books, visit our website www.jaypeebrothers.com, for detailed information on anesthesia books, visit our website www.jaypeebrothers.com, for detailed information on anesthesia books

Principles and Practice of

Pediatric Anesthesia



Editors
Snehalata H Dhayagude
Nandini M Dave

Foreword
VM Divekar

JAYPEE

Contents

SECTION 1: BASIC PRINCIPLES

1. Anatomy, Growth and Development 3

Bharati Awalegaonkar Kulkarni, Sarita Fernandes

- Anthropometry 4
- Face 5
- Teeth 5
- Fontanelles 5
- Neonatal Reflexes 5
- Upper Airway 6
- Lower Airway 8
- Small Airways, Large Controversies 8
- Chest Wall 9
- Central Nervous System 9
- The Spinal Cord 10
- The Epidural Space 11
- The Caudal Canal 11
- Heart 11
- Musculoskeletal System 12
- Neuromuscular Junction 12
- Abdomen 12
- Gastrointestinal System 13

2. Physiological Characteristics and Anesthetic Implications 14

Chandrika YR, Anuradha G

Developmental Principles: From Fetal Life to Adolescence 14

- Prematurity 14
- General Growth and Development Patterns 15
- Developmental Physiology 16
- Respiratory Physiology 18

Developmental Physiology and Anesthesia 18

- Cardiovascular Physiology 21
- Physiology of Central Nervous System 24
- Renal Physiology 25
- Hepatic Physiology 26
- Gastrointestinal System 27
- Hemopoeitic System 27

3. Essentials of Pharmacology in Neonates, Infants and Children 30

Diganta Saikia

- Pharmacokinetic Differences of Drugs in Children 30
- Pharmacodynamics of Drugs in Children 31

- Commonly Used Pharmacologic Agents in Pediatric Anesthesia 32
- Reversal of Neuromuscular Blockade 41
- Antiemetics 42
- Anticholinergics 42
- Local Anesthetics 43
- Adjuvants 44

4. Understanding the Pediatric Chest Radiograph 54
Hemant Deshmukh, Sunita Kale, Amrita Narang
- Imaging a Child 54
- Reading a Chest Radiograph 54
- Normal Chest Radiograph 55
- Signs in a Chest Radiograph 58
- Abnormal Chest Radiograph 59
- Other Congenital Lesions on a Pediatric Chest Radiograph 65
- Infective Lung Diseases 66
- Complications of Pneumonia 66
- Tension Pneumothorax 70
- Pneumomediastinum 70

5. Interpretation of Pediatric Electrocardiogram 74
Shakuntala Prabhu, Sumitra Venkatesh
- Indications 74
- ECG Recording and Interpretation 74
- Some Disease Specific ECG Changes 79
- Arrhythmias in Children 80

SECTION 2: ANESTHETIC MANAGEMENT

6. Preoperative Evaluation and Premedication 85
Rochana G Bakhshi
- Role of Surgeon 85
- Role of Anesthesiologist 85
- Role of Pediatrician 86
- The Preanesthesia Consultation 86
- Preoperative Investigations 89
- Premedication 91
- Preoperative Fasting 91
- Psychological Preparation of the Child 91

7. Induction, Maintenance and Emergence 96
Sandhya Yaddanapudi
- Preparation 96
- Induction of Anesthesia 96
- Airway Equipment and Techniques 98
- Monitoring and Documentation 102
- Maintenance of Anesthesia 102
- Emergence from Anesthesia 103
- Intraoperative Complications 104

8. Monitoring in Pediatric Anesthesia 107
Snehalata H Dhayagude
- Physical Signs 107
- Precordial/esophageal Stethoscope 108
- Electrocardiography 108
- Pulse Oximetry (SpO_2) 108
- Pleth Variability Index (PVI) 110
- Signal Extraction Technology (SET) 110
- Cutaneous Oxygen Tension PsO_2 110
- Noninvasive Blood Pressure Monitoring (NIBP) 111
- Invasive or Direct Blood Pressure Measurement 111
- Central Venous Pressure Monitoring (CVP) 111
- Noninvasive Respiratory Gas Monitoring 112
- Cutaneous Carbon Dioxide Tension ($PsCO_2$) 113
- Measurement of Other Respiratory Gases 113
- Bispectral Index Monitor (BIS) 114
- Near Infrared Spectroscopy (NIRS) 115
- Pulse Oximetry-Based Hemoglobin Determination 115
- Temperature Monitoring 116
- Neuromuscular Block (NMB) Monitoring 116
- Urine Output 118
- Blood Chemistry 118
- Other Monitoring Aids 118

9. Perioperative Fluid and Electrolyte Therapy 120
Anila Malde
- Neonatal Physiology 120
- Requirements of Neonates 121
- Intraoperative Fluid Management in Neonates 122
- Three Components of Intravenous Fluid Therapy 123
- Intraoperative Colloids 125
- Postoperative Hyponatremia 127
- Postoperative Fluid Management 128
- Correction of Water and Electrolyte Abnormalities in Perioperative Period 128
- Disturbances of Potassium Metabolism 130
- Disturbances of Calcium Metabolism 131

10. Assessment and Management of the Difficult Pediatric Airway 135
US Raveendra
- Assessment 136
- Illustrative Pictures of Difficult Airway in Children 138
- Planning and Preparation 139
- Techniques of Difficult Airway Management 140
- Choice of Anesthesia 140
- Equipment for Management of Difficult Airway 141
- Techniques of Endotracheal Intubation in Difficult Airway 145

11. Pediatric Pain Assessment and Management 154
Swati Daftary, Rajen Daftary
- Pain Assessment 154
- Neurophysiology of Pain 155
- Pathophysiology of Pain 155
- Pain Management 156
- Pediatric Pain Management Strategies 157
- Chronic Pain in Children 160
- Future of Pediatric Pain Management 160

12. Ventilatory Strategies in the Operating Room 162
Subrahmanyam M, Neha Hasija
- Respiratory Physiology 162
- Equipment 163
- Breathing Circuits 164
- Modes of Ventilation 166
- Controlled Modes 166
- Combined Modes of Ventilation 167
- Special Situations 168

13. Regional Anesthesia in Infants and Children 171
Nandini M Dave, Snehalata H Dhayagude
- Regional Anesthesia—Benefits 171
- Regional Anesthesia in Children—Awake or Anesthetized? 171

Pediatric Regional Anesthesia 171
- Factors Influencing the Choice of Technique 172
- Contraindications to Regional Anesthesia 172
- Complications of Regional Blocks 173
- Adjuvants to Local Anesthetics 173
- Individual Blocks 175
- Caudal Block 175
- Lumbar Epidural Block 177
- Spinal Block 179
- Abdominal Wall Blocks 180
- Ilioinguinal/Iliohypogastric Nerve Block 180
- Rectus Sheath Block 180
- Transversus Abdominis Plane (TAP) Block 181
- Paravertebral Block 181
- Infraorbital Nerve Block 183
- Greater Palatine Nerve Block 183
- Safety Rules for Performing Regional Anesthesia 183
- Role of Ultrasound 184
- Role of Neurostimulation 184

Local Anesthetic Toxicity 188
- Factors Influencing Toxicity of Local Anesthesia 188
- Toxic Plasma Levels of Local Anesthetics 189
- Clinical Picture of Toxicity 190
- Learning Points to Reduce Risk of Toxicity 190
- Treatment for LAST 191

14. Transfusion Therapy and Bleeding Disorders 193
Charusmita Modi
- Transfusion Therapy 194
- Blood and Blood Components 194
- Pharmaceutical Preparations 196
- Available Modifications of Blood Components 196
- Transfusion Procedure 197
- Investigations 198
- Bleeding Disorders and Transfusion Therapy 198
- Adverse Transfusion Reactions 200

SECTION 3: SUBSPECIALTY ANESTHESIA

15. Anesthesia for Surgery in the Neonate 205
Nandini M Dave
- Neonatal Physiology and the Surgical Neonate 205
- Neonatal Pharmacology and Considerations for Anesthesia 207
- Specific Neonatal Surgical Lesions 208

16. Anesthesia for Ear, Nose and Throat Procedures in Children 225
Hemalata R Iyer, Snehlata Tavri
- Anesthesia for Ear Surgery 225
- Anesthesia for Rhinologic Procedures 226
- Reduction of Nasal Bone Fracture 227
- Nasal Polypectomy 227
- Endoscopic Sinus Surgery 227
- Choanal Atresia 227
- Anesthesia for Throat Procedures 228
- Peritonsillar Abscess 230
- Supraglottitis 230
- Stridor 231
- Endoscopy of Airway 231
- Rigid Bronchoscopy 232
- Surgery for Laryngeal Stenosis 232
- Microlaryngeal Surgery 233
- Anesthesia for MicroLaryngoscopy 234
- Surgical Tracheostomy 234
- Bronchoscopy for Foreign Body Removal 235
- Esophageal Foreign Body (EFB) Extraction 236

