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IONTOPHORETIC DELIVERY OF DRUGS

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"We have to keep running to remain in the same place" - Alice in "Alice in wonderland"

Introduction

Iontophoretic drug delivery is now an accepted method of drug therapy which is gaining wide popularity especially in the area of pain relief. This technique provides a means for regulated non-invasive systemic administration of minute amounts of drug transdermally which is especially useful in patients who require long-term medication as in chronic pain, diabetics, hypertensives, rheumatoids etc. It negates the need for needle sticks, the pain and anxiety involved and minimises the trauma and risks of infection associated with it. This mode of drug delivery is simple, versatile, effective, reliable and can be tailored for individual needs.

What is iontophoresis?

Different investigators have given different definitions because one simple definition cannot explain all the mechanisms involved. But for the sake of simplicity, "Iontophoresis is a process of transportation of ionic molecules into the tissues by passage of electric current through the electrolyte solution containing the ionic molecules using a suitable electrode polarity." This means it would involve an electromotive force. In the body, ions with a positive charge(+) are driven into the skin at the anode and those with negative charge (-) at the cathode. Iontophoresis is sometimes confused with electrophoresis and electro-osmosis, the former involving movement of the colloid (dispersed phase) and the latter involving the liquid (dispersion medium), which are quite different. Iontophoresis may however cause an increased transport of method of penetration of non electrolytes through tissues.

Method of delivery

When applied topically, the current is applied through a moist electrode, the size depending on the skin region to be treated. The drug is administered through an electrode (active) which has the same charge as the drug. This is very important; if the polarity of the electrode is not the same as the ions, then penetration through the skin may not occur. The oppositely charged electrode (return) is placed some distance away at a neutral site, the size and distance of the 2 electrodes would also affect the transport of ions.

A current intensity below the pain threshold that is comfortably tolerated by the patient is passed for an appropriate length of time (usually below 5mA/cm^2). The current intensity should be gradually increased in the beginning and slowly decreased towards the end. The current can be given in any of the different waveforms, square, sinusoidal, triangular etc. The current density is the current intensity per unit cross sectional area. In practice, the density will vary from point to point and the value calculated would be an average value at the electrode surface. What happens here is, the ions transferred through the skin are taken up by the micro-circulation at the epidermo-dermal junction and the current flows back through the return electrode. If any skin irritation occurs at this stage, the current intensity should be lowered.

Various factors affect the intake of drugs by skin like lipophilicity, molecular weight, site, age of patient, drug concentration, the possibility of improving conduction of addition of salts etc.

Factors affecting iontophoretic drug delivery

1. **Ionised state of the drug:** for eg. Lignocaine is mot effective iontophoretically at a pH range of 3.4-5.2.With

iontophoresis transdermal permission is maximum at pH of 9.4 and above when it is mainly in the non-ionised state and at this pH, iontophoretic delivery is minimum.

2. **Presence of extraneous ions:** other ions of the some charge can decrease the iontophoretic delivery of the drug ions because these ions compete with the drug for the iontophoretic flux.

3. **Ionic strength:** Higher ionic strength of the solution subjected to iontophoretic current resulted in decreased iontophoretic transport of the drug into the tissues as increase in ionic strength yields higher concentration of extraneous ions which compete for the electric current.

4. **Concentration :** increased concentration of the charged molecule yields greater molecules in the tissues.

5. **Current intensity:** higher the intensity, greater then transport

6. **Polarisation:** Direct current can cause polarisation whilst pulsed current can decrease tissue polarisation.

7. **Shifts in pH in tissue and drug solutions:** With metallic electrodes, shifts in pH are noted which can affect ionisation of the drug. pH changes in the tissue can use injury due to migration of hydronium and hydroxyl ions produced by electrolysis. Separate buffered electrolyte solutions can be used which can prevent flow of ions into the tissue.

Like charges repel each other while opposite charges attract. So to assist the positively charged lidocaine ions to be transported to the skin, the ionic form must be applied under a positively charged electrode which then moves to the cathode.

Iontophoretic devices

The main manufacturing concerns as in any equipment should include safety, convenience, reliability and reproducibility of the device. The components of the equipments are:

a. DC power supply

b. A milliammeter

c. A timer

d. A rheostat

e. The 2 electrodes +ve and –ve.

Biomedical application

Iontophoresis has wide applications in Dermatology, Ophthalmology, ENT, Allergic conditions even in Cardiac and Neurological situations, but its greatest advantage is in the transport of protein or peptide drugs which are very difficult to transport trasdermally due to their hydrophilicity and large molecular size.

