Institute for Hygiene and Environmental Medicine
of the Medical University of Lübeck

Lowering the Contamination Risk of Multi-dose Containers

Results from Practical and Experimental Testing of *Minispike Plus* Extraction Cannulas

H. Ohgke and R. Krauß

Contents

Introduction and Aim of Study

1. Clinical Trial

1.1 Method
1.2 Results

2. Experimental Long Term Trial

2.1 Aim of Study
2.2. Method
2.3 Results
2.3.1 Protection from Contact Contamination
2.3.2 Sterility

3. Evaluation of results

3.1 Contamination Risk
3.2 Constructive Technical Measures
3.2.1 Particle Filter
3.2.2 Protection from Contact Contamination
3.2.3 Protection Aim: Sterility
3.3 Aspects of Handling

4. Summary

5. Literature

Introduction

Due to easy usage, decrease in disposable material and high hygienic safety (if used properly), filter cannulas for extracting medication from multi-dose containers and dissolving medicine in powder form have become a standard tool in hospitals. On closer examination however, the correct usage and application is the weak point of these products. Mere technical safety is not sufficient when using filter cannulas. When inspecting hospital wards it is observed that the tops of the filter cannulas are often left open, and the attachment cones are inevitably touched frequently during extraction of medication. Therefore the firm B. Braun Melsungen decided to develop an improved cannula known as the **“Minispike”** to guarantee simpler and hygienically safe extraction.

In addition to the particle retention filter (5µm) the new **Minispike Plus** has two filters (0.2 µm and 0.45 µm) that can retain aerosols. Therefore, as personal safety is guaranteed, this cannula can also be used to extract cytostatic medicine. A contact protection device was constructed to surround the attachment cone thereby preventing any direct contact with the substance or fingers during extraction. The screw top has been replaced by an articulated top; by gently pressing on it, it will automatically clamp onto the opening.

Aim of study

The aim of the study was to determine whether this new development led to a lower contamination frequency than conventional extraction techniques (for example steel cannulas). It was to be tested under clinical conditions (on the ward) and in a laboratory simulating clinical conditions. In both cases the frequency of bacterial contamination on the inside of the contact protection, or on the attachment cone, served as a test parameter. Under laboratory conditions the sterility of the contents of the mulit-dose containers could be checked in graded extraction frequencies.

1. Clinical Trial

In the first week of the study, the **Minispike Plus** was tested on an intensive ward, whereby the testing time for each cannula and substance was limited to 8-10 hours. The time limit and test substance could be checked by a specially developed transport medium that could be sterilised and was changed each day.
In the second week another intensive ward was added to the study and the testing time was extended to 12 hours. In the third and final week, this was extended to 24 hours for both wards. The transport medium was divided into three categories for different extraction substances. The first category encompassed diluted solutions such as Ringer's solution, isotonic NaCl solution, 5% glucose solution. Filter cannulas attached to concentrated heparin solutions were collected separately on the transport medium in the second category. A third category encompassed other substances or those that had to be dissolved - in this case Brevimytal, Nocuron, Dobutrex and Deko. The filter cannulas of these substances were also examined, but not included in the evaluation as they were only used once within the set testing period.

1.1 Method

In the laboratory the **Minispike Plus** cannulas used on the wards were categorised and numbered according to the substance, testing time and testing location. The inside of the contact protection and the surface of the attachment cone were swabbed using a sterile swab. An additional inhibiting agent test was carried out on cannulas used for the heparin solution and for the dissolved substances. A smear was done of the swab on a blood agar dish and incubated at 37 degrees Celsius for 48 hours. A semi-quantative evaluation was performed if growth appeared on the dish after the incubation period. The reason for choosing a semi-quantitive evaluation is that the method used does not enable an absolute bacterial count. The type of microorganinsm was then determined by Gram staining. In a non-systematic form, the staff was asked to evaluate the manageability of the new extraction cannulas.