17. Anesthesia for Plastic and Reconstructive Surgery 240
Neerja Bhardwaj
- Cleft Lip and Palate 240
- Anesthesia Management 241
- Craniofacial Surgery 242
- Preoperative Assessment 244
- Anesthesia Management 244
- Temporomandibular Joint Ankylosis 245
- Other Plastic Surgical Procedures 246

18. Anesthesia for Pediatric Dentistry 247
Sarita Fernandes, Deepa Suvarna
- Clinical Presentation 247
- Pediatric Dental Procedures 247
- The Dental Chair 247
- Local Anesthetics 248
- Local Anesthetic Allergy 248
- Procedural Sedation 248
- Sedative Drugs Commonly Used 249
- Reversal Drugs 251
- General Anesthesia 251
- Preoperative Evaluation and Optimization 251
- Anesthesia Management 252
- Complications 253
- Congenital Bleeding Disorders 255

19. Anesthesia for Ophthalmic Procedures 258
Renu Sinha, Bikash Ranjan Ray
- Pathophysiology 258
- Anesthetic Implications of Drugs Used in Ophthalmology: Topical and Systemic 259
- Anesthesia Goals 260
- Anesthesia Technique 260
- Clinical Presentation, Surgical Procedure and Anesthesia Management 262
- Monitoring 267
- Postoperative Care 267
- Possible Complications 268

20. Anesthesia for Major Burns and its Consequences 271
Sweta Salgaonkar, Priti Devalkar
- Understanding Burn Injury 271
- Burn Injury—Local Effects 271
- Classification of Burns 272
- Burn Severity Grading 272
- Pathophysiology of Burn Injury 273
- Management of Burns 274
- Resuscitation During Burn Shock Phase 274
- Analgesia and Anxiolysis 276
- Early Excision and Grafting Surgery 277
- Anesthesia Concerns in Early Excision 277
- Anesthesia Concerns for Delayed Excision 279
- Anesthesia Concerns for Contracture Release 279

21. Anesthesia for Pediatric Neurosurgical Procedures 281
Hemangi S Karnik, Devangi Parikh
- Pathophysiology 281
- Clinical Presentation 282
- Anesthesia Goals 282
- Anesthetic Management 282
- Possible Issues and Complications 284
- Anesthesia Considerations for Specific Surgical Procedures 285

22. Anesthesia and Pediatric Liver Diseases 289
Lakshmi Kumar
- General Principles of Pediatric Anesthesia in Liver Diseases 289
- Anesthetics and Liver Functions 289
- Physiological Jaundice in the Neonate 290
- Biliary Atresia 291
- Disorders of Bilirubin Metabolism 291
- Viral Hepatitis 292
- Wilson's Disease 292
- Non-alcoholic Steatohepatitis (NASH) and Obesity Syndromes in Children 292
- Familial Hypercholesterolemia 293
- Choledochal Cyst and Cholelithiasis 293
- Neoplasms 294
- Liver Diseases Presenting for Transplant 294

23. Anesthesia for Pediatric Urologic Procedures 297
R Jayanthi
- Renal Physiology and Anesthesia 297
- Renal Function in the Newborn 298
- Preoperative Assessment 299
- Positioning for Urological Procedures 300
- Anesthetic Management for Individual Procedures 301
- Renal Transplantation in Children 306

24. Anesthesia for Pediatric Laparoscopic Surgeries 310
Chandrashekara CR, Nandini M Dave
- Indications for Laparoscopic Procedures 310
- Contraindications 311
- Anesthetic Challenges 311
- Patient Positioning 312
- Anesthetic Management 312
- Complications of Laparoscopy 314
- Advances in Laparoscopy 315

25. Anesthesia for Pediatric Thoracic Surgery 317
Shailesh Mulgaonkar
- Physiology of Single Lung Ventilation (SLV) in Children 317
- Preoperative Evaluation 318
- Preoperative Preparation 318
- Essential Monitoring During SLV 319
- Perioperative Management 319
- Video-Assisted Thoracoscopic Surgery (VATS) 319
- Measures to Manage Desaturation During SLV 320
- Methods of Single-Lung Ventilation in Pediatric Patients 320
- Postoperative Management 323
- Postoperative Complications 324
- Postoperative Pain Control 324
- Salient Features in Managing Pediatric Thoracic Lesions 324

26. Anesthesia at Remote Locations 327
Pramila Kurkal, Shwetal Goraksha, Bhoomika Thakore, Roopali Telang
- Goals 327
- Problems 327
- Pre-procedure Planning 327
- Medications 328
- Documentation 328
- Anesthesia Technique 329
- Monitoring 329
- Recovery and Discharge Planning 330
- Individual Scenarios 330

27. Ambulatory Anesthesia in Children 336
MSRC Murthy
- Advantages 336
- Limitations 336
- Guidelines 336
- Guidelines for a Good Ambulatory Surgical Facility 341

28. Anesthesia for Pediatric Orthopedic Surgery 343
Pradnya Sawant, Varun Dua
- Anesthesia Issues 343
- Preoperative Evaluation and Premedication 344
- Tourniquets 344
- Congenital Deformities—Lower limb 344
- Congenital Deformities—Upper Limb 346
- Neurological Conditions 346
- Muscular Dystrophies 347
- Growth Disorder 348
- Infections 348
- Metabolic Disorders 348
- Scoliosis 351
- Bone Cysts and Tumors 354
- Trauma 354
- Commonly Used Regional Blocks for Orthopedic Procedures 354
- Lower Extremity Blocks 355
- Upper Extremity Blocks: Brachial Plexus Block 357

29. Anesthesia for Pediatric Trauma 360
Rakesh Garg, Uma Hariharan
- Role of Anesthesiologist in Trauma Care 360
- Types and Patterns of Pediatric Trauma 360
- Initial Assessment: Pediatric Advanced Trauma Life Support principles 361
- Primary Survey and Resuscitation 361
- Secondary Survey 363
- Monitoring 363
- Anesthetic Considerations for Specific Trauma 363
- Anesthesia for Chest/Airway Injury 364
- Anesthesia for Abdominal Injury 365
- Anesthesia for Urological/Pelvic Injury 365

- Anesthesia for Orthopedic Injury; Damage Control Resuscitation 366
- Anesthesia for Reimplantation 366
- Anesthesia for Spinal injuries 366
- Anesthesia for Ophthalmic Injuries 367
- Anesthesia for Faciomaxillary Injuries 367
- Fluid Management 368
- Pain Management 368
- Child Abuse 368
- Transfer and Transport of Pediatric Trauma Patient 368
- Pediatric Intensive Care after Trauma Surgery 369
- Brain Death and Organ Donation 369

30. Anesthesia for Pediatric Cardiac Surgery 372

Sachin Patil, Shivaji Mali

- Understanding the Cardio-pulmonary Physiology in Children 372
- Pathophysiology 373
- Classification 373
- Preoperative Evaluation 374
- Preoperative Preparation 375
- Monitoring 378
- Choice of Anesthetic Drugs and General Precautions 378
- Induction Agents 379
- Central Lines and Arterial Lines 380
- Anesthetic Considerations During Cardiopulmonary Bypass 381
- Difficulty In Weaning CPB 382
- Anesthetic Considerations for Common Lesions 382
- Postoperative Care in Pediatric Cardiac Patient 385
- Anesthesia for Closed Heart Procedures 387
- Anesthesia for Cardiac Catheterization 388
- Anesthesia for Cardiac Radiology Procedures 389
- Fast-tracking and Regional Anesthesia 390

31. Anesthetic Management of Children with Congenital Heart Disease for Noncardiac Surgery 393

Indrani Hemantkumar Chincholi

- The Neonate 393
- Classification 394
- Preoperative Considerations 394
- Risk Stratification 395

SECTION 4: SPECIAL PROBLEMS AND SITUATIONS

32. Common Pediatric Medical Conditions: Anesthetic Considerations 403

Chhaya A Divecha, Chandrika Bhat, Milind S Tullu

Upper Respiratory Tract Infection 403

- Pathogenesis 403
- Preoperative Optimization 403
- Intraoperative Management 404

