

Comprehensive Risk Analysis and Mitigation Strategies for Syringe-Based Medical Products

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Abstract. Syringe products are used in the healthcare field in many places and with high frequency. As a result, there is a proliferation of clinical adverse events in which patients and healthcare professionals can be harmed. Only by understanding these adverse events can we better address the problem. In this article, the manifestations and clinical risks of adverse events of syringes used in the clinic were sorted out by reviewing the relevant literature, and the generating conditions leading to the occurrence of adverse events of syringe-based products were identified from the perspectives of inherent risks and clinical use risks. The investigation and study found that by replacing materials, regular inspection and recall by manufacturers, emphasizing the use norms of healthcare workers, and strict supervision by relevant departments, the recurrence of clinical adverse events of syringes can be reduced, possible risks can be prevented, and a safer environment for patients and healthcare workers can be provided.

Keywords: Syringes; Clinical risk; Medical device risk events.

1. Introduction

As early as the 15th century, the Italian Catinel proposed the syringe principle. But it wasn't until 1657 that the Englishmen Boyle and Raine conducted the first human trials, and it was in 1853 Alexander Wood of Scotland and Charles Plavoz of France first combined the syringe and needle. This innovation led to the birth of the modern syringe. Wood also developed the method of hypodermic injection. In 1869, the Frenchman Luyere produced the first all-glass syringe, which greatly improved the performance of syringes and reduced the risk of infection during injections. In 1956, a New Zealand doctor, Colin Murdoch, invented the disposable plastic syringe, which was unbreakable, easy to transport, cheap, recycled, and even safer than the glass syringe. The safety of plastic syringes is even greater than that of glass syringes. In May 2012, scientists from the Auckland Bioengineering Institute in New Zealand and the Massachusetts Institute of Technology (MIT) in the United States jointly developed a syringe without a needle. Needle-free injections eliminate the pain associated with injections and can be administered more quickly and accurately. Needle-free syringes are small, portable, and can be used by patients with visual impairments; they also dramatically reduce the number of accidents involving doctors and nurses accidentally sticking themselves with needle syringes, and this needle-free injection technology can bring complete relief to needle-phobic patients. As we all know, the pre-market research of medical devices has certain limitations. There are also certain risks, such as the limited life cycle of medical devices, the combined use of drugs and devices, clinical operations, and individual patient differences, which may cause adverse events to occur during the operation and use of the product. Therefore, it is necessary to summarize the causes of risks, prevent the recurrence of adverse events, control product quality, and ensure the safe and effective use of products.

2. Product Overview

Syringes are often used with hypodermic needles to inject liquids or gases into or withdraw them from body tissues. Syringes can be made of either plastic or glass and usually have a graduated indication of the volume of liquid in the syringe. Glass syringes can be sterilized in an autoclave. Still, because plastic syringes are cheaper to dispose of, most modern medical syringes are made of plastic,

reducing the risk of bloodborne diseases. Nowadays, most syringes used for vaccination and blood sampling are made of plastic and are for one-time use only, to be disposed of after use to avoid the reuse of syringes leading to cross-infection of infectious diseases.

According to the Classification Catalog of Medical Devices, syringe products belong to the injection and puncture instruments class, with a classification code 6815. Such products are highly risky and require strict control and management to ensure the effectiveness and safety of injecting apparatuses. They mainly include single-use sterile syringes and their plugs, single-use sterile injection needles, single-use intravenous infusion needles, single-use fiber optic needles, intravenous indwelling needles, single-use dispensing injection needles, and puncture needles.

3. Risk Analysis

3.1. Inherent risks

There are three aspects of risk inherent in a product: design factors, material factors, and production quality control. Since syringe products have been around for a long time, the basic structure has mostly stayed the same. China's supervision and management of medical devices, especially using more syringe products, have been strengthened. The ability of major companies to produce standardized requirements is also gradually improved. The impact of product design and production quality control factors are even more slight and negligible. Therefore, the existing inherent risk of this product is still focused on the material risk of continuous improvement.

3.1.1 Plasticizer

Polyvinyl Chloride (PVC) is widely used in syringe products because of its stable performance and low price. PVC requires different proportions of plasticizers, heat stabilizers, colors, and other additives depending on the needs of the use. Still, additives can cause a certain degree of biotoxicity, which is hazardous to human health.

