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Needle Free Injection

Gopibabu Jampani*, Brahmaiah[1], Chandu Baburao[2]

Don Bosco P.G College of Pharmacy, Pulladigunta, Guntur, Andhra Pradesh, India.

ABSTRACT

Needle-free injection systems are novel ways to introduce various medicines into patients without piercing the skin with a conventional needle. They can take the form of power sprays, edible products, inhalers, and skin patches. While hypodermic needles were first introduced during the 1800s, needle-free systems are relatively recent inventions. Today, they are a steadily developing technology that promises to make the administration of medicine more efficient and less painful there has been a renewed interesting needle-free devices in swine due to two main factors: immunology research, indicating that targeting dendritic cells in the skin and the subcutaneous tissues results in improved immune response with minimal antigen doses, and to minimize needle-site lesions that are the result of broken needles, bacterial contamination.

Key words: needle free, power sprays, inhailers, immunology

Corresponding author

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INTRODUCTION

People are given injections to protect them from influenza, tetanus, cholera, typhoid, and other diseases. When a needle is inserted through the skin, the vaccine (or drug) it carries provides systemic immunity. This is because the vaccine gets into the bloodstream and provokes the body to create antibodies that are carried throughout the entire body [1].

In the United States, children may get over 13 vaccine injections by the age of 16. Unfortunately, there are a variety of problems associated with the hypodermic needles used for these injections. One of the most significant drawbacks is the relatively high cost of the needles. Additionally, many people have a fear of needles which causes them to avoid treatment. These drawbacks have led to the development of alternative delivery systems to needle injections[2].

Needle-free systems are designed to solve these problems making them safer, less expensive, and more convenient. It is anticipated that these systems will increase the incidence of vaccination and reduce the amount of prescribed antibiotics. Moreover, they should reduce the number of needle stick accidents that have resulted in some health care workers contracting diseases.

More than a dozen companies have developed alternatives to needle injections. Some of the different designs include nasal sprays, nose drops, flavored liquids, skin patches, air forced and edible vaccine-packed vegetables.The needle-free systems that are most like traditional injections involve the direct transfer of the medicine through the skin. One company offers an injection system where the drug is dispersed through the skin as a fine mist or powder. In this system, a tube-shaped device is held against the skin and a burst of air forces the molecules of medicine into the body. The device is designed to force the medicine far enough through the skin so it enters the bloodstream. An application for which this system is particularly useful is for patients who need daily doses of growth hormone [3].

Patches have been introduced as needle-free delivery systems. These devices, which look like bandages, slowly transfer medicine through the skin. In one type of patch, thousands of tiny blades are imbedded on its surface. The patch is covered with medicine and then placed on the skin. The blades make microscopic cuts in the skin that opens a path for drugs to enter through. When an electric current is applied, the medicine is forced into the body. This process, called iontophoresis [4].

Inhalers are another type of needle-free delivery system. In these systems, liquids or powders are inhaled and delivered into the lungs. These devices are good for delivering protein drugs because the lungs provide a rapid absorption into the bloodstream. In one system there is a pump unit that atomizes a powdered medication [5]. This allows the patient to inhale the proper amount of medicine without it getting trapped in the back of the throat. For diabetics who require daily injections of insulin, an aerosol inhaler has also been introduced.

Oral vaccines are needle-free systems that may replace vaccine injections. This technology has been difficult to perfect for many reasons. The primary problem with this type of delivery system is that the environment of the digestive system is harsh and typically destroys vaccines and other drugs. Also, vaccines do not work as well in provoking antibody production in the digestive lining. One of the latest oral vaccines involves freeze drying the medicine and mixing it with a salt buffer to protect it when it is in the stomach. Other edible forms include a sugar solution of a vaccine against the bacterium that causes ulcers. For travelers, a typhoid-vaccine capsule has been developed as an alternative to the two painful shots typically required [6].

HISTORY

As long as drugs have been known to cure diseases, people have searched for better methods of delivering them. During the early nineteenth century researchers made a series of discoveries that eventually led to the development of the hypodermic needle by Alexander Wood in 1853. This device was used to give morphine to patients suffering from sleeping disorders. In subsequent years, the hypodermic needle underwent significant changes which made them more efficient to use, safer, and more reliable. However, needles still have significant drawbacks which prompted researchers to find needle-free alternatives.