Reactive Airway Disease/Asthma 404
- Preoperative Evaluation 405
- Perioperative Management 405
- Management of Intraoperative Wheezing/Bronchospasm 406
- Extubation 406
- Postoperative Management 407
- Management in Special Circumstances 407

Nutritional Anemia 407
- Etiology 407
- Clinical Features 408
- Presurgical and Intraoperative Optimization 408
- Indications of Blood Transfusions 408

Eosinophilia 409
- Evaluation of Eosinophilia 409
- Preoperative Optimization 409
- Intraoperative Management 409
- Postoperative Management 409

Diabetes Mellitus 410
- Management Options for Diabetes Mellitus in Children 410
- Risks Associated with Diabetes Mellitus 410
- Preoperative Assessment 411
- Preoperative Management of a Child Posted for a Major Surgery 411
- Preoperative Management of a Child Posted for Minor Surgery 411
- Emergency Procedure 411
- Type 2 Diabetes 413
- Postoperative Management 413

Hypothyroidism 413
- Anesthetic Implications of Hypothyroidism 413
- Preoperative Evaluation 413
- Intraoperative Anesthetic Management 414
- Postoperative Care 414

Epilepsy 414
- Physiological and Pharmacokinetic Considerations 415
- Preanesthetic Evaluation 415

Preparing for Splenectomy 417
- Anesthetic Considerations 417
- Preoperative Management 417
- Intraoperative Management 417
- Post-Operative Management 418

Syndromic Child 418
- Etiology 418
- Preanesthetic Evaluation 418
- Anesthetic Concerns 419

33. Anesthesia Management in Special Conditions 421
Sanjay Choubey

Cerebral Palsy 421
- Pathophysiology 421
- Classification 422
- Clinical Presentation 422
- Surgical Procedure 423
- Anesthesia Technique 423
- Specific Problems (Preoperative) 424

Neuromuscular Disorders 425
- Pathophysiology 425
- Muscular Dystrophy 425
- Myotonias 426
- Congenital Myopathies 427
- Mitochondrial and Metabolic Myopathies 427
- Channelopathies 428

Childhood Obesity 431
- Description: Childhood Obesity 431
- Prevalence 431
- Pathophysiology, Clinical Presentation, Anaesthetic Issues and Pharmacokinetics of Anesthetic Agents 431
- Anesthesia Technique 432
- Possible Risks and Complications (Perioperative) 432

Obstructive Sleep Apnea 435
- Etiology of Sleep Disordered Breathing in Children 435
- Pathophysiology 435
- Clinical Presentation 435
- Diagnosis 436
- OSA severity scoring 436
- Surgical Procedure 436
- Anesthetic Considerations 436
- Postoperative Complications 437
- Postoperative Pain Relief 437

Pheochromocytoma 440
- Pathophysiology 440
- Clinical Presentation 440
- Preoperative Workup 441
- Surgical Resection of the Tumor 442
- Anesthesia Goals 442
- Anesthesia Technique 442
- Possible Complications 443

Vascular and Lymphatic Malformations 444
- Pathophysiology 444
- Classification 444
- Clinical Presentation 444
- Treatment 446
- Anesthetic Concerns and Complications 446

34. Cardiopulmonary Resuscitation in Neonates and Children 448
Aparna A Nerurkar, Naina P Dalvi
- Primary Causes of Pediatric Cardiac Arrest 448
- Strategies and Guidelines to Improve Survival 448
- Guidelines Regarding Use of AED in Children 451
- Special Situations 453
- Recent AHA Update 2015 456

35. Acute Complications During Anesthesia 459
Elsa Varghese
- Causes of Acute Problems during Anesthesia in Children 459
- Acute Cardiovascular Problems 460
- Acute Respiratory Problems 462
- Local Anesthetic Toxicity 465
- Generalized Seizures 466
- Anaphylaxis 466
- Malignant Hyperthermia 467
- Transfusion Reactions 467
- Medication Related Problems 468

SECTION 5: ANESTHETIC TECHNIQUES

36. Vascular Access in Infants and Children 473
Vibhavari Naik, Basanth Rayani
- Peripheral Vein Cannulation 473
- Ultrasound-Guided Vascular Access 473
- Peripherally Inserted Central Catheter Insertion 475
- External Jugular Vein Cannulation 475
- Central Venous Catheterization 476
- Tunneled Central Venous Catheterization 478
- Port Implantation 479
- Intraosseous Needle Placement 480
- Arterial Cannulation 481
- Umbilical Vein Catheterization 482
- Umbilical Artery Catheterization 482
- Recent Developments 482

37. Ultrasound-guided Regional Blocks 485
Sandeep Diwan
Ultrasound-Guided Plexus, Nerve and Truncal Blocks 485
- Advantages of Ultrasound Imaging in Regional Blocks 485
- Steps in Performing Ultrasound-Guided Nerve Blocks 485
- Upper Limb Blocks 486
- Lower Limb Blocks 490

Ultrasound-Guided Neuraxial Blocks 498
- Sonoanatomy of the Spine 498
- Single-Shot Caudal Block 498
- Ultrasound-Guided Catheters 499
- Equipment 499

SECTION 6: NOTES ON ALLIED TOPICS

38. Safety and Quality in Pediatric Anesthesia 503
Snehalata H Dhayagude
- High Quality Anesthesia Care has Six Attributes 503
- Assessment of Quality of Anesthesia Care 504
- Implementation of Quality Improvement 504
- Common Causes of Undesirable Events During Anesthesia 505
- Anesthetic Training Should Incorporate 505
- Specialty Professional Training has Evolved into Multidisciplinary Education (MDE) Involving Many Steps 506

39. Ethical Issues in Pediatric Anesthesia 507
Rachana D Chhabria
- Informed Consent 507
- Assent 508
- Mature Minor 508
- Special Situations 509
- Research in Pediatric Patients 509
- Obligations of Pediatric Anesthesiologists 510

40. Simulation in Pediatric Anesthesia 512
Nandini M Dave, Amit Nagpal
- Types of Simulation 512
- Conceptual Issues About Patient Simulation 513
- Setting of the Simulation Exercise 513
- Pediatric Simulators 515
- Applications of Simulation in Pediatric Anesthesia 516

APPENDICES

Appendix I. Index of Syndromes and Anesthetic Implications 519
Appendix II. Pediatric Drug Index 526
Appendix II. Quick Reference Tables and Formulae 534

Photo Gallery *539*
Index *547*

3

CHAPTER

Essentials of Pharmacology in Neonates, Infants and Children

Diganta Saikia

JAYPEE BROTHERS

INTRODUCTION

Pharmacokinetics and pharmacodynamics of drugs are different in children from those in adults. These differences make children respond differently to drugs, including anesthetics and other perioperative medications. Many perioperative medications used in children, especially in neonates and infants, are not extensively clinically studied and data is frequently extrapolated from adult literature. However, doing this in clinical practice may result in inappropriate selection of drugs, therapeutic doses and frequency of administration and may cause overdosing and serious drug toxicity in children. Thus, clear understanding of these pharmacokinetic and pharmacodynamic differences between children and adults is mandatory for anesthesiologists to provide safe anesthesia to children.

PHARMACOKINETIC DIFFERENCES OF DRUGS IN CHILDREN

Children, especially neonates and infants have a different body composition, reduced hepatic metabolic and renal function, decreased body fat and muscle mass as a proportion of body weight and lower protein binding of drugs than in adults. These differences together with some other fairly less significant factors (Table 1) produce differences in pharmacokinetics of drugs in children from those in adults. The pharmacokinetic differences are most marked in neonates and young infants and may persist over the first decade of life.

