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A REVIEW ON NEEDLE FREE INJECTION TECHNOLOGY

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ABSTRACT

The Needle-free injection (NFI) systems are one of the novel method to introduce various medicines. Needle free injection technology was developed to reduce the number of needle stick accidents and associated problems. The needle injection has many complications like anxiety, fever, avoidance, disgust and needle stick injuries. Therefore NFI systems are used to overcome these complications. This needle free injection review work mainly focused on the types of needle free injections, and its working, advantages and disadvantages, preparation method of needle free injection, and its working, evaluation methods. Needle free injection technology is growing and has the potential to make the administration of medicine more efficient, safe and convenient

INTRODUCTION:

Injections are the most popular route for delivering drugs in the body in order to prevent and to treat various diseases. Injections are the major source of disease transmission, i.e., particularly when the needles are used incorrectly or when the reuse of the injection takes place. To overcome the problems related to needle based injections, needle free injection technology (NFIT) has been introduced. These needle free injection technology has been gained popularity during the past few years and offer many benefits. By using these needle free technologies we can inject liquid as-well-as solid (powdered) dosage form. Since 1930 onwards needle free injection devices are available for humans use. Needle free injection can be according to the International Organization for Standardization (ISO) as the injection of pharmaceutical dosage forms into the skin by pressure and not penetrating the skin with a needle. Jet injection is often termed as a synonym of needle free injection technology. In older needle free injection technology same nozzle faces and fluid pathways are used to dose all the individuals; thereby causing potential safety hazards of transferring blood-borne pathogens between the individuals. And in new generation of needle-free technology uses disposable single-dose cartridges which can eliminate the re-use of the nozzle face and fluid path. In the newer devices the use of disposable nozzle face allows the fast and easy nozzle changes, when necessary and when transferring to a different form. Needle-free injection systems are the novel

way used to introduce various medicines into the patients without piercing the skin with a conventional needle. Needle-free systems were first described by Marshall Lockhart in the year 1936 in his patent jet injection. Then in the early 1940's Higson and others developed a high pressure "guns" using a fine jet of liquid to pierce the skin and deposit the drug in underlying tissue. Needle-free injection device mainly consists of three components. They are:

- Injection device
- Nozzle
- Pressure source

1. Injection device:

These injection devices consist of a drug chamber and these drug chambers are designed in such a way that the self-administration is possible. The injection device is made up of plastic. Sterility is maintained throughout the device. Needle-free syringe which is made up of plastic and this device should be sterilized.

2. Nozzle:

The nozzle mainly serves as a passage for the drug and serves as the skin contacting surface. Nozzle contains an orifice through which the drug enters into the skin when injected. The diameter of orifice is 100 μm. The nozzle can fire the drug particles at an typical speed of 100 m/s with an depth of 2 mm. The most common orifice size is 0.127mm, comparable to a 25-guage needle. Therefore this injection is painless the patient feels tap of gas on the skin which is like flicking with your finger against on your skin.

3. Pressure source:

Pressure source is one of the most important for delivering a drug forcefully into the systemic circulation via the skin. The pressure source is a mechanical method which can store the energy in a spring and can be released by pushing a plunger to provide the necessary pressure. It can also be a pressure storage method that utilizes the compressed gas in the gas cartridge. The most popular gases which can be used in the devices are co_2 or nitrogen. Pressurized metal air cartridges are often provided for access in portable units.

