**Introduction:**

Lidocaine or lignocaine is a common local anesthetic and antiarrhythmic drug. Lidocaine is used topically to relieve itching, burning and pain from skin inflammations, injected as a dental anesthetic or as a local anesthetic for minor surgery. Higher serum concentrations of local anesthetics cause cardiovascular effects.Therefore, it is essential for monitoring such drugs

**Indications:**

Local and regional anaesthesia by infiltration, nerve block, epidural, or spinal techniques; acute treatment of ventricular arrhythmias from myocardial infarction or cardiac manipulation

Ophthalmic: To provide local anesthesia to ocular surface during ophthalmologic procedures

Rectal: Temporary relief of pain and itching due to anorectal disorders

Topical: Local anesthetic for oral muscous membrane; use in laser/cosmetic surgeries; minor burns, cuts, and abrasions of the skin

Oral solution (viscous): Topical anesthesia of irritated oral mucous membranes and pharyngeal tissue

Patch : Relief of allodynia (painful hypersensitivity) and chronic pain in postherpetic neuralgia

**Pharmacodynamics/Kinetics:**

Absorption:

Distribution: Vd: 1.1-2.1 L/kg; alterable by many patient factors; decreased in CHF and liver disease; crosses blood-brain barrier

Protein binding: 60% to 80% to alpha1 acid glycoprotein

Metabolism: 90% hepatic; active metabolites monoethylglycinexylidide (MEGX) and glycinexylidide (GX) can accumulate and may cause CNS toxicity

Bioavailability: 85%

Half-life elimination: Biphasic: Prolonged with congestive heart failure, liver disease, shock, severe renal disease; Initial: 7-30 minutes; Terminal: Infants, premature: 3.2 hours, Adults: 1.5-2 hours

Excretion: Urine (<10% as unchanged drug, ~90% as metabolites)

**Dose :adults: ventricular fibrillation: I.V** 1-1.5mg/kg

**Therapeutic and Toxic Levels:**

The monitoring of lidocaine levels in the blood is critical. Common toxic reaction seen with this drug includes arrhythmias, bradycardia, heart block etc.

Therapeutic Levels: 1.5-5.0mcg/ml

Potentially Toxic level: >6mcg/mL

Toxic level: > 9mcg/mL**3**

**Assay Parameters:**

Sample:

1 mL serum or plasma (0.5 mL minimum)

Container:

Red top (no additive) tube, lavender top (EDTA) tube, or green top (heparin) tube. Do **not** use a serum separator tube. Containers are laboratory and methodology specific.

Collection:

Routine venipuncture. Separate serum or plasma from cells as soon as possible. A consistent sampling time, ideally a trough level 30 minutes prior to next dose should be used to monitor patients on chronic therapy.

Storage Instructions:

Maintain sample at room temperature or refrigerate. 3

**Analytical Methods:**

Commercial reagent-based techniques represent the primary methodology for the analysis of lidocaine such as serum Enzyme immunoassay (EIA); enzyme multiplied immunoassay technique (EMIT); fluorescence polarization immunoassay (FPIA); gas-liquid chromatography (GLC); high performance liquid chromatography (HPLC); liquid chromatography/tandem mass spectrometry (LC/MS-MS).

**GLC:**

Although numerous GLC procedures have been developed, which measures either intact drug or variety of derivative or degradation product. None is satisfactory as CBZ undergoes partial degradation during GLC. The best approach is to analyze the intact drug and to use C13 CBZ as an internal standard, but this approach requires spectrometric detection.

**HPLC:**

High Pressure Liquid Chromatography: it is a common analytical method used to measure therapeutic drug levels prior to the advent of immunoassays. The principle of HPLC technology is based on the fact that separation of a substance depends on the relative distribution of mixture constituents between two phases, a mobile phase (carrying the mixture) and a stationary phase. Substances that are distributed preferentially in the mobile phase move through the system more rapidly than do the substances that are distributed in the stationary phase.

The basic pathway in HPLC involves six elements:

1) Solvent (mobile phase) reservoir

2) Pump

3) Sample injector

4) Column

5) Detector

6) Output data-processing unit

In HPLC, a liquid containing the sample is injected at one end of the column. The column contains a medium which helps separate the molecules in the liquid. High pressure is used to overcome the resistance to flow. As the liquid flows, some molecules move faster than others due to differences in solubility and polarity. The exact time that each molecule takes to flow through the column is measured by a detector. The retention time is calculated. An internal standard, a compound similar in structure to the specimen to be analyzed, is also run through the column. By comparing the retention time of the sample to the internal standard, the molecule (or drug) can be identified. The concentration of the molecule can also be determined from the peaks produced during the run. The peak size is used to calculate the quantity of the drug in the specimen.

**FPIA:**

Fluorescence Polarization Immunoassay: This method uses a fluorescent molecule as the label instead of an enzyme, making it more sensitive. In FPIA, the patient sample is incubated with a known quantity of the fluorescent-labeled drug and an antibody specific for the drug. As in EMIT, the labeled and unlabeled drugs compete for the binding sites of the antibody. Polarized light is emitted in certain angles depending on whether the fluorescent-labeled drug is bound to antibodies or not. Since this is a competitive assay, the greater the amount of drug in the sample, the lower the amount of fluorescence.

**EMIT:**

The EMIT (Enzyme Multiplied Immunoassay Technique) homogeneous enzyme immunoassay is a versatile methodology designed to measure microamounts of drugs and drug metabolites in human biological fluids.The EMIT technology is based on competition for the target analyte antibody binding sites. Analyte in the sample competes with the drug in the enzyme reagent that is labeled with G6PDH. Active enzyme G6PBH converts thecoenzyme (NAD) in the antibody reagent to NADH, resulting in a kinetic absorbance change that is measured photometrically.

**Conclusion:**

The unpredictable relationship between dose and lidocaine concentration, its narrow therapeutic index, and the presence of numerous clinically significant drug interactions support the need to individualize and maintain therapy using TDM. The accepted therapeutic range for lidocaine is 1.5–5 μg/mL when the drug is used for the treatment of seizures and neuralgia.

**References:**

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