Neonates and preterm infants have delayed gastric emptying rate until 6–8 months of age.[1,2] Thus, absorption as well as peak bioavailability of orally administered premedicants and postoperative pain medications are slower in this group of children. Sublingual and nasally administered drugs (e.g. sublingual fentanyl citrate and nasal midazolam) produce rapid onset of action as these agents skip first pass hepatic metabolism and quickly attain peak plasma level.[3] Locally applied medications (such as local anesthetic creams, analgesic patches etc.) are rapidly absorbed in neonates and infants because of their highly perfused, relatively large and thin skin surface area compared to older children and adults.[4] There is potential for drug overdose by this route. Absorption and bioavailability of rectally administered drugs are variable and unpredictable. Drugs administered into the lower part of the rectum initially bypass the liver.[5] Intramuscularly administered drugs exhibit more rapid onset of action with higher bioavailability in children because of higher cardiac output and increased muscle blood flow.[6] However, intramuscular injection is painful and is usually avoided in children. In infants, epidural space is highly vascular with smaller absorptive surface. Consequently, systemic absorption of epidurally administered drugs is faster in neonates and in infants until six months of age.[7]

Volume of distribution is high in infants because of increased total body water content (as increased ECF) than in older children and adults.[8] Preterm and term infants have higher proportion of extracellular fluid (ECF) (approximately 63% and 45%, respectively) compared to older children and adults (20%). Consequently, they

Table 1: Summary of pharmacokinetic differences of drugs in neonates and in infants

Drug absorption	• Delayed gastric emptying in neonates and young infants	• Absorption of oral medications is slower
	• Sublingual and nasally administered drugs bypass first pass hepatic metabolism	• These drugs quickly attain peak plasma level producing rapid onset of action
	• Highly perfused, relatively large and thin skin surface area	• Rapid absorption of large amount of locally applied drugs (i.e. EMLA cream) may produce drug toxicity
	• Smaller and highly vascular epidural space	• Systemic absorption of epidural drugs is faster
Volume of distribution	• Increased total body water content (mostly as increased extracellular fluid)	• Require larger boluses of drugs, such as atracurium, succinylcholine, etc. (water soluble drugs)
	• Distribution of higher percentage of CO to larger brain and liver masses	• Induction with intravenous agents is faster
	• Reduced body fat and muscle mass relative to body weight	• Increased and prolonged effects of lipid soluble drugs (i.e. propofol, thiopentone etc.)
Drug clearance	• Activities of the liver enzymes as well as the hepatic blood flow are reduced	• Hepatic drug metabolism and biotransformation are reduced
	• Renal glomerular filtration and tubular functions are reduced	• Drug elimination is delayed. Half-life of amino glycoside and cephalosporin antibiotics may increase

require higher bolus doses of water soluble drugs like succinylcholine, atracurium, etc. compared to older children and adults. In neonates and infants a higher percentage of cardiac output is distributed to their relatively larger cerebral and hepatic masses which causes rapid induction of anesthesia with intravenous agents.[6] Recovery on the other hand is slower because redistribution to well-perfused and deep under-perfused tissues is more limited. Preterm and term neonates have reduced body fat (3% and 12%, respectively as a proportion of body weight which doubles by 4–5 months of age) and muscle mass relative to their body weight than older children and adults.[6] Thus, they have reduced volume of distribution and hence increased and prolonged plasma level of drugs, such as thiopentone that redistribute into fat and muscles (lipid soluble drugs).[9]

The activities of most of the liver enzymes as well as the hepatic blood flow are reduced in neonates. Microsomal activity of cytocrome P450 enzyme system is reduced at birth.[10] Phase-I reactions reach adult levels a few days after birth whilst phase-II reactions mature by 3 months.[11] Consequently, hepatic drug metabolism and biotransformation are reduced in neonates. However, drug metabolism and clearance is higher in children between 1 and 2 years of age because of mature hepatic enzyme systems and increased hepatic blood flow. The renal function in preterm and term infants is less efficient than in adults because of reduced glomerular filtration and tubular function. In term neonates, renal drug clearance becomes normal (adult level) by 3 and 4 weeks of age while glomerular filtration rate and tubular function reach adult level between 20 weeks and 2 years of life.[9]

Neonates have lower albumin and α1-acid glycoprotein (AAGP) concentrations.[12] This results in decreased protein binding and increased plasma level of free active form of highly protein bound drugs, such as thiopentone, bupivacaine, etc. and may cause enhanced clinical effects.

Blood-brain barrier (BBB) function attains adult level by the end of neonatal period.[13] Protein-bound drugs do not normally cross the BBB. Relatively lipid insoluble (partially ionized) drugs, such as morphine cross immature BBB of premature neonates easily. Term neonate's mature BBB allows passive diffusion of protein unbound, fat soluble drugs, such as bupivacaine to pass across it. Fentanyl moves in and out through the BBB with the help of ATP dependent active transport systems. CNS pathology, such as cerebral ischemia and inflammation may influence opioid transport and distribution across BBB.[14]

PHARMACODYNAMICS OF DRUGS IN CHILDREN

Older children respond to pharmacological agents much the same way as adults.[15] However, infants and neonates exhibit different pharmacodynamic responses towards many preoperative medications. Both in premature and term neonates neuromuscular blocking agents are more sensitive because of underdeveloped neuromuscular junction.[16] MAC of all inhalational anesthetics is reduced in neonates than in infants (Table 2).[17] Spinal block remains for shorter duration and requires higher dose of amide local anesthetics to produce same dermatomal level of anesthesia as in adults. While, bronchodilators are not effective because of paucity of bronchial smooth muscles, prokinetic drugs are fully effective only in older children. Neonatal heart stores less calcium and life-threatening bradycardia and hypotension may follow administration

JAYPEE BROTHERS

of calcium channel blockers, such as verapamil.[18] Also externally administered calcium produces exaggerated responses. One should be aware that at birth, in both preterm and term infants, coagulation cascade is immature and may influence perioperative hemostatic effects.[18] And, responses to benzodiazepines vary in children until the age of 10 years because of immature inhibitory GABA receptors.

COMMONLY USED PHARMACOLOGIC AGENTS IN PEDIATRIC ANESTHESIA

Inhalational Agents

Pharmacokinetics

The rate of rise of alveolar anesthetic concentration (wash-in) of inhalational agents in infants and children is more rapid than in adults. This is caused by a greater alveolar ventilation relative to functional residual capacity (5 to 1 in neonates, 1.5 to 1 in adults), distribution of a greater proportion of the cardiac output to the vessel-rich group of tissues, and lower blood/gas as well as tissue/gas solubility of more soluble inhaled anesthetics, such as halothane and isoflurane in children than in adults.[9]

Rapid "wash-in" of volatile agents causes relatively rapid induction of anesthesia in younger children than in adults. Induction is more rapid with poorly soluble agents (such as sevoflurane) because of their reduced uptake from the lungs. However, as MAC of poorly soluble agents is higher in infants and young children thus, the speed of induction also depends on the rate of increase of inspired concentration as well as maximum inspired concentration of these agents. Therefore, the rate of induction is accelerated if the inspired concentration (of poorly soluble agents) is rapidly increased to a very high level in larger increments.[9] Also, induction becomes faster if respiration is assisted and then controlled after the child is asleep.

The rate of wash-out of anesthetics in older children is similar to that in adults. In neonates and infants, however, this is more rapid. Less soluble agents (sevoflurane and desflurane) are washed-out faster.[19] Emergence from desflurane is faster than emergence from isoflurane and sevoflurane. Recovery from halothane anesthesia is also relatively faster (equivalent to isoflurane) in neonates and in infants because a higher percentage of halothane is eliminated by hepatic metabolism.[9]

KEY POINT

To enhance the speed of induction, the inspired concentration of more soluble agents (i.e. halothane) should not be rapidly increased to a very high level. This may produce inadvertent cardio respiratory instability

Pharmacodynamics

Minimum alveolar concentration (MAC): In children, MAC varies significantly with age (Table 2). MAC is highest during the first year of life although at different time periods for different agents.[20] MAC of all volatile agents except sevoflurane is lower in neonates compared to both children and adults. MAC value of sevoflurane is 3.3% (highest) in both neonates as well as in infants younger than 6 months. MAC in preterm neonates is studied only for isoflurane and found to be lower than for full-term infants. Beyond first year of life MAC value for all volatile anesthetics decreases as age increases.[21,22] MAC of all volatile agents is 15 to 40% higher in children between 1 and 12 years of age than in young adults.[21] MAC, however, does not vary significantly (10% or less) between children of this age group.

Addition of 60% nitrous oxide decreases the MAC values of sevoflurane by 20 to 25%, halothane by 60%, isoflurane by 40% and desflurane by 25%.[23-25] A reduction in body temperature, cerebral palsy and cognitive disorders also decreases MAC of volatile anesthetics in children.[26,27]

Individual Inhalational Agents

The most widely used inhalational anesthetics in the practice of pediatric anesthesia are nitrous oxide, sevoflurane, and isoflurane. Halothane is low-priced and thus is still being used, albeit less commonly, in many lesser developed and developing countries.