ADVANTAGES

- Broken needles can be eliminated
- Consistent vaccine delivery.
- Dose can be reduced vaccine volume.
- Higher antigen dispersion.
- Elimination of worker needle sticks.
- Elimination of needle disposal.
- Painless and can be removed the stress.
- Avoids problems of reconstitution and any effect of shearing.
- Elimination of needle phobia.
- Self-administration is possible with needle free injections.
- A good dose response with increased drug doses.
- These needle free injection system can prevent the skin puncture hazards and its destruction; and also does not cause any problem of bleeding or bruising.
- Safety, use of needle-free injections avoids risks of accidental needle stick injuries for friends, family and healthcare workers. Contaminated needles can transmit HIV, hepatitis, and other blood-borne pathogens, and pose a major risk to health

DISADVANTAGES

- Higher start-up costs.
- Infrastructure for exhaustible gas systems.
- Worker confidence in NFID
- Method is complex
- Expensive method
- All systems are not fitted into one size.
- personnel training and maintenance is required
- administration of drug molecule through Intravenous route is not possible
- Easily transmission of disease from one person to another if the needle is used for different patients
- Increased chance of overdose

TYPES OF NEEDLE FREE INJECTION SYSTEMS

Needle free technologies are of three types: Powder injections, Liquid injections, Depot or projectile injection

Powder injections: [7-8]

In these type of powder injection systems, certain amount of pre measured powdered medication is placed in the drug cassette which is opened by the compressed gas and thus the medication is to be delivered into the tissue.

Design of powder injection systems

This type of powder injections consist of a chamber which is filled with solid drug content and consists a nozzle which is used for firing the drug particles into the skin by utilizing the compressed gas as a power source. These powder injections contain a diaphragm (a few microns thick) on either side of the chamber which is used to cover the drug chamber.

Mechanism of powder injection system:

(a) The drug Particles can exist along with a gas stream from the nozzle.

(b) The drug Particles can impinge on the skin surface which leads to form a hole on the surface of the skin with the progression of a injection.

(c) The Drug particles get deposited in the form of a spherical pattern at the end of the hole and thus penetrate the drug across the stratum corneum.

(d) After the penetration of a drug into the skin, the drug particles get distributed completely into the stratum corneum and the viable epidermis.

Advantages of Powder injections [9-10]

• A minor volume of the drug material is shot through the skin as in form of powder instead of liquid form, hence these powder injection is painless.

• The therapeutic agent will be more stable and there is no need of cold storage

1) Liquid injections: [9-10]

Liquid injection can mainly works on the principle of "if a high enough pressure can be generated by the fluid in the intimate contact with the skin, and then the liquid will punch a hole on the skin and delivered the drug into the tissues and under the skin." Although the same principle is to be applied as in powder injection, but there is a difference in the actual design and operation of the powder injection devices. These liquid injection systems can use either gas or spring, pistons, drug loaded compartments and nozzles. Nozzle orifice size is about 150 to 300 μm

Mechanism of liquid injections

• When a piston is Impact on the liquid reservoir in the nozzle these will increases the pressure, which shoots the jet out of the nozzle at high velocity (velocity > 100m/s)

• Due to The effect of the jet on the skin surface it starts the formation of a hole on the skin through erosion, fracture, or other skin failure mechanisms.

• The depth of the hole in the skin is increased which increases the impingement. If the rate of formation of hole is less than the rate of jet impinging the skin, then some of the liquid splashes back towards the injector.

• The accumulation of fluid in the hole occurs because of a deeper hole in the skin which slows down the incoming jet. Hence, further development of a hole is stopped. The dimensions of the hole are established very early in the process (a few tens of microseconds) from the time of impact. Stagnation of the jet at the end of the hole disperses the liquid into the skin in a near-spherical shape

3 - Depot or projectile injections

For the delivery of drug into the muscles the depot or projectile injections were developed. These depot injections may create a drug reservoir in the muscles. The drug from the reservoir is continuously released for certain period of time.

TYPES OF NEEDLE FREE INJECTION DEVICES BASED ON POWER SOURCE: [11]

There are 2 types of Needle-free injection devices based on the power source. They are; Spring-Powered: Compressed gas powered.

1) Spring powered:

Cost of these spring powered devices is less, but these devices have a limited range of force and reduced versatility. Primarily these types of spring powered devices have been used for the administration of drugs via subcutaneous.