The first air-powered needle-free injection systems were developed during the 1940s and 1950s. These devices were gun-shaped and used propellant gases to force fluid medicines through the skin. Over the years, the devices have been modified to improve the amount and types of medicines delivered, and the efficiency and the ease of use [7].

Today's Situation

Two factors have recently rekindled the interest of pharmaceutical companies in needle-free injection systems.

The first factor is major changes in the perspective of those involved in patient care as they have started taking into account the following major public health concerns.

- Needle phobia was recognized as an important issue as it concerns up to 30% of the population, of which severe cases can lead to avoidance behaviours that entail serious medical consequences.
- Contamination risks and injuries have become a major professional concern for healthcare professionals with the development of the HIV and hepatitis viruses.
- Many efforts have been made to improve overall patient care and comfort, including the development of self-injection procedures for chronic diseases (such as diabetes) [9].
- The second factor is the increase in value of the injectable drug market, due largely to a switch from low-cost drugs (such as common antibiotics, now mainly oral) to complex

molecules (the result of advances in biotechnology) with high added value (recombinant hormones, growth factors, cytokines and, in the near future, gene therapy).

NEEDLE FREE INJECTION PREPARATION

Raw Materials Used

Since these devices directly contact the body, they must be made from materials that are pharmacologically inert. The materials also must be able to withstand high temperatures because they are heat-sterilized. Air forced injection systems are available in different shapes as sizes. The outer shell of the device is made from a high strength, lightweight thermoplastic such as polycarbonate. Polycarbonates are polymers produced synthetically through various chemical reactions. To make the polymer easier to mold, fillers are added. These fillers make plastics more durable, lightweight, and rigid. Colorants are also incorporated into the plastic to modify the appearance. Prior to manufacture, the plastics are typically supplied in pellet form with the colorants and fillers already incorporated. Air-forced systems typically use carbon dioxide or helium gas to propel the medicine into the body [10].

Certain types of medicines work better with needle-free injection systems than other. Insulin, which must be administered daily to diabetics, can be incorporated into an inhaler system. Lidocaine hydrochloride, a local anesthetic is suitable to be delivered needle free. Other medicines suitable for needle free systems include Fentanyl (an Opioid analgesic), Heparin (an anticoagulant) and a variety of vaccines. Various adjunct ingredients included in these medicines include cyclodextrins, lactose, liposomes, amino acids and water.

Design

The air-forced needle-free injection systems are typically made up of three components including an injection device, a disposable needle free syringe and an air cartridge. The injection device is made of a durable plastic. It is designed to be easy to hold for self-administration of medicine. The needle-free syringe is also plastic. It is sterilized and is disposed after every use. For portable units, pressurized metal air cartridges are included. Less mobile devices have air hook-ups that attach to larger containers of compressed air. Some air-forced systems use a re-usable spring to generate the pushing force instead of pressurized air cartridges[11].

The Manufacturing Process

There are numerous methods of producing each needle-free injection system. The following process focuses on the production of an air-forced system. These systems are made through a step by step procedure which involves molding the pieces, assembling them, and decorating and labeling the final product. The individual pieces are typically produced off-site and assembled by the needle free injection system manufacturer. All of the manufacturing is done under sterile conditions to prevent the spread of disease.

Making the pieces

- 1 The first step requires the production of the component plastic pieces from plastic pellets. This is done by a process called injection molding [12]. Pellets of plastic are put into a large holding bin on an injection molding machine. They are heated to make them flowable.
- 2 The material is then passed through a hydraulically controlled screw. As the screw rotates, the plastic is directed through a nozzle which then injects it into a mold. The mold is made up of two metal halves that form the shape of the part when brought together. When the plastic is in the mold, it is held under pressure for a specified amount of time and then allowed to cool. As it cools, the plastic inside hardens.
- 3 The mold pieces are separated and the plastic part falls out onto a conveyor. The mold then closes again and the process is repeated. After the plastic parts are ejected from the mold, they are manually inspected to ensure that no significantly damaged parts are used.

Assembling and labeling

- 4 The parts are next transported to an assembly line. In this production phase various events occur. Machines apply markings that show dose levels and force measurements. These machines are specially calibrated so each printing is made precisely. Depending on the complexity of the device, human workers or machines may assemble the devices. This involves inserting the various pieces into the main housing and attaching any buttons [13].

Packaging

- 5 After the assembly step, the injection devices are put into packaging. They are first wrapped in sterile films and then put into cardboard or plastic boxes. Each part is packaged so movement is minimal to prevent damage. For consumer products, an instruction manual is included along with safety information. These boxes are then stacked on pallets and shipped via truck to distributors [14].