Table 2: MAC of commonly used inhalational agents in various age groups and effects of N_2O on MAC reduction

Agent	*MAC with oxygen (%)*			*MAC with 60% N_2O (%)*
	Neonates	*Infants*	*Older children*	*In older Children*
Halothane	0.87	1.2	0.98	0.35
Isoflurane	1.6	1.86	1.2	0.72
Sevoflurane	3.3	3.3	2.5	2.0
Desflurane	9.2	9.92	8.72	6.4

JAYPEE BROTHERS

Nitrous Oxide

Nitrous oxide (MAC 104% at sea level, in adults) is commonly used as a "carrier agent" to facilitate induction and intubation of children under deep volatile anesthesia. It reduces cardiovascular side effects of some volatile anesthetic agents, such as halothane by decreasing their MAC during induction. Nitrous oxide is a powerful analgesic and provides excellent analgesia for short painful procedures.[28] Analgesic effect of nitrous oxide is especially useful when opioids are either not justified or contraindicated for pain management in children undergoing painful procedures.[29] N_2O tends to diffuse into the closed spaces and may be relatively contraindicated in endoscopic procedures, gastrointestinal surgery, in middle ear and some ocular procedures, and in children with emphysema.[30] N_2O is less emetogenic in children.

KEY POINT

Omitting nitrous oxide during anesthesia may be associated with higher incidences of awareness in children and requires meticulous consideration, assessment, and monitoring[9]

Halothane

Halothane is less commonly used even in third world countries nowadays because of its poor cardiovascular profile. Halothane blunts baroreceptor reflex response and thereby makes neonates and infants vulnerable to direct cardiorespiratory depressant actions of anesthetics.[31] Halothane depresses myocardial contractility in children more than isoflurane and sevoflurane.[9] Benign arrhythmias (such as PVC's, nodal rhythm, bigemini, as well as supraventricular arrhythmias, etc.) occur frequently, especially in spontaneously breathing children and in presence of increased plasma catecholamines and respond well to deepening of anesthesia and correction of hypercarbia.[32] Halothane decreases heart rate, particularly markedly in neonates, and may cause junctional rhythm, bradycardia and even cardiac asystole. Halothane-induced bradycardia needs early correction with intravenous atropine (10 μg/kg).[33] Rapid rise in alveolar concentration because of its relatively reduced solubility and high potency may produce unintended cardiorespiratory instability in neonates and infants during induction, especially if inspiratory concentration is raised in larger increments and if ventilation is controlled rather than allowing spontaneous ventilation.[34] Control of depth of anesthesia by changing inspiratory concentration (i.e. by changing vaporiser dial setting) is poorer with halothane because of its slower "wash-out" due to higher solubility. MAC of halothane is highest during first six months of age (maximum 1.2%) and comes down by 30% in full term neonates.[35,36] Unlike in adults, halothane causes less sensitisation of myocardium to catecholamines in children in the presence of hypercarbia. Consequently, during halothane anesthesia, low dose epinephrine (10 μg/kg) can be safely administered to children who otherwise have a normal cardiovascular system.[37] Hepatotoxicity following halothane occurs much less frequently in children and current evidence is not enough to disapprove repeat anesthetic with halothane.[22,9]

KEY POINT

During induction, halothane concentration should be increased gradually in small increments (at a rate of 0.5–1.0% every 3 to 4 breaths) until the desired stage of anesthesia is achieved

Isoflurane

Isoflurane is commonly used only for maintenance of anesthesia in children. It is pungent and causes irritation of the respiratory tract. However, following induction with other agents children tolerate addition of isoflurane and emerge from it smoothly during recovery.[30] Lesser blood solubility permits better control of depth of anesthesia by changing (increasing or decreasing) inspiratory concentration. Fall in alveolar concentration and thus recovery from isoflurane anesthesia is faster than halothane.[38] The MAC of isoflurane varies with age and is highest in infants aged between 1 and 6 months (1.86%). In preterm newborns MAC is 10–12% lower than it is in term neonates.[39] Sudden increase in the inspired concentration of isoflurane does not cause tachycardia and hypertension in children because of central sympathetic response as is seen in adults.[30] Cardiac output is better preserved during isoflurane than during halothane anesthesia. In children with severe liver disease isoflurane is the anesthetic of choice as it maintains total hepatic perfusion better than halothane and only a little amount (0.2–0.3%) is metabolized in the liver. During isoflurane anaesthesia, cerebral blood flow velocity (CBFV) varies proportionately with end tidal carbon dioxide.[40]

KEY POINTS

- Isoflurane is not a preferred agent for induction of anesthesia in children
- Breath holding and laryngospasm in unpremedicated children may slow the rate of isoflurane induction

Sevoflurane

Sevoflurane has a pleasant odor, does not irritate the respiratory tract and has little effect on hemodynamics.

JAYPEE BROTHERS

Sevoflurane's low blood solubility causes rapid wash-in consistent with rapid induction and faster recovery from anesthesia in children. Anesthetic depth can be controlled more easily. MAC is highest (3.3%) and alike in both neonates and infants up to the age of 6 months (2.5 for older infants and children).[24,41,42] This very high MAC value more than offsets the reduced solubility of sevoflurane in neonates and infants. Therefore, excessive concentration of sevoflurane cannot be administered to neonates and infants with current vaporizer design which is advantageous as anesthetic overdose is very unlikely to occur during induction.[9] However, inability to deliver large concentration causes difficulty in rapidly inducing deep level of anesthesia with sevoflurane in neonates and infants compared to older children. Sevoflurane induction requires rapidly increasing the inspired concentration from 0 to 8% following administration of 70% nitrous oxide in oxygen for 1–2 minutes in spontaneously breathing children.[9,43] Ventilation should not be controlled with higher inspired concentration, as in during induction, as it may produce cardiovascular instability especially in neonates and infants. Attaining a deeper state of anesthesia with sevoflurane is difficult and IV anesthetic may be required. Sevoflurane produces mild cardiovascular depression. Cardiac arrhythmias are uncommon. Compared to halothane, sevoflurane causes more respiratory depression and upper airway narrowing in spontaneously breathing children.[44] Incidence of emergence delirium during recovery is higher than with halothane.[45,46]

KEY POINT

After induction, inspired concentration of sevoflurane should be maintained at a higher level for few minutes in spontaneously breathing children until the IV catheter is inserted[9]

Desflurane

Desflurane is least soluble (blood/gas solubility 0.42) of all modern volatile anesthetics. Uptake from lungs is minimal and alveolar concentration rises very rapidly to near inspiratory concentration. Induction of anesthesia is faster and precise control of depth of anaesthesia is easy. However, induction in children is associated with higher incidences of coughing, breath holding and laryngospasm as desflurane is more pungent than sevoflurane and irritates the airway.[47,48] Thus, desflurane is not recommended for induction of anesthesia in children. Of all volatile anesthetics, desflurane is least potent with a MAC between 8% and 10% in infants. Desflurane MAC is highest (9.92%) in infants between 6 months and 1 year. It is minimally metabolized (0.02%) in the body. Desflurane rarely causes arrhythmias and does not alter cardiovascular variables at 1 MAC.[23] It exaggerates airway narrowing markedly in susceptible children.[49] Recovery from desflurane is faster than sevoflurane but is associated with higher incidences of emergence delirium than with sevoflurane and halothane.[50] Desflurane anesthesia may be beneficial in neonates as it does not cause post anesthetic apnea, particularly in expremature neonates and infants.[51]

KEY POINT

Desflurane is better used as a maintenance agent in children. Use of closed circuit is recommended

Intravenous Anesthetic Agents

Propofol

Propofol, an alkylphenol, is widely used for both induction and maintenance of general anesthesia in children. It is also used in children undergoing brief radiological as well as medical procedures. Because of larger volume of distribution children need higher doses to achieve the same plasma concentration as adults. Recommended dose for induction of anesthesia in infants and children is 2.5–3.5 mg/kg over 20–30 seconds.[52] Children may require larger doses (4–5 mg/kg) for acceptance of face mask.[53,54] More rapid injection may produce sudden hypotension. Hypovolemia, sedative premedication and induction with sevoflurane and nitrous oxide reduce the propofol dose requirement for induction of anesthesia. More than 5 mg/kg (4.7–6.8 mg/kg) of propofol is necessary for successful LMA insertion when opioid is not coadministered.[55] At a much higher dose (>6 mg/kg) appropriate intubating conditions are achieved in unpremedicated children and endotracheal intubation can be performed without use of muscle relaxants.[56] There has been no recommended dose of propofol for induction of anesthesia in neonates and they probably require lower doses.[9] Neonates and infants have lower clearance of propofol because of reduced hepatic metabolism. Intermittent bolus or continuous infusion may lead to propofol accumulation and delayed awakening from anesthesia. Initial propofol dose for continuous infusion (Table 3) during short radiological or medical procedures is 200–250 µg/kg/minute (12–15 mg/kg/hour).[9,57] Infusion dose requirement to prevent movement during procedure is higher for younger children and for children having cognitive impairment. For ICU sedation a lower initial dose (1–4 mg/kg/hour) should be administered which can be titrated later to the desired response.[58,59] Pain with IV injection is a major disadvantage and is best reduced by pretreatment with