DEHP is widely used as a plasticizer in PVC products. The temperature, the input liquid's fat solubility, and the contact duration with the PVC material can determine the amount of dissolution. The acute toxicity of DEHP is slight, and some studies have indicated that the LD50 of experimental animals receiving this compound by various routes (e.g., orally or by local injection) ranges from 14 to 50 g/kg, and the LD50 of intravenous injection is even as high as 200 mg/kg. LD50 for intravenous injection is as high as 200 mg/kg [1]. Under normal conditions, a small amount of DEHP is excreted in urine or feces within 24 hours. However, the main metabolite of DEHP, Phthalic acid mono-2-ethylhexyl ester (MEHP), accumulates in human tissues over a long period, with a bioaccumulation time of up to 6 months or even longer. The chronic toxicity of DEHP is mainly manifested in the effects on the reproductive system, the blood system, and hepatotoxicity because medical devices made of PVC can be affected by chemical reactions. Because of the PVC material, the medical devices will affect the nature and effectiveness of the output liquid through chemical action, etc., and even affect the human body's toxicity and life and health in more serious cases.

3.1.2 Heat stabilizer

PVC can only be plasticized at a processing temperature of $>160^{\circ}\text{C}$. However, the molecular chain growth during heating generates active tertiary carbon atoms, which can easily form and shed HCl with the attached chlorine and hydrogen atoms. Adding a heat stabilizer eliminates the unstable part that causes the start of HCl removal and quickly binds the removed HCl, thus inhibiting the decomposition of PVC [2]. The common heat stabilizers in PVC are lead salts, organotin, and metal soaps. Lead salt heat stabilizers due to heavy metal lead, migration, and accumulation in the body will inevitably cause damage to the human nervous system, resulting in intellectual and motor abnormalities and damage to the bone marrow hematopoietic system, leading to anemia. The commonly used organotin stabilizer in China is methylation mercaptide. Wang Wei et al. [3] conducted an acute oral toxicity test on SFP-grade mice using Methyltin Mercaptide ide according to

the national standard. They obtained the result that Methyltin Mercaptide is of intermediate toxicity. Meanwhile, TMT (trimethyl tin chloride), a highly toxic impurity, is easily generated in the production control of TMT. According to the case analysis of Zhu Haibing et al. [4], it can be known that TMT causes moderate or severe poisoning in human beings, which leads to dizziness, mental and behavioral abnormality, and memory loss in patients. However, China's national standard for organotin stabilizers, GB/T26026-2010, "Methyltin Mercaptide," does not contain a limit for TMT and lacks a standard for the industry, posing a certain hygiene risk for producers and users. Metal soap heat stabilizers are the main components of composite heat stabilizers, mostly fatty acids (lauric acid, stearic acid, etc.) of metal (barium, cadmium, zinc, calcium, etc.) salts, this type of heat stabilizers in addition to the role of HCl, but also can be replaced with a lively allyl chloride atom.

3.1.3 Rubber materials

It is generally accepted in the industry that the oxidation susceptibility of syringes may originate from the manufacturing process, formulation, and sterilization [5] and that the main factor influencing their test results is the quality of the piston. However, these fail to explain "why the level of oxidation susceptibility of small-volume syringes is higher than that of large-volume syringes, even if they are from the same manufacturer." Zhao et al. examined the structure and material properties of syringes. They determined that the main influence on the oxidizability of syringes is the rubber material of the piston and that the better the quality of the rubber material, the more chemically stable the material is, and the less oxidizable (reducing substances) are dissolved, and that for syringes made of the same rubber material, the smaller the nominal volume, the larger the relative surface area of the piston in contact with the liquid, and the more oxidizable substances are dissolved [6]. The smaller the nominal volume of the syringe made of the same rubber material, the larger the relative surface area of the piston in contact with the solution, the more oxidizable substances are dissolved, and the higher the difference in the consumption of potassium permanganate solution. From this, it is inferred that in the process of syringe production, especially for syringes with specifications of 1 ml or even smaller volume, even if the rubber material fully meets the standard requirements of YY/T 0243, taking into account the joint influence of plastic components, lubricants, and other factors, the product will still have the risk of failing to meet the standard, which will result in unnecessary losses.

3.2. Clinical Use Risks

3.2.1 Structural integrity

Adverse events of structural incompleteness in clinical use include compression, cracking, or rupture of the pressure cannula, rupture of the syringe cartridge adapter, or separation of paired components leading to internal exposure of the electronics. Obvious impurities and foreign objects, product breakage, non-sterility due to package seal failure, and clogged and broken filters.

3.2.2 Specification selection

Different specifications for patients can vary significantly or even lead to serious consequences. Lee MD et al. focus on severe vision loss after intracorneal injections of silicone crystalline suspension using prefilled syringes (PFS), a study conducted by researchers from the Casey Eye Research Institute, the Department of Physics at the Oregon Health and Science University, and the Veteran's Affairs Portland Health Care System Division of Ophthalmology, conducted by researchers in a retrospective case series and experimental study. The researchers queried retina specialists and reviewed the charts of 12 patients who developed vision loss after receiving intracorneal injections of silicon crystal suspension. They found that retina specialists noted increased vision loss with silicone crystal-suspended intracorneal injections. Laboratory experiments demonstrated that injection force was also greater at higher injection speeds for all syringe types. Silicon crystal suspensions consistently had greater injection force than pre-filled syringes [7].