Quality Control [15]

Quality control checks are done throughout the manufacturing process. Line inspectors check the plastic components to assure they conform to predetermined specifications. Visual inspections are the first test method, but measuring equipment is also used to check the dimensions including size and thickness. Instruments that can be used include laser micrometers, calipers and microscopes. Inspectors also check to make sure the printing and labeling is correct and that all the parts are included in the final packages.
Since these devices can have various safety issues, their production is strictly controlled by the Food and Drug Administration (FDA). Each manufacturer must conform to various production standards and specifications. Announced and unannounced inspections may occur to ensure that these companies are following good manufacturing practices. For this reason detailed

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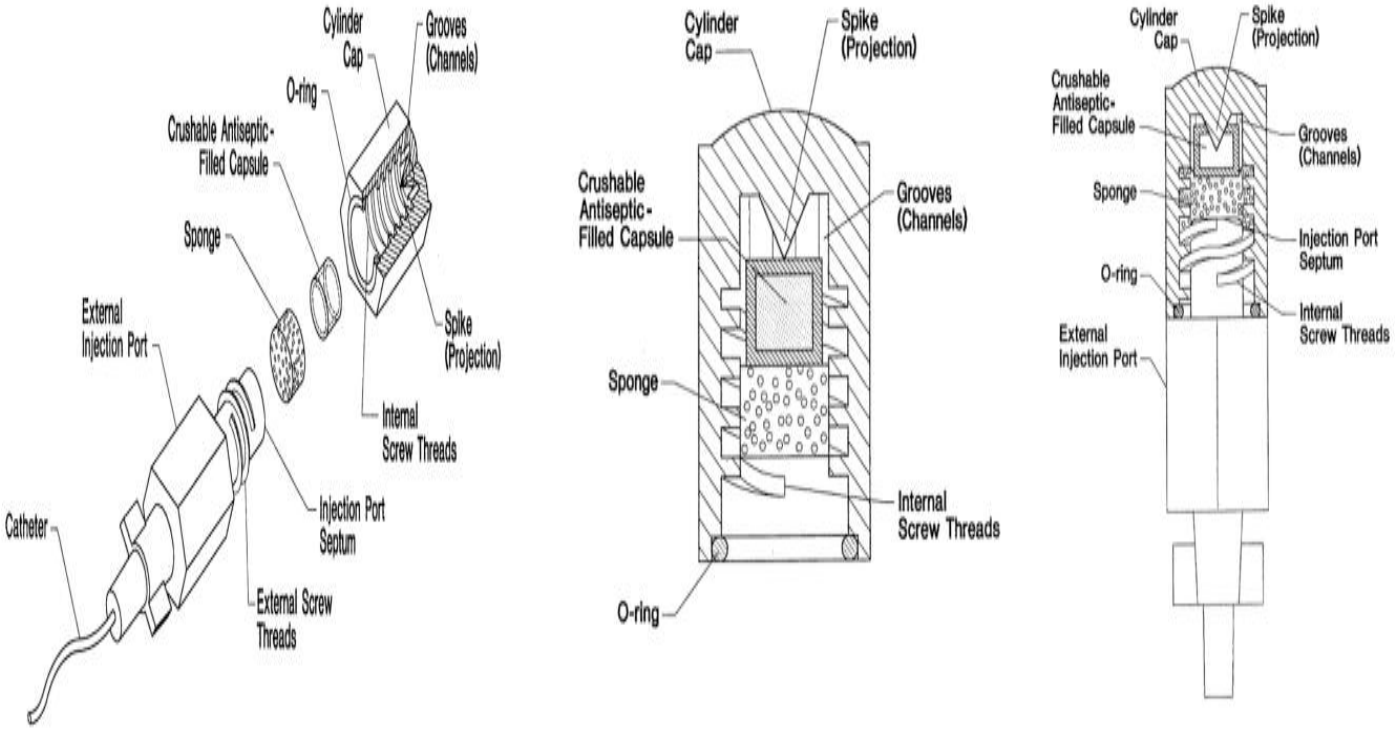
records must be kept related to production and design.



Needleless valve connectors for vascular catheters

Schematic of the antiseptic-barrier cap studied, including the injection port and cover [16]. It can be seen that when the cap is affixed to the membranous surface of the needleless connector or injection port, the spike ruptures the antiseptic-filled capsule, and the capsule sponge becomes saturated with chlorhexidine and maintains continuous contact with the entire membranous surface [17].