JAYPEE BROTHERS

Table 3: Continuous infusion scheme for propofol

Infusion rate	*Time*			
	0–15 min	*15–30 min*	*30–60 min*	*1–4 hours*
Propofol (mg/kg/h)	15	13	11	10 - 9

intravenous lidocaine (0.5–1.0 mg/kg) after applying tourniquet proximal to the site of injection 30 seconds prior to administration of propofol.[9] Propofol decreases mean arterial pressure by 20–30% from baseline and causes apnea in up to 40% unpremedicated children following induction.[60,61] Anaphylaxis to propofol itself is rare.[56] Propofol causes dose dependent bronchodilatation and is beneficial in asthmatic children.[62] It depresses laryngeal and pharyngeal reflexes and can be used at a dose of 1–2 mg/kg bolus to avert cough and to successfully break laryngospasm.[63] Propofol also possesses useful antiemetic properties. Prolonged sedation with propofol at a rate of more than 5 mg/kg/h (70 µg/kg/min) for more than 48 hours may produce propofol infusion syndrome (PRIS) manifested as insidious onset of lipemia, metabolic acidosis, hyperkalemia and rhabdomyolysis. This may result in profound myocardial instability and cardiovascular collapse and does not usually respond even to advanced resuscitative efforts.[56]

Thiopentone

Thiopentone is a short-acting barbiturate with sedative hypnotic and anticonvulsant properties. It is beneficial when cardiovascular stability is necessary as it maintains SVR and causes less reduction in MAP than propofol.[29] Unlike propofol, IV injection of thiopentone is painless. Induction of anesthesia is smooth and occurs in one arm brain circulation time.[64] Awakening from anesthesia is quiet although occasionally interrupted by shivering. Thiopentone induction dose is inversely related to the age.[65,66] Because of reduced protein binding neonates require a lower induction dose (3–5 mg/kg) of thiopentone. Infants have higher volume of distribution and require higher doses (6–8 mg/kg) than older children (4–6 mg/kg). Elimination is slow in neonates because of reduced metabolism by immature hepatic enzyme systems.[67] Thiopentone may accumulate following repeated injection or continuous infusion because of its low hepatic extraction ratio (0.3) and thus may cause prolonged sedation.[56] Acute tolerance to thiopentone may also occur in children.[68] Recovery of psychomotor skills is delayed following thiopentone induction than following propofol.[69] Thiopentone does not suppress laryngeal and pharyngeal reflexes. It causes direct myocardial depression and mild peripheral vasodilatation and may precipitate hypotension in hypovolemic chidren.[70] Thiopentone is absolutely contraindicated in presence of variegate (South African genetic porphyria) as well as acute intermittent prophyria. To safeguard from life-threatening complications, however, thiopentone is best avoided in presence of all kinds porphyria in children.

KEY POINT

Thiopentone should not be used in children coming for day care surgery

Ketamine

Ketamine, phencyclidine derivative, produces dissociative anesthesia and is an excellent analgesic and amnesic.[71] After IV (Table 4) administration, onset of anesthesia occurs within 30 seconds and duration of action persists for 5–8 minutes. However, analgesic effects of bolus ketamine is more prolonged and may prevail for as long as 4 hours.[72,73] Top-up doses (0.5–1.0 mg/kg) may be administered as and when necessary.[9] Recovery is relatively slow and is associated with higher incidences of nausea and vomiting and emergence reactions.[74] Coadministration of an antisialagogue is necessary to prevent excessive airway secretion and thereby reduce the consequent risk of laryngospasm.[75] Ketamine in low doses (1–2 mg/kg IV or 3–5 mg/kg IM) is frequently used for short procedures outside the operation theatre because of relative preservation of airway tone.[76,77] Coughing and airway obstruction may occur even with low doses especially when combined with other sedating medications.[78-80] Heart rate increases and so does cardiac output and systemic blood pressure.[81] Ketamine maintains peripheral vascular resistance and pulmonary to systemic blood flow ratios and has little effect on shunting magnitude or direction in children with cyanotic heart disease.[82] It is beneficial for induction of anesthesia in hypovolemic children or in children with congenital cyanotic heart disease. Ketamine is a significant bronchodilator and has been an induction agent of choice in children with severe bronchial asthma.[83] Intramuscular Ketamine (3–5 mg/kg) is useful as a premedicant or preinduction agent for

Table 4: Doses of ketamine through various routes

	Oral (mg/kg)	*IM (mg/kg)*	*IV (mg/kg)*	*Epidural/ Caudal (mg/kg)*
Premedication	5	3–5		
Short procedure		3–5	1–2	
Induction		5–10	1–3	
As adjuvant				1 or 0.5 (S (+) ketamine)

JAYPEE BROTHERS

children who are developmentally delayed or those who are too scared to be separated from parents or to come to the operating theatre.[9] Other uses of ketamine include as oral premedicant (5 mg/kg), as an adjunct to local anesthetic (1 mg/kg or 0.5 mg/kg, preservative free S (+) ketamine) to increase duration of epidural block, or as an adjunct to opioids for postoperative pain relief. Ketamine increases ICP and IOP and thus should not be used in children with intracranial hypertension and perforating eye injury. Ketamine is associated with higher incidences of laryngospasm in children with URTI.[84,85] Ketamine has psychotropic and epileptogenic effects and hence should be avoided in children with psychiatric or seizure disorders.[86,87]

Etomidate

Etomidate is a rapidly acting carboxylated imidazole derivative with a short duration of action. In children, induction occurs within 20–30 seconds after IV injection (0.2–0.3 mg/kg) and action lasts for 2–6 minutes.[88] Etomidate is highly protein bound and has a longer terminal half-life (4.6 hours).[89,90] Induction dose is 30% higher in children compared to adults because of higher volume of distribution.[91] IV etomidate is painful and is better administered through large veins. Induction is frequently associated with involuntary muscle movement, increased muscle tone and myoclonus. On the other hand, etomidate has minimal cardiovascular and respiratory effects and is suitable for induction in children with poor cardiac reserve.[92,93] In children with traumatic brain injury induction with etomidate reduces intracranial pressure, improves cerebral perfusion and decreases cerebral oxygen consumption.[94] Because of its better hemodynamic profile etomidate is also frequently used in emergency department for rapid sequence intubation in children.[95-97] However, etomidate is known to suppress adrenal function and inhibit cortisol synthesis. Even a single bolus injection may block cortisol production or negatively influence adrenal function in critically ill children for at least 24 hours.[98,99]

KEY POINT

Critically-ill children may require corticosteroid supple-mentation following administration of etomidate to secure their airway[100,101]

Sedatives

Midazolam

Oral midazolam (0.3–0.5 mg/kg, maximum 20 mg) is commonly used as premedicant in children to reduce separation anxiety and distress at induction.[29] Peak plasma level is achieved after 30–60 minutes.[102,103] Maximum sedation and anxiolysis after intranasal administration (0.1–0.2 mg/kg) is obtained at 20 minutes.[104] However, nasal midazolam causes nasal mucosal irritation and has a long lasting bitter after taste and is better avoided.[105,106] IV midazolam (0.1–0.2 mg/kg, up to 0.5 mg/kg) is used for sedation of ventilated children in ICU. Bolus midazolam injection in neonates and infants may cause profound hypotension particularly if the infant is receiving fentanyl.[107] Neonates and infants are susceptible to have prolonged sedation because of reduced hepatic metabolism and clearance than older children. Older children have higher clearance and require higher sedating doses. Intravenous midazolam reduces hypoxic ventilatory response and may cause respiratory arrest.[108,109] It reduces pharyngeal muscular tone and may cause upper airway obstruction, especially in children with obstructive sleep apnea.[110]

KEY POINT

Midazolam sedation requires appropriate respiratory monitoring, es-pecially in children with obstructive sleep apnea

