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AN OVERVIEW ON NEEDLE FREE INJECTION SYSTEM

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Abstract:
Needle free injection system are to introduce the various medicines into patients without piercing the skin with a conventional needle. Needle-free technology offers the many benefit of reducing patient concern about the use of needle. Needle free injection is the very effective injections a wide range of drugs and bioequivalent to syringe and needle. It results in less pain, and is strongly preferred by patients. Additional benefits include very fast injection compared with conventional needles and no needle disposal issues. Not only benefit of the pharmaceutical industry to the increasing product sales, it has the added potential to increase compliance with dosage regimens and improved outcomes. Today, they are a steadily developing technology that promises to make the administration of medicine more efficient and less painful.
***Keywords**: NFID ,Injection, Skin, Subcutaneous, Pressure*

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INTRODUCTION:

At present scenario, many researchers are working to develop technology that promises to make the administration of medicine more efficient and less painful. There are a variety of problems associated with the hypodermic needles used in injections. These include relatively high cost of the needles, lack of reusability that is needle syringe should be sterilized, additionally; many people have fear of needles or needle-phobia, which cause them to avoid treatment. These drawbacks have led to development of alternative delivery system to needle injections. Needle-free injection system was designed to solve this problem making them safer, less expensive and more convenient[1].

The term needle free is used to describe an extensive range of drug delivery technologies, which consist of technologies that do not have a needle but make use of electrophoresis to drive drugs through the skin, technologies that use one or more very small needles, but needle nevertheless. Needle free devices are taken to the form of power sprays, edible product, inhalers and skin patches. Devices are available in reusable and disposable forms, for home or physician office use, and also versions for multiple patients and institutional uses. This technology avoids various disadvantages that are associated with needle use[2]:

- The risk of cross contamination from needle stick injury.
- Under or overdosing which results in poor injection technique in patients.
- Needle phobia.
- Injection site pain.
- Poor complains resulting in long-term worsening of conditions.
- The decreased costs due to the patients visiting the hospitals for injection

ADVANTAGES

- No under or overdosing condition of the drugs.
- Useful in case of patients with needle phobia.
- compliance especially in chronic administration of drugs.
- No specific disposal requirements.
- No risk of cross contamination from needle stick injury.
- Better drug stability during storage as it is delivered in dry powder form.

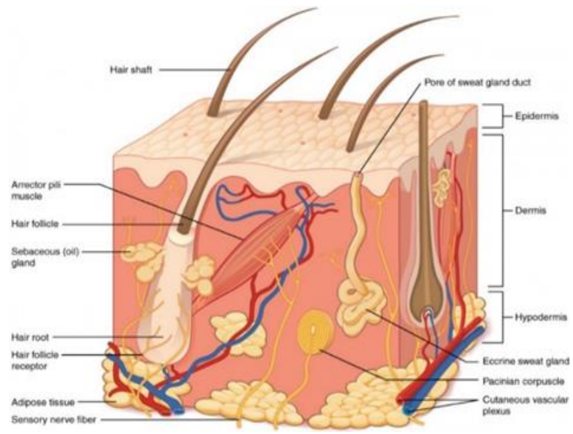
DISADVANTAGES

- Higher star-up costs.
- Infrastructure for exhaustible gas system.
- Higher requirement for training and maintenance.
- No one size fits all NFID.
- Worker confidence in NFID[3]

STRUCTURE OF HUMAN SKIN

Human skin is generally made of two layers.

- Epidermis



- Dermis

Figure 1: Layer of skin

Epidermis

It is the external layer of the skin which is mainly composed of various layers of keratinocytes, melanocytes, Langerhans cells and Merkel cells. It acts as a physical and chemical barrier between the body and external environment. It has four layers:

1. Stratum basale
2. Stratum spinosum
3. Stratum granulosum
4. Stratum corneum

Dermis

It is the area of supportive connective tissue between the epidermis and subcutis. The dermis mainly consists of sweat glands, hair roots, nerve cells and fibers, blood and lymph vessels. Its main function is to protect the body from stress and strain [4].

Hypodermis

It is the layer of loose connective tissue and fat that lies beneath the dermis. Its role is to put together the skin and underlying bone and muscle and supply it with blood vessels and nerves.

NEEDLE-FREE INJECTION TECHNOLOGY: ORIGIN AND METHODOLOGY

In the 1930s the Needle-free technology, first called jet injectors, was developed. Over 50yr, it was extensively in used mass vaccination programs in people for smallpox, polio, and measles. Mechanical compression is used to force fluid through a small orifice, a high-pressure stream is produced that could penetrate skin and subcutaneous tissue to deliver the vaccine. In most of the older devices the same nozzle faces and fluid pathways are used to dose all the individuals; thereby causing potential safety hazards of transferring blood-borne between individuals. In people, new generation needle-free technology uses disposable single-dose cartridges eliminating re-use of the nozzle face and fluid path. Most needle-free technology in production animals use non-disposable nozzle faces. 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 [5].