Dermatology

- In hyperhidrosis, especially palmar and plantar – probably by obstructing the sweat ducts. No side effects when compared to anti- cholinergics.
- Copper- iontophoresis for fungal infection and male contraception, zinc for ulcers, iodine for reduction of scar tissues, iron/titanium oxide for tattoo removal.
- Histamine in allergy testing.
- In the diagnosis of cystic fibrosis to increase sweating by pilocarpine and confirm diagnosis by the concentration of

sodium and chloride in the sweat.

- In scleroderma, for iontophoretic delivery of hyaluronidase.

Ophthalmology

- Iontophoretic induction of various drugs like atropine, scopolamine, sulfadiazine, fluorescein, gentamycin etc .

ENT

- For providing anaesthesia of the external ear canal and middle ear and in maxillo facial prosthetics surgeries.

Dentistry

- To prevent dentin hypersensitivity and for providing local anaesthetic for multiple tooth extraction.

Neurophysiological and Neuropharmacological studies

- As a research tool, micro-iontophoresis can be used to study neuro muscular junction, peripheral and central nervous system and smooth muscle preparations.

Delivery of drugs

- Antihypertensives, anti-diabetics, anti-rheumatoids, hormones, vasodilators: Metaprolol, propranolol, insulin, methylcholine, bleomycin, steroids have all been introduced iontophoretically.

Musculo skeletal disorders

- Magnesium sulphate for bursitis, Calcium for myopathy, Silver for c/c osteomyelitis, local anaesthetics and steroids into elbow, shoulder and knee joints.

