESTHESIA AND THE DEVELOPING BRAIN

Brain development begins during the last trimester of intrauterine life; human brain is not fully developed at birth and continues to grow over the first couple of years of postnatal life.[44]

According to a Danish study young children exposed to a brief, single anaesthetic did not show any evidence of adverse long-term effects on the brain.[45] Based on the work of Ikonomidou *et al*.[46] it is widely accepted that the commonly used general anaesthetics potentiate inhibitory transmission through gamma-amino-butyric-acid type A (GABAA) receptors and the excitatory transmission is reduced through N-methyl-D-aspartic acid (NMDA) glutamate receptors at the peak of synaptogenesis causing apoptotic neurodegeneration.[47] Furthermore, based on the studies by Jevtovic-Todorovic *et al*. it appeared that exposure to general anaesthetics at the peak of synaptogenesis causes significant learning and memory deficit later in life.[47]

In the adult, GABAA receptor activation leads to an influx of chloride ions (Cl^-) into the cell. This results in hyperpolarisation and can lead to neuroprotection in many models of hypoxia and ischaemia. However, in the developing brain, especially during synaptogenesis, intracellular concentration of Cl^- is high; activation of GABAA receptor results in Cl^- efflux and depolarisation of the neuron. Consequently, depolarization-mediated rise in intracellular calcium concentration reaches levels that can be harmful to the cell, suggesting that this excitotoxic action of GABAA contribute to neuronal injury.

Several human cohort studies demonstrated an association between major surgery in the neonatal period and poor neurodevelopmental outcome. Premature infants who underwent laparotomy had poorer neurodevelopmental outcome and children born with esophageal atresia had increased long-term learning emotional and behavioural problems.[48]

Wilder *et al*.[49] using a large birth cohort maintained at the Mayo Clinic studied children who had a surgery before the age of 4 years, and they found the risk of learning disability increased with the number of anaesthetics a child had received. Interestingly, there was no evidence for an increased risk of association after just one exposure. The association between disability and multiple exposures to anaesthetics persisted when adjustment was made for chronic illness.

Di Maggio *et al*.[50] performed a study comparing children who had hernia repair before the age of 3 matched with those who had no surgery. After adjusting for confounding factors, they found children who had hernia repair had twice the risk of diagnosis of behavioural or developmental disorder.

Olney *et al*. have proposed that anaesthetic drug effects on foetal and neonatal GABAA and NMDA receptors cause translocation of a Bcl-2-associated protein to mitochondrial membranes, leading to an apoptotic cascade.[51]

Warner DO *et al*. analysed data from Mayo Anaesthesia Safety in Kids (MASK) study, in which unexposed, singly exposed and multiply exposed children to general anaesthesia before 3 years of age were studied. The children underwent Operant Test Battery (OTB) testing at ages 8-12 or 15-20 years using five tasks that generated 15 OTB test score. They hypothesised that children exposed to general anaesthesia show deficits on OTB tests.[52]

Mc Cann ME *et al*. in a controlled trial studied infants of less than 60 weeks postmenstrual age undergoing inguinal herniorrhaphy with no previous exposure to general anaesthesia or risk factors for neurological injury. The full scale intelligence quotient (FSIQ) on Wechsler preschool and primary scale of intelligence, third edition (WPPSI III) was measured at 5 years of age. They discovered that slightly less than 1 hour of general anaesthesia in early infancy doesn't alter neurodevelopmental outcome at 5 years of age.[53]

Melatonin, beta estradiol, L carnitine, xenon prevent anaesthesia-induced apoptotic neuronal degeneration.[51] *In vivo* dexmedetomidine dose dependently prevent isoflurane-induced injury in the hippocampus, thalamus, and cortex which causes impairment of long-term memory.[51]

SUMMARY

Anaesthetising the paediatric patients can be fascinating, albeit challenging, even for experienced anaesthesiologists. It is evident that the paediatric population differs even amongst themselves physiologically, anatomically as well as pharmacologically depending upon their age group. It is imperative to have thorough knowledge about the pharmacological difference for each age group alongwith the PK and PD interactions of anaesthetic drugs to prevent therapeutic misadventures. Target controlled infusions in paediatric and the neurodevelopmental outcome of anaesthetic drugs is still being studied. We have tried to review the literature and articles specific to paediatric anaesthesia and pharmacology briefly.

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Conflicts of interest

There are no conflicts of interest.

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