In the Needle-free injection technology a compressed gas (typically air, CO2 or nitrogen) uses to propel the vaccine at high velocity through a tiny orifice by generating force. When administered through the skin, an ultra-fine stream of fluid penetrates the skin, delivering the vaccine in a fraction of a second to the skin, subcutaneous tissue, and underlying shallow muscle. One major objection to needle-free injections has been the wetness associated with residual vaccine on the skin surface. This wet appearance may cause the vaccine administrator to think that the vaccine was improperly administered. Needle-free injection technology has been designed to deliver antibiotics, iron dextran vaccine comfortably, accurately, and quickly without the use of a needle. In contrast, needle-based injections may result in animal stress, vaccine residues, injection site lesions, and broken needles. Needle-free injection is precise, reliable, and virtually the same every time. There are 3 stages in needle-free delivery, and the total amount of time required to deliver the vaccine is less than 1/3 of a second. The three stages are,

- Stage 1, the peak pressure phase, optimal pressure used to penetrate the skin (0.025sec);
- Stage 2, the delivery or dispersion phase (-0.2 sec)
- Stage3, the drop-off phase (<0.05 sec).

This pressure profile is consistent with each administration of vaccine ensuring each animalis vaccinated at the proper tissue depth. This is not the case with needle-syringe administration of vaccine, which is equipment (e.g., needle length and gauge) and technique dependent. In the case of vaccine dispersion, an enhanced dispersion field is a significant consideration that affects the animal's immune response to a given antigen. Traditional needle and syringe administration results in a bolus forming in the tissue adjacent to the tip of the needle. The needle- free injection technology improves the dispersion of medication throughout the tissue. As the fluid stream forces its way through the tissue, it follows the path of least resistance, resulting in a widely dispersed, spider-web-like distribution of the medication. Slightly reduced force in the dispersion phase allows the fluid to disperse in the tissue. This wide dispersion of vaccine in a needle-less injection system the fluid stream creates a local high pressure point at the skin's surface which punctures the skin allowing the drug to pass through. A stream diameter of approximately 100 um and traveling at 100 m/s can achieve the desired injection depth of 2 mm. A comparison of relative diameters for a 24-gauge (diameter of 460 um) needle, a 100 mm injection stream and a human hair. From this figure it is seen that the needle-less stream is much smaller than the average injection needle [6].

Figure 2. Schematic representation of injection via typical Needle-free system

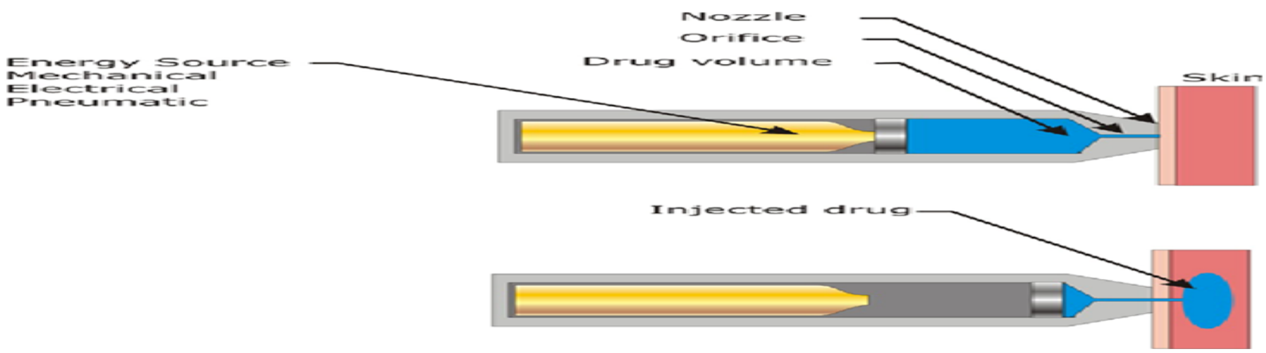


Figure 3: Components of needle free injection system

COMPONENTS OF NEDDLE FREE INJECTION DEVICE

Component 1 - Injection device: It has a drug chamber and is designed such that self-administration is possible. The device made up of plastic.
Component 2 - Nozzle: The nozzle serves as passage for the drug and serves as the skin contacting surface. The nozzle has an orifice through which the drug enters skin when injected. The diameter of orifice typically is 100 µm. The nozzle fires drug particles at a typical speed of 100 m/s with a depth of 2 mm. The most common orifice size is 0.127mm.
Component 3 - Pressure source: It is important for delivering a drug forcefully into the systemic circulation via the skin. The most popular gases used in devices are carbon dioxide or nitrogen. Pressurized metal air cartridges are often provided for access in portable units [7].