1.2 Results

The presentation of results does not list specific types of micro-organisms, because the Gram staining showed growth only of micrococci and spore forming bacteria (no pathogenic or facultatively pathogenic germs were detected). The extent of contamination was divided into growth above and below 5 cfu (colony forming units) per agar dish and also into “non-countable” (more than 1000 cfus per agar dish, whereby individual cfus could no longer be distinguished). The extraction frequency was 12 - 18 times per filter cannula in 24 hours. Theoretically it would be possible for liquid to collect within the contact protection - this however was not found in any of the examined **Minispike Plus** cannulas.

The semi-quantitive presentation of the contamination of the cannulas (Table 1) shows very low germ counts.

There is a tendency of increased germ growth in the cannulas the longer the clinical trial ran (Illustration 1). The new cannulas were recieved positively by the entire staff. On daily visits to the wards, one could observe that the tops were on when the cannulas were not being used.

2 Experimental Long Term Trial

2.1 Aim of Study

On intensive wards multi-extraction systems are rarely used for longer than 24 hours. On general wards however, the substances are used less but stand around longer. This means that long term use (> 24 hours) of filter cannulas on general wards is an important practical aspect of everyday clinical life. Therefore a long term trial simulating clinical extraction conditions was carried out in the laboratory to register the change in the frequency and extent of germ contamination and in substance contamination over a 96 hour period.

2.2 Method

Sixty-four sterile infusion bottles were each filled with 100 ml casein-peptone-soya nutrient stock. Sixty bottles were numbered and stored on a laboratory shelf out of direct light. Four bottles were used as controls (one bottle per day).

To disinfect the rubber stoppers on the bottles, they were wiped with a 70% alcohol solution which was allowed to soak in for 60 seconds. Then, after hand disinfection, the sterile tip of the filter cannula was inserted through the rubber stopper into the bottle.

The extraction frequency found in the clinical trials (12 per 24 hours) was used as a base for the experiments. The long term trial ran for 96 hours. The extraction was performed with 1800 2ml+5ml syringes by different people with varying degrees of knowledge and routine in filling syringes. Laboratory staff, secretaries, medical students, nurses, and trainees took part in the experiment - all of whom were acquainted with the concepts “sterile”, “disinfected” and “contaminated”.
Each person’s normal activities were interrupted and they were then requested to perform the extraction task. Hand disinfection was not explicitely required, but left to what the person deemed correct, thereby closely simulating the clinical situation.

For each extraction a sterile syringe was removed from the packaging and the filter cannula was opened. Then the syringe was filled with a maximum of 1 ml of the nutrient solution and the filter cannula top was closed again. The syringe and contents were then discarded.
The extractions were carried out half-hourly, the first 8 from 10.00 to 13.30, and the remaining 4 until 09.30 the following day; each was signed.

After the first day 15 bottles were taken out and, analogous to the clinical trials, swabbed, a smear was done on blood agar and incubated for 18 hours at 37°C. The 15 bottles were then kept in a dustfree cupboard at room temperature for 5 days and then incubated for 24 h at 37°C. During this period the filter cannula remained in the bottle. Extractions continued to be performed on the other 45 bottles, whereby 15 bottles were removed every 24 hours and treated as described above.

If the bottles of nutrient solution showed signs of clouding after the incubation period,the contents were cultured aerobically and anaerobically up to seven days.

2.3. Results

2.3.1 Contact Protection

After completing the four day experiment 45 of 60 cannulas showed no germ growth (75%). The remaining ones displayed growth rates under 5 cfus (semi-quantiative method). None of the germs found were of medical relavance. Compared to the clinical trial there was no tendency of increased germ growth with longer usage.

2.3.2 Sterility

Three of the 60 bottles that were used as multi-dose containers were no longer sterile; two after the first day, and one after the fourth day. In all three cases there was no contamination of the cannulas.

3. Evaluation of Results

3.1 Contamination Risk in Multi-Dose Containers

Using multi-dose containers for sterile medication makes economic and ecological sense. However, sterility of the contents has to be guaranteed for the entire period the container is used. Former investigations show that (depending on the extraction technique) the contamination risk for the sterile contents of the multi-dose containers increases with the number of extractions.