Clonidine

Clonidine, a mixed alpha-1 and alpha-2 adrenoceptor agonist with predominant alpha-2 actions has dose dependent sedative, anxiolytic and analgesic effects.[111] Oral clonidine (3–5 μg/kg) is used as a premedicant in children. Orally administered clonidine is absorbed slowly and peak effects occur only after 60–90 minutes.[112] Smooth induction of anesthesia under sedation ("steal induction") is possible in most of the children after oral premedication.[113] Clonidine premedication reduces MAC, prolongs postoperative analgesia, and attenuates surgical stress responses in children.[113,114] Clearance of clonidine in neonates is about one-third of that described in adults. Intravenous clonidine (1–2 μg/kg) is used in children to prevent or treat emergence dysphoria.[115] Clonidine is also used as an adjunct to local anesthetics to prolong block duration and decrease analgesic requirement. Low dose clonidine (1–2 μg/kg) does not significantly reduce heart rate and blood pressure in children and prophylactic atropine is probably not necessary.[29]

KEY POINT

Clonidine may produce apnea in ex-premature neonates

Dexmedetomidine

Dexmedetomidine, a selective α-2 adrenergic agonist, has 8-fold higher affinity for α-2 compared to α-1 adrenergic

JAYPEE BROTHERS

receptors. Predominant α_2 effects of dexmedetomidine may cause hypotension and bradycardia in children in a dose dependent manner apart from its primary effects of sedation and anxiolysis.[116,9] High dose dexmedetomidine may produce hypertension especially in infants and children who require top-up bolus doses to prolong sedation.[117] Dexmedetomidine also provides modest analgesia and decreases opioid requirement during surgery.[118,119,120] It is gaining popularity as a sedative agent for ICU patients, and for procedures outside the operation room in children mainly because of its minimal effects on respiration and a shorter half-life than clonidine. Even though change in airway diameter is minimal and possibility of airway obstruction is very unlikely, measures to rescue compromised airway during dexmedetomidine sedation is mandatory.[121] A loading dose of 1 μg/kg intravenously over 10 minutes is followed by infusion at 0.5–1 μg/kg/hour. Recovery profile following dexmedetomidine infusion is slower compared to propofol for sedation during MRI.[122,123] Dexmedetomidine sedation provides definite advantages for awake procedures (such as awake fiberoptic intubation as well as for awake craniotomy) as it permits arousal with gentle stimulation.[124,125] Dexmedetomidine has also been found to be useful in reducing the incidence of emergence delirium.[126]

KEY POINT

Dexmedetomidine induced bradycardia and hypotension should be managed by decreasing the infusion dose and administering a bolus of balanced salt solution, if necessary

Opioids

Morphine

Intravenous morphine, commonly in the form of continuous infusion (0.05–0.2 mg/kg/hour), is most frequently used to manage acute postoperative pain in children.[127] PCA device is used to administer morphine intravenously commonly in children older than five years of age.[128] As gestational and postnatal age increase, postoperative morphine requirement also increases.[129,130] Critically ill children receiving supplemental analgesics and hypnotics, and/or who experience fall in hemoglobin saturation at night because of obstructive sleep apnea should receive lower doses.[131,132] Morphine can also be administered orally (as short or long acting formulations), rectally and as intermittent IV bolus. Because of first pass hepatic metabolism oral bioavailability of morphine is only approximately 35%.[9] As adjuvant to local anesthetics, or even sometimes alone, morphine can also be administered into epidural or caudal space either as a single bolus or as continuous infusion.[127] Clearance of morphine is age dependent, being lowest in preterm infants and highest in young children. Critically ill children also have reduced clearance of morphine. Respiratory depression is the most important unwanted effect of all opioids in infants and children. Morphine causes respiratory depression by diminishing respiratory rate and tidal volume. However, at reduced infusion rates (10–30 μg/kg/h) morphine renders adequate postoperative analgesia and does not induce respiratory depression.[133] Rapid IV administration of morphine may result in systemic hypotension because of histamine release and consequent vasodilation.[134] Morphine-induced vomiting in postoperative children is dose dependent. Higher incidence (>50%) of vomiting occurs in children who receive more than 0.1 mg/kg of morphine.[135,136]

Fentanyl

Fentanyl is commonly used as perioperative analgesic in infants and children during general anesthesia. Perioperative fentanyl (1–3 μg/kg IV) blunts surgical stress response and provides better hemodynamic stability than morphine.[137] High dose fentanyl (10–100 μg/kg IV) maintains cardiovascular stability and is often administered as a sole anesthetic in high risk neonatal and in pediatric cardiac surgical procedures.[9] A continuous infusion (0.5–2.5 μg/kg/h) is frequently used in ICU setting to provide sedation and analgesia in mechanically ventilated infants and children.[138] Clinical effects of fentanyl last shorter because of its redistribution and rapid hepatic clearance. Fentanyl clearance is greater in older infants and children than in adults but is prolonged in neonates and in children with congenital cyanotic heart disease.[139,140] Respiratory depression is less in neonates after doses as high as 10 μg/kg because of increased volume of distribution.[29] Rapid bolus injection of fentanyl may produce chest wall and glottic rigidity and bradycardia due to increased vagal tone.[141,142] These can be reversed by administration of naloxone or using a muscle relaxant and control ventilating the child.[142] Fentanyl may sometimes depress the baroreceptor reflex control of heart rate in newborns.[143] Bolus administration of midazolam and fentanyl together may produce severe hypotension.[93] Oral transmucosal fentanyl (OTF) was previously used for premedication in children. However, this product is no longer marketed in US.[127] Fentanyl patch provides extended release of fentanyl and is used in children who require long-term fentanyl to combat chronic pain but are either unable to take orally or are noncompliant to oral medications. For this, fentanyl transdermal therapeutic system (TTS) has been developed that releases fentanyl at a lower dose (12.5 μg/h) required to control cancer pain in children.[144] Fentanyl is also used as an adjuvant to local

JAYPEE BROTHERS

anesthetics for supplementation of caudal or epidural analgesia.

KEY POINT

Fentanyl may produce prolonged respiratory depression in preterm neonates because of its markedly prolonged clearance

Remifentanil

Remifentanil is a highly potent synthetic opioid with rapid onset of action. Remifentanil provides intense analgesia and anesthesia with cardiovascular stability. It is particularly beneficial for sick neonates and infants because of faster clearance than older children.[145] Remifentanil has a very brief elimination half-life (3–6 minutes) and clinical effects disappear within 10 minutes of intravenous injection.[145,9] For prolonged analgesia, a loading dose of 0.1–0.25 μg/kg is followed by a continuous infusion 0.25–0.50 μg/kg/min. Remifentanil propofol combination can be effectively used to provide anesthesia in children for a variety of short surgical and nonsurgical procedures. Bolus remifentanil (3 μg/kg) can also be used to supplement propofol (4 mg/kg) to facilitate endotracheal intubation without the use of a muscle relaxant.[146] Initial bolus dose of remifentanil may be associated with bradycardia and hypotension because of direct negative chronotropic action.[147] Respiratory depressant effect of remifentanil is less in younger children.[148]

KEY POINT

Concomitant use of a vagolytic agent should prevent remifentanil-induced bradycardia and hypotension

Tramadol

Tramadol is a weak opioid and is effective against moderate to severe pain in children. It is used as perioperative analgesic (1–2 mg/kg) in children and to treat postoperative shivering. Clearance in children is similar to that in adults.[149] Compared to other opioids, tramadol causes lower incidence of respiratory depression and similar incidence of other opioid-related unwanted effects, such as nausea, vomiting, pruritus, etc.[150] Rapid IV injection may result in flushing, sweating, dizziness and nausea.[127] Tramadol lowers seizure threshold. Coadministration with 5-HT3 antagonist results in reduced efficacy of tramadol.[151] Oral route is useful as a transition after IV administration. Initial oral dose of 2–3 mg/kg is followed by 1–2 mg/kg 4–6 hourly. Tramadol has also been used caudally and epidurally as adjuvant to local anesthetics to prolong postoperative analgesia in children.