TYPES OF NEEDLE-FREE INJECTION SYSTEM

Needle-free injection drug delivery systems are classified as follows:

1. Powder injections
2. Liquid injections
3. Depot or Projectile Injection.

System Type 1 - Powder injections Design of powder injection system

These injections consist of a chamber filled with solid drug content and a nozzle for firing drug particles into the skin by utilizing the power source which typically is compressed gas.

Mechanism of powder injection

(a) Particles exist from the nozzle along with a gas stream.
(b) Particles impinge the skin surface leading to formation of a hole into the skin with the progression of the injection.
(c) Drug particles get deposited in a spherical pattern at the end of the hole and penetrate across the stratum corneum.
(d) After their penetration into the skin, drug particles get distributed completely into the stratum corneum and the viable epidermis [7].

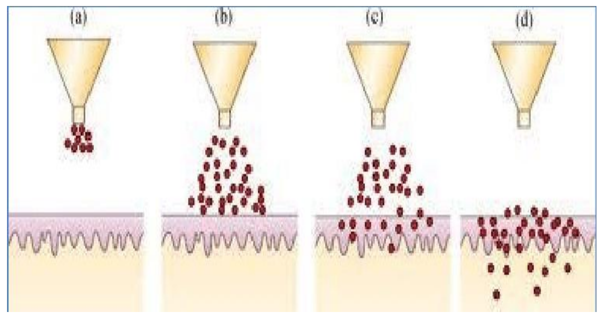


Figure 4. Mechanism of a powder injection System

Type 2 - Liquid injections

The basic principle of this injection is "if a high enough pressure can be generated by a fluid in intimate contact with the skin, then the liquid will punch a hole in to the skin and be delivered in to the tissues in and under the skin."

Mechanism of liquid injections

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

- The effect of the jet on the skin surface starts the formation of a hole in the skin through erosion, fracture, or other skin failure mechanisms.
- Further impingement of the jet increases the depth of the hole in the skin. If the volumetric rate of hole formation is less than the volumetric rate of jet impinging the skin, then some of the liquid splashes back towards the injector.
- The accumulation of liquid in the hole occurs because of a deeper hole in 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 [8].

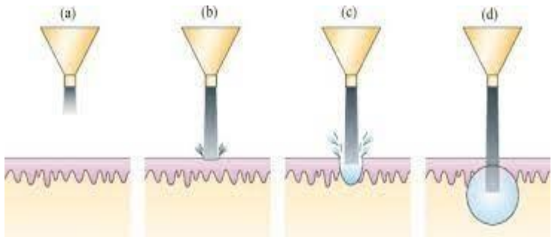


Figure 5. Mechanism of a liquid injection System

Type 3 - Depot or projectile injections

These systems are designed for administration of a drug into muscles. They create a store of drug into muscles that is released continuously over a desired time period [9].

MANUFACTURING OF NEEDLE FREE INJECTION SYSTEM

Design

The air forced needle free injection systems are usually made up of three components which include an injection device, a disposable needle free syringe and an air cartridge. The syringe is sterilized prior since it is the only piece of the device that touches the skin. The syringe is fabricated such that, it should be disposed after every use.

Raw material

Since these devices directly come in contact with the body, they must be fabricated from pharmacologically inert materials. The materials must be capable to endure high temperatures since they are heat sterilized. The external body of the device is made up of a thermoplastic which has characteristics such as high strength, lightweight. The example of such thermoplastic is polycarbonate. In order to make the polymer significant to mold, fillers are added. Due to the addition of fillers the plastics become more durable, lightweight, and rigid. To modify the overall appearance, colorants are included into the plastic [9].

The manufacturing processes

There are various methods of producing needle free injection system. The manufacturing process involves steps such as molding the pieces, assembling them, decorating and labeling the final product. All of the manufacturing process is done under sterile conditions to avoid the spread of disease.

a. **Molding the pieces**
b. **Assembling and labeling the pieces**
c. **Packaging**

Quality control

Quality control checks are performed regularly during the manufacturing process. Dimensions such as size and thickness are checked by test methods such as visual inspections and measuring equipment dimensions. Laser micrometers, calipers and microscopes can be used to test the systems. Inspectors also confirm that the labeling and printing on the device is proper and complete and all parts are properly assembled in the device. Production of needle free devices is totally controlled by FDA due to the safety issues. Each manufacturer is expected to follow various production standards and specifications. Announced and unannounced inspections are regularly conducted to ensure that the companies are following good manufacturing practices (GMP). The manufacturers must also maintain a detailed record of production and design operations.