2. **Compressed Gas-Powered:**

The compressed gas powered devices has the ability to deliver the large volumes

of medicaments. And have greater flexibility and have Sustained force of generation.

HOW IS A NEEDLE-FREE INJECTION SYSTEM MADE? [12, 13, 14, 15]

Needle free injection system is a novel way of introduction of various medicines. The medicines can take in the form of power sprays, edible products, inhalers, and skin patches. The recent invention is the needle-free system while the hypodermic needles were first introduced in the 1800s. Today, this technology is a steadily developing technology that makes the administration of medicine more efficient and less painful

1) Raw Materials

Pharmacologically inert material have been used for the preparation of needle free injections(NFI), these needle free injection devices direct contact with the human body that's why these devices are sterilized. These needle free injection device outer shell is made of light weight with high strength thermoplastic materials such as polycarbonate. Due to the addition of fillers to the plastic the plastic materials become light weight, rigid, and more durable. Overall appearance is modified by using colorants.

1) **DESIGN:**

Needle free injection device consists of these 3 components. They are:

Injection device and disposable needle free syringe and an air catridge. Durable plastic material are used in the preparation of needle free injection, these device are made in order easy for the administration of self medication. The syringe is disposed after every use.

2) **The Manufacturing Process**

Various number of methods is available for the production of needle-free injection device. The following Process is mainly focused on the preparation of an air-forced system. These air forced systems are made by using following procedure which involves the molding of the pieces, assembling the pieces, and then decorating them and then labeled the final product. Typically the individual pieces are produced off-site and these pieces are assembled by the needle free injection system manufacturer. To prevent the spread of disease the manufacturing processes of the needle free injection systems must be done under the sterile condition.

Making the pieces;

In the first step plastic pieces produced from the plastic pellets. It is done by the process called as the injection molding. Plastic pellets are put in a large holding bin on the machine known as injection molding. These plastic pellets are then heat to make a flow. After than the material is to be passed through an hydraulically controlled screw.

As these screws rotate, the plastic is to be directed through a nozzle which is then injected into a mold. The mold which is composed of 2 metal halves that form the shape of the part when brought together. When the plastic is in the mold, for a specified period of time it is held under the pressure and then allowed to cool. After cooling, the plastic which is inside gets hardens. Then the mold pieces are to be separated and then the plastic part falls out onto a conveyor. Then the mold closes again and the entire process is repeated again. After the plastic parts are ejected from the mold, then the manual inspection are carried out during the process to ensure that there is no significantly damaged parts are used.

Assembling and labeling

Now these parts are to be transported to assembly line. In this production phase various events are occurring. Markings are to be done on the machine that shows dose levels and the force measurements. These machines are specially calibrated so printing is made precisely. Depending on the complexity of the device, either human workers or machines can assemble the devices. This involves the inserting of various pieces into the main housing and attaching any buttons.

Packaging

After the assembling, then the next step is packaging. Packaging involves 2 steps. The first step is wrapped the product in a sterile films and the second step is put the primary packing into a cardboard or plastic boxes. Each part is packaged so movement is minimized to prevent damage. For consumer products, instruction manual and safety information is put in packaging. Then these boxes are shipped via truck to distributors.

Quality Control

Quality control can checks the quality of the product during the manufacturing process. Line inspectors can generally check the plastic components during production, and then they conform and give the assurance that the specific product will meet its predetermined specification. Visual inspection is the first step, but measuring of the equipment is also important to check the dimensions of the equipment including size and thickness. Instruments that can be used include laser micrometers, calipers and microscopes. Inspectors can check whether the labeling and the printing of the equipment are correct and that all the parts are included in the final packages. Since these type of devices may have various safety issues, production of these equipments is strictly controlled by the Food and Drug Administration (FDA). Each manufacturer must conform to the various production standards and specifications. Inspections may be occurring in 2 ways. They are Announced and unannounced inspections. These inspections may occur to ensure that the companies are following good manufacturing practices or not. For this reason production and design records must be kept in detailed.