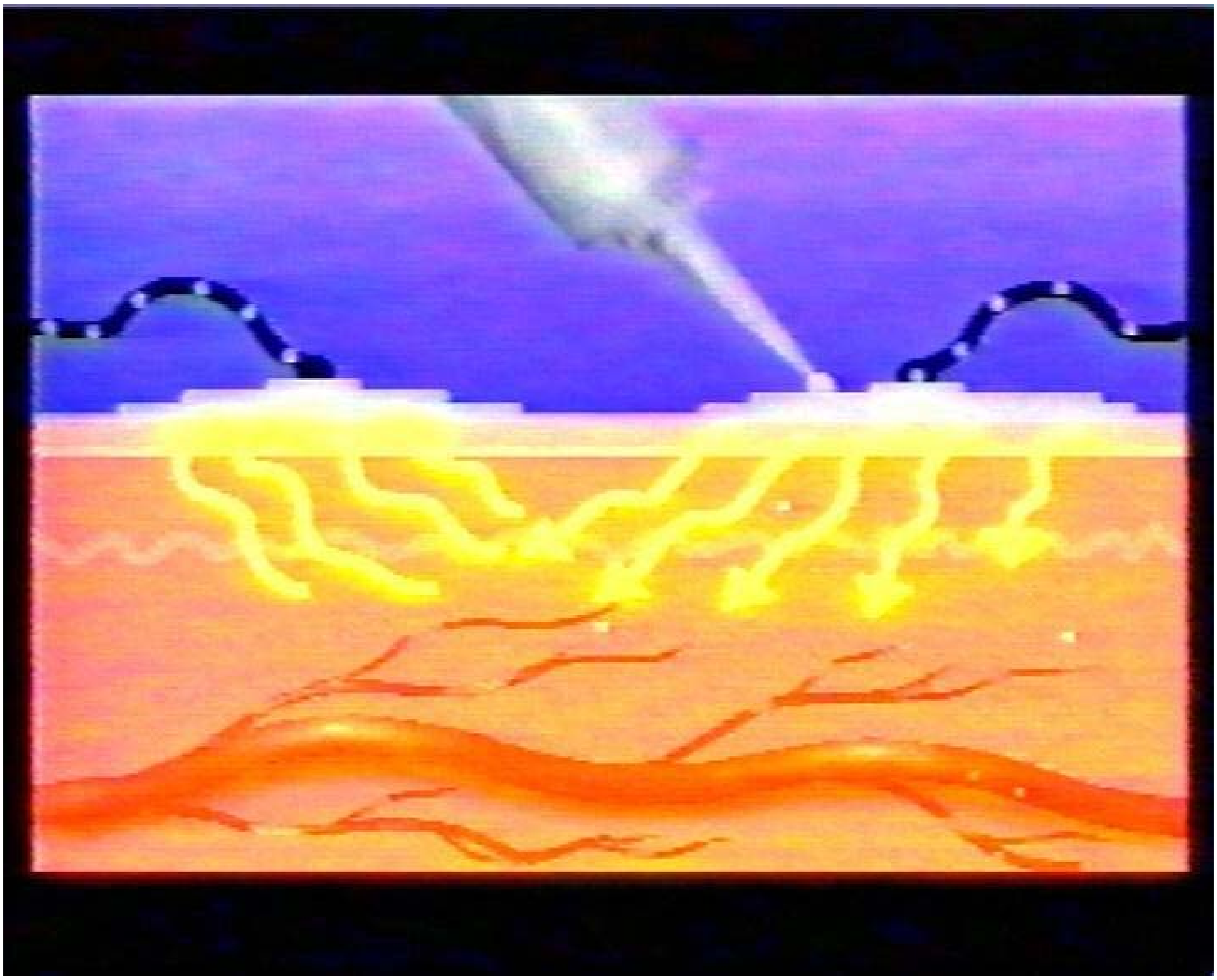
Cardiology

- Iontophoretic transmyocardial drug delivery of anti-arrhythmic drugs which would avoid high systemic toxic levels is being done in animals.

For relief of pain

- Iontophoretic histamine delivery as counter-irritant
- In painless venipuncture
- For post-operative pain relief
- For iontophoretic delivery of local anaesthetics for referred pain
- Anti-inflammatory drug delivery

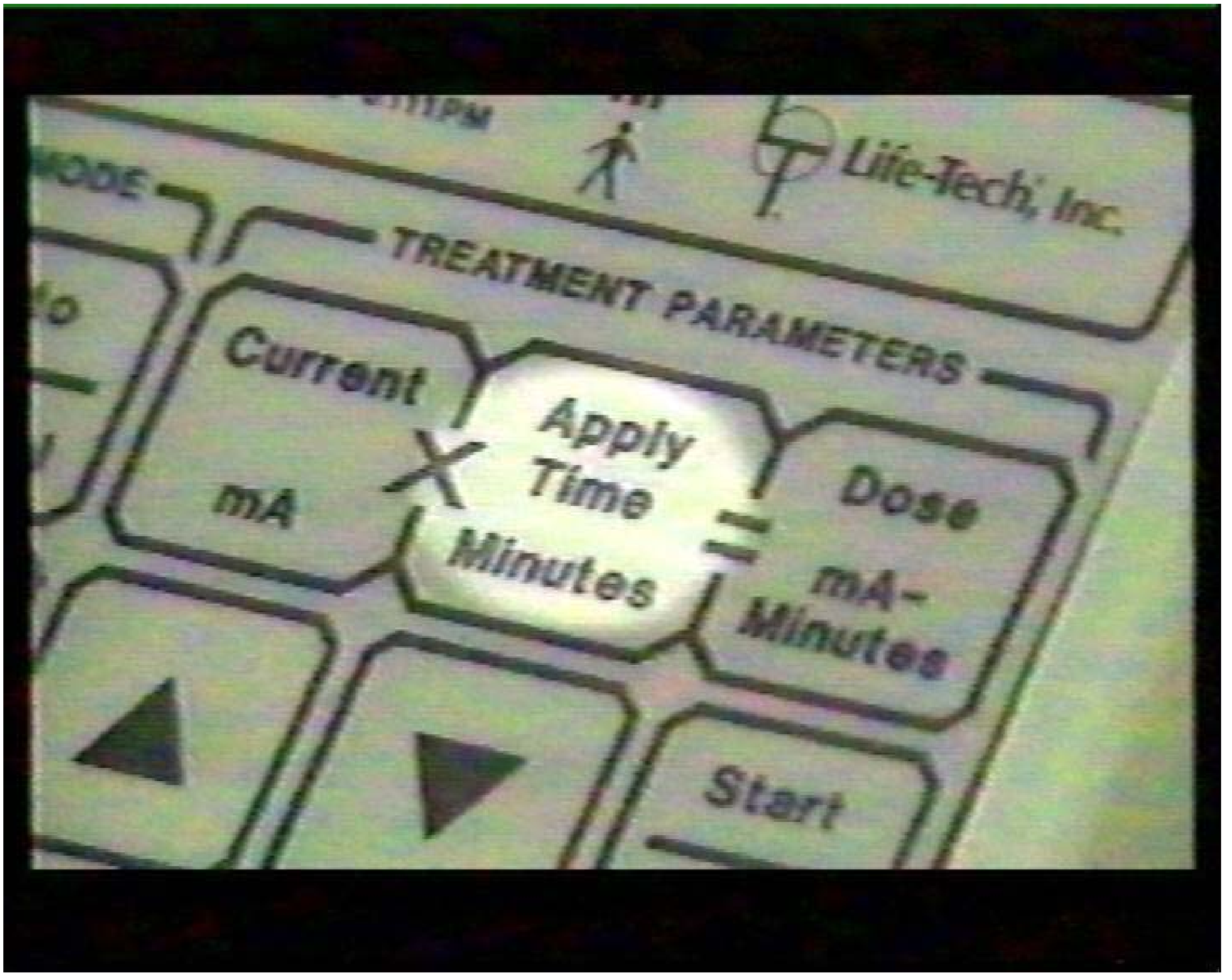
This is an area which has wide scope for expansion. We have seen the varied applications and the potential for improvement for this method of drug delivery. Further research is required to perfect this technique. There are several devices now available in all sizes and shapes to suit individual needs and ensure absolute safety. With even pencil shaped transdermal applicators now available for self administration, iontophoresis may prove to be an important alternative method of drug delivery in the near future.