FUTURE WITH NEEDLE LESS TECHNIQUE

Many of these needle-free alternative technologies are in the development stage. Companies are still working on producing devices that are safer and easier to use. They are also working on alternatives which can deliver even more types of medicines. Inhalers are being improved as are nasal sprays, forced air injectors and patches. In the future, other foods may be genetically enhanced to deliver vaccines and other drugs. These include foods like bananas and tomatoes. In fact, bananas are being looked at as carriers for a vaccine to protect against the Norwalk virus. Tomatoes that protect against hepatitis B are also being developed. In addition to new delivery systems, scientists are also investigating methods for producing longer lasting drugs that will reduce the number of needle injections [18].

Novel Antiseptic-Barrier Cap

The antiseptic-barrier cap studied (Saralex, Menyhay Medical), consists of 3 parts: an outer cap with internal female threads and a spike inside the closed end, a capsule containing

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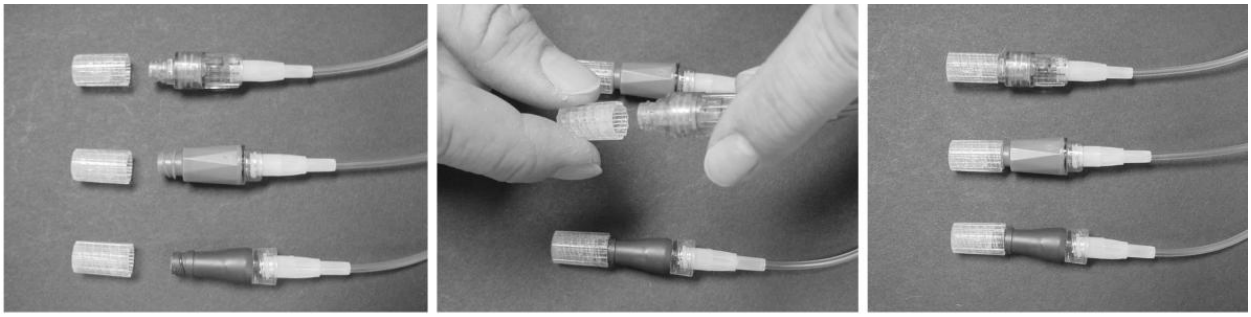
0.25 mL of 2% chlorhexidine gluconate in 70% isopropylalcohol, and a sponge (Fig 1). The cap has been designed so that, when it is threaded onto a luer-adaptable needleless connector or injection port, the spike ruptures the antiseptic capsule, saturating the sponge between the septum and the capsule. When the cap is tightened, the antiseptic-impregnated sponge[20] is brought into continuous contact with membranous surface of the connector or port until the cap is removed. After removal of the cap, there is no need to disinfect the membranous surface before access.

Design of the Simulation Study

Needleless luer-activated valved connectors from 3 manufacturers (Clear link [Baxter Healthcare],[21] Posi Flow [Becton-Dickinson], and Micro CLAVE [ICU Medical]) were studied.

All of the connectors have a membranous surface that is designed to be accessed by a blunt luer-lock male connector



Thirty-six connectors from each manufacturer were tested concurrently in a simulation trial. One device of each type was used as a negative control (they were accessed without precontamination). The remaining 35 devices from each manufacturer were contaminated by immersing the membranous surface in a suspension of *Enterococcus faecalis* [22] containing1108 colony-forming units/ml, after which the septum was allowed to dry in a protected aseptic container for24 hours (final inoculum on the septum, ~105 colony-forming units) [23].

Implications

Advantages of needle-free vaccine delivery over conventional needle-syringe administration include elimination of broken needles, lower vaccine volume and greater antigen dispersion, elimination of accidental worker needle sticks, elimination of needle disposal, and less pain and stress [24].

Adoption of NFIDs has been slow due to the cost of the unit and associated maintenance and gas infrastructure costs, greater complexity than needle syringe devices, higher labor costs, and requirement for training.

Immune responses to vaccines administered by NFID and needle-syringe technology are similar [25]

Further studies under field conditions in commercial swine operations are needed to confirm the advantages of NFID vaccine delivery over conventional needle-and-syringe vaccine delivery [27]

CONCLUSION

For the easy incorporation of drug in to body and to reduce the phobia towards injections can be done by the use of needle less injections and the drug with in less quantities can be given by this the drug can be easily diffused in to body without passing first pass metabolism. For the emergency inoculation of drug this technique is used.