MECHANISM OF WORKING

Needle-free injection technology is mainly works by forcing the liquid medication at the high speed through an tiny orifice that is held against to the skin. The orifice diameter plays an important role in working of the equipment. While come to the orifice diameter it is smaller than the diameter of the human hair. This smaller diameter of orifice can produce ultrafine stream of high-pressure fluid that can be penetrated into the skin without using a needle. The design of the instrument has a major influence on the accuracy of the subcutaneous delivery and the stresses imposed on the product to be delivered. The design of the equipment must be ensure to produce sufficient high pressure which is required to puncture the skin, while the subsequent pressure is reduced to ensure that the molecule is deposited comfortably at a level that does not reach the muscle tissue. High-pressure delivery could leads to damage of the fragile molecules, such as monoclonal antibodies. For Successful delivery of such molecules, therefore, requires a device with carefully controlled power, nuances. Therefore several companies that are involved in development of this technology, such as, Antares Pharma Inc, Aradigm Corporation, Bioject Medical Technologies Inc and Biovalve Technologies Inc.

Ideal Needle free injectors must be made from material having following characteristics [16, 17, 18, 19, 20]

(1) Pharmacologically inert material should be used.

(2) The equipment should be heat resistant so that the equipment can withstand at the very high temperature used during heat sterilization.

(3) Outer shell material which is made up of light weight and should have high strength.

Example; polycarbonate.

Evaluation

The injector expels at a high pressure liquid jet having the static pressure of greater than 10 MPa and the velocity of 100m/s from the nozzle. This liquid jet disperses in the dermis and hypodermis.

THE MECHANICAL TESTING SYSTEM FOR NEEDLE FREE INJECTIONS (NFI) ARE*:*

(1) ***Ex Vivo*** **Skin technique: -** It uses skin cross section and photography and its analysis. In this the skin tissue like per fused porcine forelimb is isolated. A dye named Herlitz No.1 is used and filled up to 0.3ml to 0.5ml in injector. The tissue is

dissected and photographed. The two evaluation parameters such as penetration depth and tissue reached are noted.

(2) (2) Synthetic Acceptor Gel: - It uses a polyacrylamide gels (8-40%) having young modulus up to 1000KPa are used with digital image analysis and a high speed camera that shows penetration kinetics

APPLICATIONS OF NEEDLE FREE INJECTION TECHNOLOGY [21, 22, 23, 24]

1. Mass immunizations such as measles, smallpox.
2. Proteins, peptides, monoclonal antibodies, small molecules and vaccines can be delivered by using intraject technology
3. Powderject (Powderject pharmaceuticals) technology is used to deliver insulin to hairless guinea pigs, delivery of large macromolecules across the skin, for intradermal DNA immunization against influenza virus in mice.
4. Jet injectors technology can delivers proteins such as β-interferon as well as small organic conventional therapeutic agents such as lidocaine (lignocaine) for local anesthesia.
5. The Disposable Syringe Jet Injector (DSJI) Project is supporting clinical research on the delivery of vaccines with jet injectors. Current research work includes following applications
6. Measles-mumps-rubella vaccine
7. Yellow fever vaccine
8. DTP-Hib-hep B vaccine
9. BCG vaccine
10. Hyperhidrosis
11. Hemophilia

CONCLUSION

Needle free injections are more efficient and much safer than the conventional needle injection and easy to use. Needle free injection technology is much safer and have no disposal problem these needle free injections are easily acceptance by patients, and lowering costs and continuing development all make needle free injection technology is one of the best way for vaccinations and insulin self treatments. Organizations such as WHO and CDC (Centre for Disease Control) and groups like Gates Foundation have been supported for the development of needle-free injections as an alternatives for drug delivery through needle injections and can prevent the transmission of disease through re-use of needles.

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