Picture -1 Iontophoretic Delivery of Drug

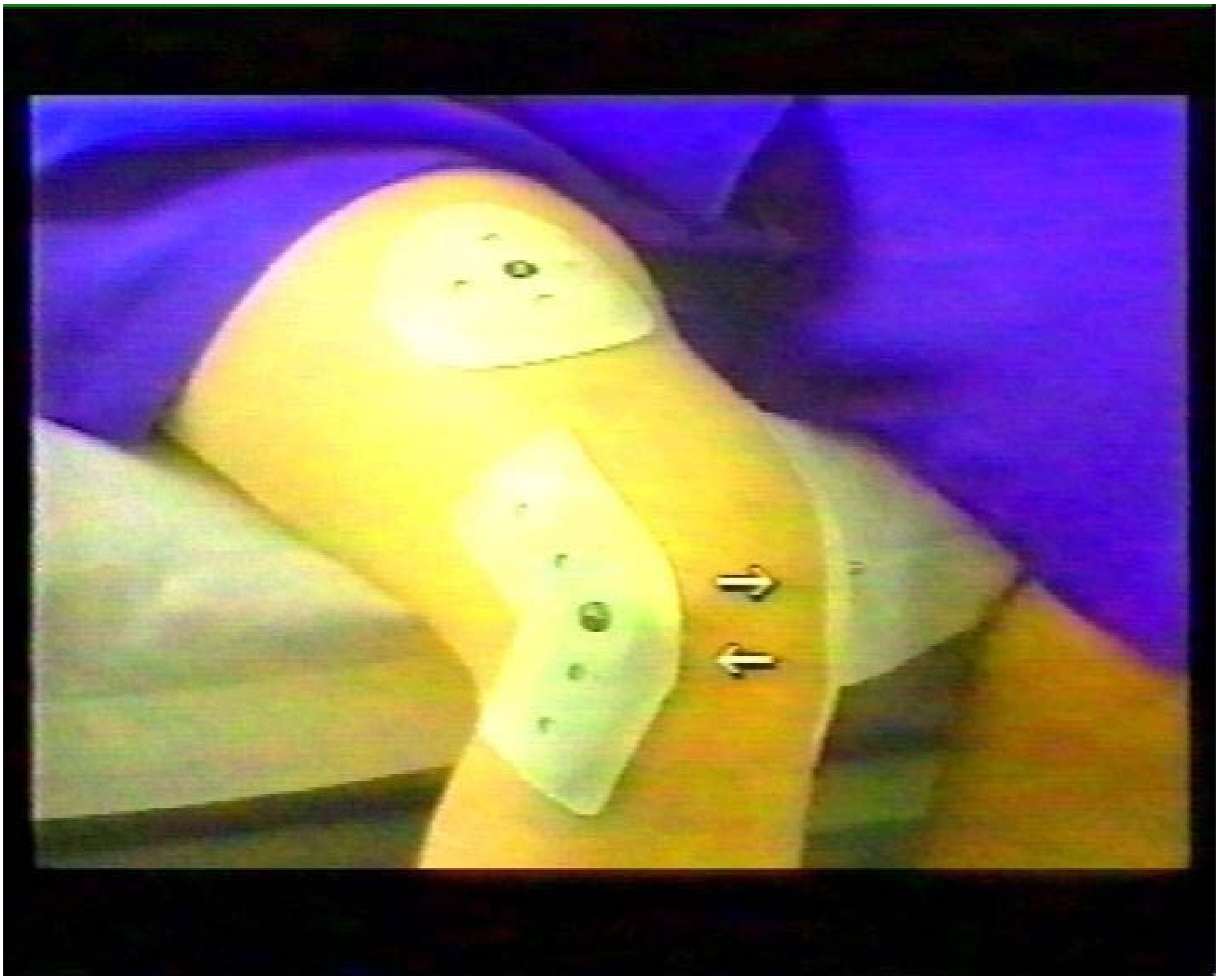
Picture -2 Iontophore Equipment

Picture -3 Iontophore



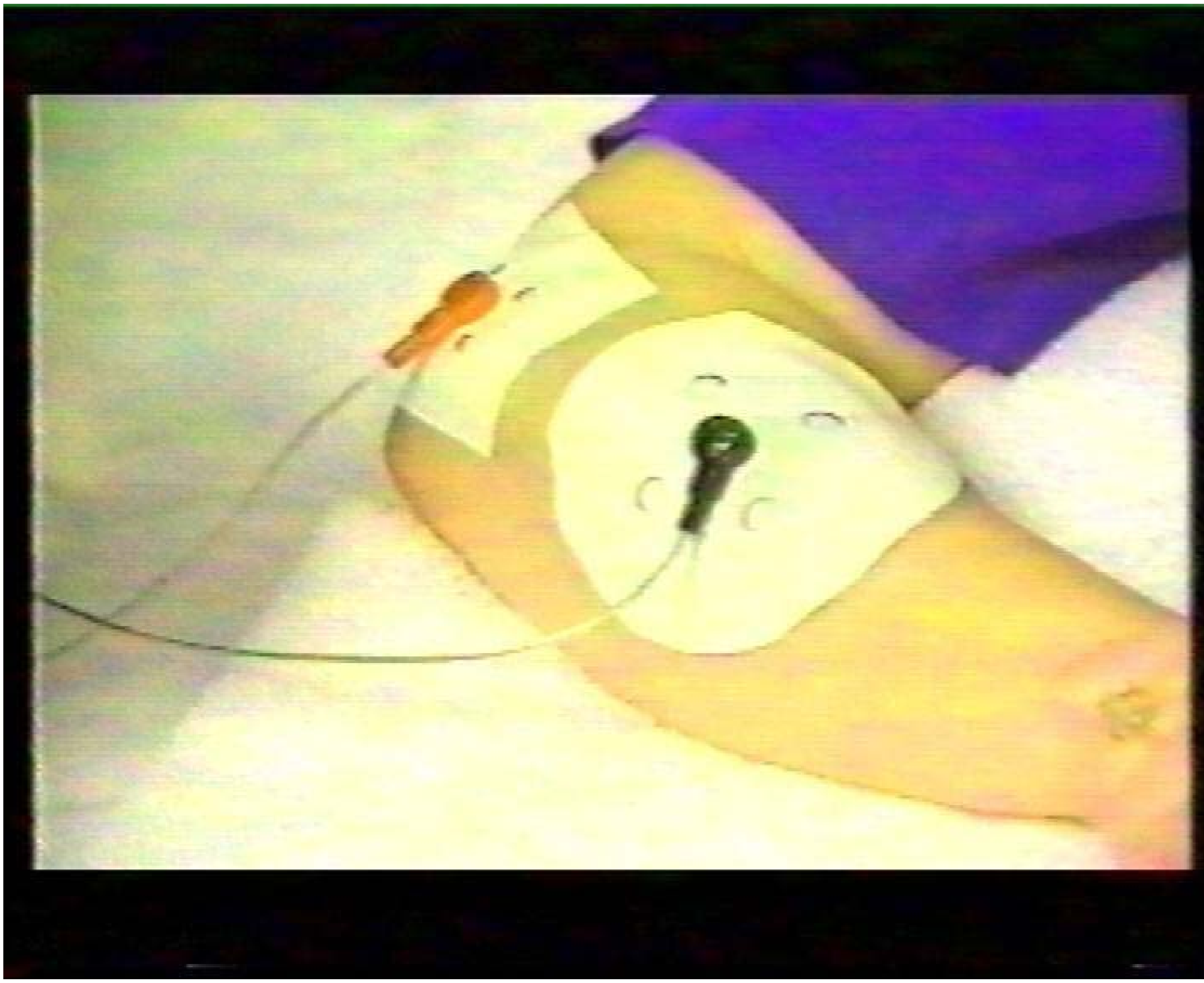
Picture -4 Application of Current

Picture -5 Electrodes of Different Sizes & Shapes



Picture -6 Electrode Placement

Picture -7 Drug Introduced into the Electrodes



Picture -8 Electrodes with Drug Connected to Iontophore

For Further Reading:

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4. Prien T. Intradermal anaesthesia: comparison of several compounds. Acta Anesthesiol Scand 1994:38:805-7.

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