REFERENCES

[1] Maki DG, Mermel LA. Infections due to infusion therapy. In: Bennet JV, Brachman PS, eds. Hospital Infections. Philadelphia: Lippincott-Raven Publishers; 1998:689-724.
[2] Arnow PM, Quimosing EM, Beach M. Clin Infect Dis 1993; 16:778-784
[3] Pittet D, Tarara D, Wenzel RP. JAMA 1994; 271:1598-1601
[4] Rello J, Ochagavia A, Sabanes E, et al. Am J RespirCrit Care Med 2000; 162:1027-1030.
[5] Marrie TJ, Costerton JW. J Clin Microbiol 1984; 19:687-693.
[6] Donlan RM, Murga R, Bell M, et al. J ClinMicrobiol 2001; 39:750-753.
[7] Murga R, Miller JM, Donlan RM. J Clin Microbiol 2001; 39:2294-2297.
[8] Bjornson HS, Colley R, Bower RH, Duty VP, Schwartz-Fulton JT, FischerJE. Surgery 1982; 92:720-727.
[9] Mermel LA, McCormick RD, Springman SR, Maki DG. Am J Med 1991; 91(Suppl 3B):197S-205S
[10] Safdar N, Maki DG. IntensiveCare Med 2004; 30:62-67.
[11] Sitges-Serra A, Puig P, Linares J, et al. JPEN J Parenter Enteral Nutr1984; 8:668-672.disinfection of catheter hubs 27
[12] Raad I, Costerton W, Sabharwal U, Sacilowski M, Anaissie E, Bodey GP. JInfect Dis 1993; 168:400-407
[13] Cheesbrough JS, Finch RG, Burden RP. J Infect Dis1986; 154:579-589.
[14] Safdar N, Maki DG. Chest 2005; 128:489-495
[15] Tan L, Hawk JC III, Sterling ML, Arch InternMed 2001; 161:929-936.

[16] Centers for Disease Control and Prevention. Public Health Service guidelinesfor the management of health-care worker exposures to HIV andrecommendations for postexposure prophylaxis. MMWR Recomm Rep1998; 47(RR-7):1-33.
[17] Centers for Disease Control and Prevention. Guidelines for the managementof occupational exposures to hepatitis B, hepatitis C, and HIVand recommendations for postexposure prophylaxis. Atlanta: Centers forDisease Control and Prevention; 2001.
[18] Available at: http://www.cdc.gov/ncidod/dhpq/gl_occupational.html. Accessed December 13, 2005.
[19] Danzig LE, Short LJ, Collins K, et al JAMA 1995; 273:1862-1864.
[20] Kellerman S, Shay DK, Howard J, et al. J Pediatr 1996; 129:711-717.

[21] Cookson ST, Ihrig M, O'Mara EM, et al. Infect Control Hosp Epidemiol 1998; 19:23-27.
[22] McDonald LC, Banerjee SN, Jarvis WR. Infect Control Hosp Epidemiol 1998; 19:772-777.
[23] Do AN, Ray BJ, Banerjee SN, et al. Bloodstream infection associatedwith needleless device use and the importance of infection-control practices
[24] Royer G, Charreyre C, Milward F. ProcAASV. Kansas City, Missouri. 2006; 239–241.
[25] Thacker EL, Nilubol D, Evans R. Proc AASV. Orlando,Florida. 2007;135–138.
[26] Babiuk S, Baca-Estrada ME, Foldvari M, Baizer L, Stout R, Storms M, Rabussay D, Widera G, Babiuk L. Mol Ther. 2003;8:992–998.
[27] Wesley RD, Lager KM. Am J Vet Res. 2005;66:1943–1947*
[28] Apley M, Thacker B Research Abstract. 2003. Available at: http://www.pork.org/porkscience/research/documents/02–136-apley.abs.9–26–03.pdf. Accessed 3 July 2008.
[29] Senn MK, Bradford JR, Cook DL, LoskutovA. Proc AASV. DesMoines, Iowa. 2004;263–265.
[30] Houser TA, Sebranek JG, Baas TJ, ThackerBJ, Nilubol D, Thacker EL. 2002. Available at: http://www.ipic.iastate.edu/reports/02swinereports/asl-1814.pdf. Accessed 3 July 2008
[31] Paquin G, Achacha M, Toburen T. Proc AASV. Toronto, Ontario, Canada.