UNIT 11 LOCAL ANESTHETICS

Structure

11.1 INTRODUCTION

Local anaesthetics are those agents that reversibly block impulse conduction in a restricted area of the body where it is applied by topical application or local injection.

Objectives

After studying this unit, you should be able to:

- know about local anaesthetics and skeletal muscle relaxants;
- enumerate their pharmacological actions and toxicities;
- state the therapeutic indications for the use of these agents; and
- compare and contrast the different groups of compounds.

11.2 LOCAL ANESTHETICS

All the local anaesthetics possess varying degree of water and lipid solubility. Both the properties are essential for a local anaesthetic, lipid solubility helps in migration of active drug into the neuronal fibre and water solubility is essential to get the drug to site of action from the site of administration.

Local anaesthetics can also be classified into two categories based on their chemical structure:

a) **Ester linked local anaesthetics** e.g. cocaine, procaine, tetracaine, benzocaine, chloroprocaine.

b) **Amide linked local anaesthetics** e.g. lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine.

Local anaesthetics block both the generation and conduction of the nerve impulse. By depressing higher centers, local anaesthetics stimulate CNS and produce restlessness, tremor, mental confusion and convulsion. In toxic doses, it causes respiratory depression, coma and death. **Cocaine** is a powerful stimulant while procaine and other agents produce less CNS stimulant effect. Local anaesthetics are myocardial depressant and decrease heart rate and amplitude of myocardial contraction. **Bupivacaine** is more cardiotoxic and can produce ventricular tachycardia or fibrillation. Local anaesthetics also produce decrease in blood pressure which may be due to sympathetic blockade. Only cocaine has the property to raise the BP due to its sympathomimetic property. Local anaesthetics are readily absorbed through mucous membranes and damaged skin. These are weak bases and at tissue pH diffuse through the connective tissue and cellular membranes to reach the nerve fibres where ionization can occur. The important therapeutic uses of local anesthetics are to produce:

- Surface anaesthesia.
- Spinal anaesthesia.
- Infiltration anaesthesia.
- Nerve block or conduction block and
- For systemic use in the treatment of cardiac arrhythmias (Details are given in chapter 'Antiarrhythmic agents').

11.2.1 Individual Agents

Lignocaine

Lignocaine stabilizes the neuronal membrane by inhibiting ionic fluxes required for initiation and conduction of impulses thereby affecting local anaesthetic action. Drowsiness following the administration of lignocaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption. Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension and cardiovascular collapse, which may lead to cardiac arrest.

Lignocaine injections are indicated for production of local or regional anaesthesia by infiltration techniques such as percutaneous injection, peripheral nerve block, spinal or subarachnoid block.

Benzocaine

It is a local anaesthetic belonging to the ester group. It is poorly absorbed from the intact epidermis and is generally employed for topical anesthesia. Benzocaine has been termed as 'one of the most widely used and safest external analgesic and that the incidence of sensitivity of benzocaine is quite low'. Its male genital desensitizing product has been termed as premature ejaculation remedy.

Dibucaine

It is another local anaesthetic with longest duration of action but due to its toxicity, it is used only for surface anaesthesia.

Bupivacaine

It is a potent and long acting local anaesthetic used for spinal, infiltration, epidural and nerve block anaesthesia.

Benoxinate

It is a surface anaesthetic used in eye for producing corneal anaesthesia for opthalmological procedures.

Oxethazaine

A potent local anaesthetic used for anaesthetizing gastric mucosa. Along with antacid in suspension form it is used in gastritis, gastric irritation and gastroesophageal reflux.

Ropivacaine

It is a newer, long acting local anaesthetic, which produces less cardiotoxicity. It is used mainly for nerve block and in postoperative pain.

SAQ 1

a) ___ is a potent local anaesthetic used for anaesthetizing gastric mucosa.

b) ________ is a local anaesthetic with longest duration of action.

c) ____________is cardiotoxic and can produce ventricular fibrillation.

11.3 SKELETAL MUSCLE RELAXANTS

11.3.1 Introduction

Skeletal muscle relaxants are agents that act peripherally at the neuromuscular junction or centrally in the cerebrospinal axis to reduce muscle tone. Skeletal muscle relaxants are classified into two main groups.

11.3.2 Neuromuscular Blockers

d-Tubocurarine is an alkaloid obtained from *Chondrodendron tomentosum* plant. It initially produces motor weakness followed by flaccid paralysis after parenteral administration. The paralysis occurs in following order e.g. paralysis of fingers, toes, eyes, ears producing diplopia, speech slurring, difficulty in swallowing; the muscles of neck, limb, trunk, paralysis of diaphragm and death occur due to hypoxia. In higher doses, d-tubocurarine can produce blockade of autonomic ganglia.

Pancuronium is a synthetic steroidal compounds and approximately five times potent than d-tubocurarine. **Vecuronium** is congener of pancuronium with short duration of action. **Atracurium** is competitive blocker similar to pancuronium in properties and duration of action. **Succinylcholine** is a structural analogue to acetylcholine (Details are discussed in chapter 'Cholinergic agents'). The therapeutic uses of peripherally acting skeletal muscle relaxants are as follows:

- As a adjuvant to general anaesthetics (specially in major surgical procedures e.g. abdominal and thoracic surgery, orthopaedic procedures, intubation etc).
- Succinylcholine is used for surgical procedure of brief duration (endotracheal intubation, bronchoscopy, esophagoscopy, laryngoscopy etc).
- Succinylcholine is used to control convulsion from electroconvulsive therapy.
- In the treatment of tetanus and status epilepticus.
- As a diagnostic tool for myasthenia gravis.