Mechanism of working

Needle-free injection technology uses force generated by a compressed gas (typically air, CO_2 or nitrogen) to propel the vaccine at high velocity through a tiny orifice. When administered through the skin, an ultrafine stream of fluid penetrates the skin, delivering the vaccine in a fraction of a second to the skin, subcutaneous tissue, and intramuscular tissue. Injection event requires less than 0.5 seconds [10].

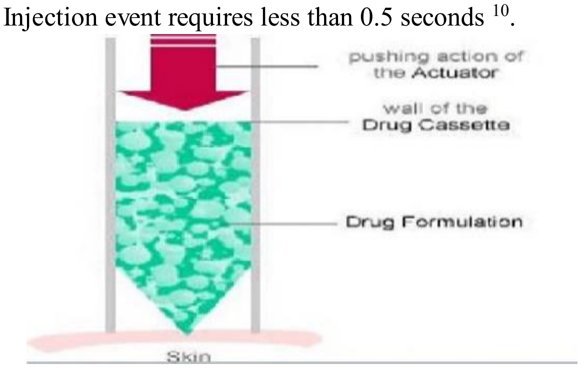


Figure 6. Mechanism of working of needle free injection system

RECENT NEEDLE-FREE INJECTION TECHNOLOGIES

1. Biojector

It is the only system for intramuscular use which is approved by FDA. More than 10 million injections have been administered successfully using the Biojector 2000, with no reports of major complications. This system proved to be safe and successful in the case of higher risk conditions like delivering drug to HIV or hepatitis infected patients.

Figure 7. Biojector needle free injection device

2. Serojet

The device is designed for delivering Serostim recombinant human growth hormone administered subcutaneously. The Serojet device is tailored from Vitajet technology. This is used for treatment of HIV associated wasting in adults and was approved by FDA in March 2001 for marketing.

3. Iject

The Iject is a pre-filled single-use disposable injection device configured to administer 0.5 to 1.00 ml subcutaneous or intramuscular injections. This small, lightweight, gas-powered injection system designed for home or professional use having two versions, one is a pre-filled, single-use disposable injector, and the second is a reusable injector that accepts pre-filles medication cartridges.

Figure 8. Injex

5. Zetajet

It consists of two components, the portable injector and an auto disabling disposable syringe. It is intended to deliver vaccines and injectable medications either subcutaneously or intramuscularly and is indicated for both professional use and home use for patients who self-inject. The syringe assembly has a unique "auto-disable" feature that prevents re-use of the syringe [7].

Figure 9. Zetajet

6. Cool click

Bioject developed it for delivering Saizen recombinant human growth hormone. In some children, naturally occurring growth hormone is absent or is produced in inadequate amounts. In these cases, Saizen or growth hormone replacement must be injected to maintain normal growth[11].

Figure 10. Cool click

APPLICATIONS OF NFI TECHNOLOGY

- Mass immunizations such as measles, smallpox.
- A local anaesthetic called lidocaine hydrochloride can be administered without using a needle.
- Needles-free injection can be used to provide heparin (an anticoagulant), erythropoietin, lidocaine hydrochloride (a local anaesthetic), and several vaccinations.
- Patients who are minors Children become particularly difficult dental patients because they are so terrified and don't comprehend why the procedure is necessary.
- Patient adults Many folks are terrified of both the discomfort associated with getting dental work done and syringes with needles. The "needle-free syringe" will help to solve this issue.
- Haemophilia- The first needle-free reconstitution device with a prefilled diluent syringe was developed for haemophilia, a hereditary condition.
- Hyperhidrosis-This skin condition causes excessive sweating, which makes the palms and other body parts damp.

CONCLUSION:

Needle-free injection systems have potential to improve efficiencies. Major advantages of needle-free systems are the elimination of broken needles, a more constant delivery of vaccines and drugs, and decreased worker safety risk. Needle free injection systems are customizable to each operation and can be modified to optimize productivity. Needle free injection technology offers effective injectors for a wide range of drugs & bioequivalent to needles and syringes. Needle free devices have demonstrated consistent delivery to the epidermis, the dermis, the subcutaneous and the intramuscular space. They offer less pain, avoid needle stick injuries and contamination, allows self-administration and results in no needle phobia and are thus strongly preferred by the patients. Some of them are ideally suited to chronic injections of varying doses of insulin, proteins and monoclonal antibodies.

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