KEY POINT

Caudal tramadol is not recommended due to risk of potential neurotoxicity[152,153]

Buprenorphine

Buprenorphine is a partial μ agonist, 25–50 times more potent than morphine. It is highly protein bound and cleared from plasma mostly by hepatic extraction and extensive first pass hepatic metabolism. Decreased hepatic blood flow prolongs duration of action of buprenorphine.[127] After a single bolus dose buprenorphine clearance is higher in children than in adults.[154] Buprenorphine produces similar analgesic and CNS effects as morphine. Sublingual buprenorphine is rapidly absorbed and produces clinical effects in 30–60 minutes and has been used as a premedicant in children.[155] Intravascular buprenorphine produces equivalent but longer postoperative analgesia compared to morphine.[156,157] However, respiratory depressant effect of parenteral buprenorphine is greater and longer lasting compared to morphine.[158] Other adverse effects, such as sedation, nausea and vomiting, dizziness, and sweating, etc. are similar to those produced by other morphine like opioids. Caudal buprenorphine (2.5–4 μg/kg), either alone or combined with caudal bupivacaine provides postoperative analgesia up to 24 hours in children without any major opioid-related side effects except higher incidence of nausea and vomiting.[159,160]

KEYPOINT

Caudal buprenorphine cannot be advocated for use in children as it has not undergone adequate safety evaluation and is associated with higher incidence of nausea and vomiting[161,159]

Non-Opioid Analgesics

Ketorolac

Ketorolac is useful as an adjuvant to prolonged postoperative pain management in children, mostly as a transition from IV (0.2–0.6 mg/kg stat followed by 0.2–0.4 mg/kg 4–6 hourly for 5 days) to oral route (0.2 mg/kg 4–6 hourly).[162] Ketorolac suppresses platelet function and may increase surgical bleeding.[9] Increased incidence of bleeding is seen especially in children undergoing adenotonsillectomy and particularly when administered during or at the beginning of the surgical procedure before hemostasis is achieved. Ketorolac is safe in preterm and term infants and can also be safely used to treat postoperative pain in children undergoing cardiac surgery.[163,164] Ketorolac is also safe for orthopedic procedures except spinal fusion

JAYPEE BROTHERS

where large doses may adversely affect bone healing.[165-168] Rapid IV administration of ketorolac may cause sudden and profound bradycardia.[169]

KEY POINT

Ketorolac should be administered only after adequate hemostasis is achieved particularly in children undergoing adenotonsillectomy

Acetaminophen (Paracetamol)

Acetaminophen has opioid sparing effects.[170] Oral acetaminophen (20–40 mg/kg) administered before induction is rapidly absorbed and produces effective therapeutic blood level at the time of emergence even after very brief surgical procedure.[9] Absorption via rectal route (40 mg/kg) is unpredictable and time delays of 60 minutes or so has been observed before peak clinical effects occur after achieving peak plasma concentration.[171] For long duration surgical procedures rectal administration at the beginning is helpful to provide necessary blood concentration at emergence until the child is ready for oral medication.[172] The superiority of IV route over oral and rectal routes has not been proven.[173] However, IV paracetamol is being increasingly used in neonates. The recommended dose is 7.5 mg/kg/ 6 hour for neonates after 10 days of age through to infants of 10 kg and a dose of 15 mg/kg/6 hour (max daily dose 60 mg/kg) is recommended for infants and children between 10 and 40 kg.[174] Neonates have larger volume of distribution and smaller clearance. Hepatotoxicity, even though rare, occurs commonly because of overdose.[175] IV paracetamol is painful. However, amongst two IV paracetamol formulations (i.e. acetaminophen and propacetamol) acetaminophen is less painful and should be administered over a period of 15 minutes.[176] IV paracetamol is expensive and should be restricted to use in infants and children who do not tolerate enteral or rectal preparations.[177,178]

KEY POINT

Maximum dose of oral paracetamol should not exceed 90–100 mg/kg/day

Diclofenac

Diclofenac is effective for treatment of acute pain in children and can be used as a component of balanced analgesic regimen perioperatively in pediatric anesthesia practice.[179] It is readily absorbed via oral, rectal and intramuscular routes. Diclofenac is highly bound to plasma proteins (mostly albumin, >99.5%), has a smaller volume of distribution and undergoes extensive first pass hepatic metabolism.[180,181] Intramuscular route should be avoided as it produces long-term muscular pain.[182] Timing of administration via oral or rectal route is important for optimal therapeutic effects during surgical procedure or at the time of awakening from anesthesia. When administered before surgery, diclofenac significantly reduces the number of children requiring rescue pain medications post operatively.[183-187] Diclofenac is associated with less postoperative nausea and vomiting probably because of its better analgesic effects that reduces necessity of other emetogenic rescue analgesics.[179] Incidence of serious adverse effects, such as GI bleeding and allergic-type reactions in children following administration of diclofenac is low (<3/1,000 children). Therapeutic doses of diclofenac do not inhibit platelet aggregation and thus is not associated with increased perioperative bleeding that requires surgical intervention.[188-190] In asthmatic children single therapeutic dose of diclofenac has been shown to produce no significant incidence of bronchospasm.[191] There have been no recommended optimum doses of diclofenac for acute pain in children. A 2009 Cochrane review revealed a range of 0.5–2.5 mg/kg (both oral as well as rectal) in the single dose being used by different researchers.[179,192,193]

KEY POINT

Oral and rectal doses of diclofenac are equivalent and peak bioavailability occurs approximately one hour after administration through these routes

Neuromuscular Blocking Agents

Neuromuscular blocking agents are less frequently used in present day pediatric anesthesia practice.[194,195] Indications for tracheal intubation are decreasing as in many cases airway is managed with supraglottic devices, such as LMA or i-Gel without using a muscle relaxant. A volatile agent when combined with propofol and an opioid (such as remifentanil) gives optimum intubating conditions and also provides sufficient muscle relaxation during surgical procedure and is frequently used in many cases instead of a neuromuscular blocking agent.[196] Regular use of regional anesthesia has also reduced the necessity of neuromuscular blocking drugs in children under general anesthesia. However, in some cases use of muscle relaxant is necessary for smooth and rapid endotracheal intubation, to paralyse skeletal muscles to make surgical procedure easier or to facilitate mechanical ventilation in intensive care.[30] Monitoring of neuromuscular function is essential as clinical clues of depth of neuromuscular blockade are absent during inhalational anesthesia until the child is fully awake afterwards.[197]

Dose requirement for neuromuscular blocking agents is dependent on required plasma concentrations and volume of distribution of these agents. These two factors are very much related to the age of the child and consequently

JAYPEE BROTHERS

for detailed information on anesthesia books, visit our website www.jaypeebrothers.com, for detailed information on anesthesia books, visit our website www.jaypeebrothers.com, for de

Principles and Practice of
Pediatric Anesthesia

Salient Features

- Includes contributions from experienced anesthesiologists from across the country
- Provides exhaustive information on wide ranging topics related to all aspects of pediatric anesthesia
- Divided into sections: Basic Principles, Anesthetic Management, Subspecialty Anesthesia, Special Problems and Situations, Anesthetic Techniques, and Notes on Allied Topics
- Presents detailed discussion on the basic principles as well as the practical approach to management of various clinical scenarios in neonates and children
- Includes essential chapters provided by specialists from radiology, cardiology, pediatric medicine and transfusion medicine
- Provides appendices for quick reference to pediatric drug dosages, syndromes, and handy formulae and tables
- Meticulously edited all chapters and added touch of excellence with appropriate updates
- A valuable resource to postgraduate students and to practising anesthesiologists.



Snehalata H Dhayagude DA FRCA (UK) is practising pediatric anesthesiology for over 40 years, and presently she is a Consultant Pediatric Anesthesiologist in Bombay Hospitals and Research Centre, Mumbai, Maharashtra, India. She was Head, Department of Pediatric Anesthesia at BJ Wadia Hospital for Children, Mumbai. She started the annual Pediatric Anesthesia Lecture Series for postgraduate students in 1998. She was Founder President of the Indian Association of Pediatric Anesthesiologists (IAPA), which was registered in 2006. She represented India at the World Assembly of Pediatric Anesthesia at Washington DC in 2012. She has contributed to chapters in various journals and was guest editor for the World Clinics Anesthesia, Pain and Critical Care—Pediatric Anesthesia Issue. She is an active participant in pediatric anesthesia forums and workshops. Her vast repertoire of knowledge and experience has been the driving force behind the creation of this book.



Nandini M Dave MD DNB PGDHHM PGDMLS is an Additional Professor, Department of Anesthesiology at Seth GS Medical College and KEM Hospital, Mumbai, Maharashtra, India. She is a recognized teacher for DM (Pediatric Anesthesia) Course, which commenced in 2014 at KEM Hospital with Medical Council of India (MCI) approval. She is also a Faculty for Pediatric Anesthesia Fellowship Course from 2009. She is a recipient of several scholarships, including the Hargobind Foundation and JASCAP Foundation Scholarships. She is an Instructor for Basic Life Support (BLS) Course, Advanced Cardiac Life Support (ACLS) Course and Simulation, and is currently pursuing a PhD in Medical Simulation. She has contributed to chapters in several textbooks and has bagged many publications to her credit. She is an Executive Committee Member of Indian Association of Pediatric Anesthesiologists (IAPA) and participates regularly in national and regional conferences.

Available at all medical bookstores
or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
ANESTHESIA

ISBN 978-93-85891-70-0

9 789385 891700