3.2.3 Operational risk

Improper handling by personnel is also a risk. When cleaning the barrel adapter and the inside of the pressure sleeve, the water should not contain esters, ethers, chlorides, N-alkyls, ethanol, detergents and sanitizers, and any substances containing dimethyl benzyl, ammonium chloride, and dimethyl ethyl benzyl [8].

Care must be taken during high-pressure syringes to ensure a tight connection between the filling tube and the injection barrel and that no air is drawn into the barrel. If the injected air is not properly removed before transferring the injection, it will cause injury or even death to the patient [9].

Needle stick injuries are one of the most common occupational risks for staff. Clinical nursing staff are busy at work and often use syringe needles and various sharp instruments, in addition to being in a state of chronic tension and high pressure, so it is very easy to lead to syphilis, hepatitis B virus, HIV, and other blood-borne infectious diseases brought about by needlestick injuries [10].

4. Risk Response Recommendations

4.1. Product Technology Upgrade

The unavoidable use of plasticizers in the production of medical devices makes PVC medical devices subject to strict regulation by national government agencies. The use of PVC material for infusion packages in the medical device industry not only has adsorption losses of certain drugs but also the leaching of chemicals such as plasticizers added to it can affect the safety of a medication. Polypropylene is a non-PVC packaging material with less adsorption of drugs and is more environmentally friendly, safer, and more promising in terms of medical device adsorption of drugs.

In recent years, common metal soap heat stabilizers are compound calcium-zinc heat stabilizers, which are environmentally friendly. Cheng et al., through rheological experiments and large-scale production of the application of calcium and zinc heat stabilizers of PVC material examination, found that environmentally friendly calcium and zinc heat stabilizers can replace the toxic lead salts heat stabilizers [11].

TOPAS® COC resin - a new prefilled syringe material with excellent properties. A large European region is switching to plastics for prefilled syringes instead of glass. Prefilled syringes are an excellent alternative to glass because of their improved breakage rate during manufacturing, reduced quality, lack of metal leachate, optimal water vapor permeability, long-term shelf life, and transparency that is as good as glass. Polyplastics' COC resin TOPAS® is considered the optimal plastic material for this application because it meets the above characteristics, has high mold transcription properties due to its high fluidity, and has a good cost/performance ratio.

4.2. Reinforcement of Standardized Training

Since injection products are mainly used in medical institutions, it is recommended to Strengthen the standardized training in the use of the link, continuously improve the level of understanding of the user of syringe products and related adverse events, raise the awareness of the risk of product use, and reduce the risk of use due to errors and mistakes.

The service life of pressure cannulae varies depending on the pressure occurring during injection, the frequency of use, and the cleaning and sterilization techniques used. Generally, the expected service life is at least 30 days and may exceed 2 years if used properly. Wipe the inside of the pressure sleeve and the inside of the syringe cartridge adapter with a lint-free towel moistened with water. Alternatively, place or soak the entire base and pressure cannula in a solution of mild soap and warm water to remove any hardened contrast material. A lint-free cloth can remove dust from the console and powerhead. When cleaning the touchscreen, clean the surface regularly with a non-abrasive cloth and any ammonia-free window cleaner available on the market [12].

4.3. Regulatory Efforts

It is recommended that manufacturers collect post-market surveillance information (including alerts and recalls) on syringe products promptly, update the alerts in the product insert labeling information, and update the warning information in the product specification labels promptly. Information further improves and clarifies the product's contraindications and suspected adverse events. The labeling of product instructions should be updated promptly, and the contraindications and suspected adverse events should be further improved and clarified so that users can be advised to avoid the risks of use effectively.

5. Conclusion

In recent years, due to the prevailing international demand for mass vaccination and the revision of the corresponding technical requirements of international standards, as well as the continuous development of the domestic syringe industry and technology, the positive role of syringe-based products in treating patients requires that lessons be learned from adverse medical events and the prevention of medical errors. This is not a task for one party but requires multi-party cooperation. Manufacturers need to control the quality control of syringes strictly, timely collect post-marketing surveillance information, instructions, and labeling content to give warning information; government departments to be able to real-time supervision, do regular risk and benefit assessments, reduce inherent risk, be able to develop safer syringe products; healthcare workers to carry out effective training to enhance safety awareness, the correct use of syringe products. This is responsible for both them and their patients. It is hoped that there will be cheaper products with the same or even better results, reducing external risks. In the future, research on syringes will focus on the invention and development of micro-syringe technology to reduce the pain caused by injections and to continuously improve the therapeutic effects of medications to treat patients better.

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