11.3.3 Centrally Acting Muscle Relaxants

These agents reduce skeletal muscle tone by a selective action on cerebrospinal axis without affecting consciousness.

Mephenesin was the first drug used as muscle relaxant but due to its serious side effects e.g. haemolysis, hypotension and thrombophlebitis, it is not clinically used now. **Chlorzoxazone** is related to mephenesin. It is used in painful skeletal muscle spasm and is used in combination with paracetamol and diclofenac. **Methocarbamol** produces skeletal muscle relaxation by preferential blockade of polysynaptic spinal reflexes. It is indicated in skeletal muscle spasm, in surgery, orthopaedic procedures, neurological diseases and tetanus. **Carisoprodol** is used for the treatment of muscle spasm. It has antipyretic and weak antiadrenergic activity. It is used in musculoskeletal disorders. **Orphenadrine** is a centrally acting, anticholinergic muscle relaxant drug. It is used in musculoskeletal disorders, trauma, sports injuries, low backache, tension headache, sprains and strains, parkinsonism including the drug induced. **Tizanidine** is indicated in spasticity due to neurological disorders e.g., multiple sclerosis, chronic myelopathy, degenerative diseases of the spinal cord, cerebrovascular accidents and cerebral palsy; painful muscle spasm associated with static and functional disorders of the spine (cervical and lumbar syndromes); painful muscle spasm following surgery e.g., for herniated intervertebral disc or for osteoarthritis of the hip. It produces its actions by acting on alpha adrenergic neurons in the spinal and supraspinal levels. **Baclofen** is a powerful neuronal depressant. It reduces the release of excitatory transmitter and is antinociceptive in animal studies. It is mainly used in the treatment of spasticity in multiple sclerosis, spastic spinal paralysis etc. It is also used in the treatment of trigeminal neuralgia.

SAQ 2

a) Skeletal muscle relaxants that act at neuromuscular junction are called _______.

b) _____________is used to avoid convulsion and coma from electroconvulsive therapy.

c) ____________is an α-adrenergic receptor agonist that produces skeletal muscle relaxation by acting on supraspinal and spinal levels.

11.4 SUMMARY

- Local anaesthetics can also be classified into two categories based on their chemical structure:

  a) **Ester linked local anaesthetics** e.g. cocaine, procaine.

  b) **Amide linked local anaesthetics** e.g. lidocaine, bupivacaine, dibucaine.

- Local anaesthetics block both the generation and conduction of the nerve impulse.

- All local anesthetics are myocardial depressants and decrease the BP. Only cocaine has the property to raise the BP due to its sympathomimetic property.

- Neuromuscular blockers are not absorbed orally and have to be administered by the parenteral route.

- Neuromuscular blockers produce motor weakness followed by flaccid paralysis after parenteral administration.

- These agents reduce skeletal muscle tone by a selective action on cerebrospinal axis without affecting consciousness.

11.5 TERMINAL QUESTIONS

1. Classify local anesthetics.

2. What is the mechanism of action of local anesthetics? What are their therapeutic indications?

3. What are the different types of skeletal muscle relaxants? Classify them.

4. What is the difference in mechanism of skeletal muscle relaxation produced by the neuromuscular blockers and centrally acting agents?

5. What are the therapeutic indications for the use of skeletal muscle relaxants?

11.6 ANSWERS

Self Assessment Questions

1. a) Oxethazine b) Dibucaine c) Bupivacaine
2. a) Neuromuscular blockers b) Succinylcholine c) Tizanidine

Terminal Questions

1. For convenience, local anesthetics are classified on the basis of their chemical structure into two major groups:

   a) **Ester linked local anaesthetics** e.g. cocaine, procaine, tetracaine, benzocaine, chloroprocaine.

   b) **Amide linked local anaesthetics** e.g. lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine.

2. Local anaesthetics stabilizes the neuronal membrane by inhibiting ionic fluxes required for initiation and conduction of impulses, thereby affecting sensory perception. They are indicated for production of local or regional anaesthesia by infiltration techniques such as percutaneous injection, peripheral nerve block, spinal or subarachnoid block. These are employed for short or minor surgical procedures like tooth extraction, burn dressing, skin graftings, etc.

3. Skeletal muscle relaxants are agents that act peripherally at the neuromuscular junction or centrally in the cerebrospinal axis to reduce muscle tone. They can be classified on the basis of their site of action:

   Peripherally acting agents: d-Tubocurarine, Atracurium, Pancuronium, Vecuronium, Succinylcholine

   Centrally acting muscle relaxants: Chlorzoxazone, Carisoprodol, Tizanidine

4. The peripherally acting agents act either on the neuromuscular junction and block the interaction between acetylcholine and the nicotinic receptors. Thus the action potential required for muscular contraction is not developed and muscle weakness and paralysis is produced. On the other hand, the centrally acting agents act either at the level of the spinal cord or the motor cortex and reduce the outflow of motor impulses. This in turn decreases the muscle tone.

5. The therapeutic uses of skeletal muscle relaxants can be enumerated as follows:

   - As a adjuvant to general anaesthetics (specially in major surgical procedures e.g. abdominal and thoracic surgery, orthopaedic procedures, intubation etc).

- Succinylcholine is used for surgical procedure of brief duration (endotracheal intubation, bronchoscopy, esophagoscopy, laryngoscopy etc).
- Succinylcholine is used to control convulsion from electroconvulsive therapy.
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