The main sources for this kind of contamination are:

- Microbially contaminated hands and working surfaces. During extraction germs are rubbed off the skin or swirled up from the working surface, thereby contaminating the cone of the extraction cannula or syringe and possibly carrying germs into the container. The majority of the germs are attached to dirt particles or small skin scales or as a conglomerate of different germs. These kind of particles are relatively large with a median diameter of 13 µm (3).
- Direct contact of the cannula cone with hands or objects transfers germs in the same manner as air transfer.
- Extracting the medication with a contaminated syringe poses a major threat to the sterility of the container contents. This error can occur if Hughes phenomenon is not observed (2).

3.2. Constructive Technical Measures to avoid Contamination Risk

Increased knowledge of contamination sources and pathways led to development of extraction cannulas that lowered the risk of contamination. Extraction with a two-way cannula (which filters the air entering the container during pressure balance) showed much better results in contamination experiments than other techniques (1,2,4). Nevertheless the authors unanimously agreed that further improvement was necessary.

The development of the new "**Minispike Plus**" cannula satisfies a number of these requirements.

3.2.1 Particle Filter with 5 µm Pores

In addition to the ventilation filter, the new particle filter also protects the patient from dust and rubber particles or not fully dissolved medication. It is located between the cone and the tip of the needle. It also presents a barrier to germ laden

particles from the surroundings, as these are generally larger than the size of the pores. A remaining risk would be if the liquid medication were to dissolve germ aggregates, thereby enabling individual germs (0.5-2.0 µm) to pass through the filter.

A more likely risk would occur if the rubber stopper were not thoroughly disinfected, so that germs would be carried into the container by the point of the cannula.

3.2.2 Protecting the Cone from Contact Contamination

To decrease the risk of germ infiltration from a contaminated cone, the **Minispike Plus** was developed with a special contact protection shield to surround the cone. The top of this shield can be closed when the container is not being used. It is an articulated top that clamps down on the opening by gentle pressure, so that contamination is largely avoided. In the clinical trial 23% of 210 cannulas revealed germ growth.

From the point of view of hygiene the surrounding conditions were by no means aseptic, but corresponded to the normal conditions on a ward. However, the amount of germs detected was extremely low and did not rise with increased usage. The tendency for germ growth to increase with increased extraction frequency could not be replicated in the laboratory experiments. Kunz and colleagues (2) detected germ contamination in 20% of the experimental cases if a contaminated syringe was used. It cannot be excluded that our results are also affected by this type of inaccessible technical error.

3.2.3. Protection Aim: Sterility

Although one of the research endeavours is to reduce cone contamination to an absolute minimum, the main aim is to maintain the sterility of the medication. In this respect the simulation experiment - up to 48 extractions within 4 days - showed very good results.

As contamination frequency was low and the rate and length of usage did not correspond to the lack of sterility in the container, we would like to draw the following conclusions:

Multi-dose containers with **Minispike Plus** cannulas do not have to be used up within 4 days. This finding is of great practical importance, e.g. on wards that use diluted heparin solutions for a large number of patients (intensive wards, dialysis units). If medication is used over this length of time then other factors affecting it, (such as light, temperature, disintegration in aqueous solutions etc.) should be taken into consideration.

Only 3 (5%) of the 60 multi-dose containers were not sterile after the experiment (2 after 1 day and 1 after 4 days). Interestingly enough no bacteria was detected on the cone or the inside of the contact protection of these 3 containers.

In earlier experiments the ventilated two-way-cannulas (Minispike) displayed contamination rates as high as 15% (2), 14% (4) and 28% (1). Therefore a rate of only 5% can be viewed as a great improvement. To date this has only been achieved under ‘locally aseptic’ extraction conditions (i.e. disinfected hands and surroundings (1)). Such conditions were not adhered to in our experiments.

3.3. Aspects of Handling

- The ventilation valve facilitates handling procedures, as it creates a pressure balance whenever excess pressure occurs, thereby preventing medication from escaping.

- The staff is also protected from dermatotoxic and allergizing substances due to the following mechanism:
  the inner stopper of the top seals off the cone, so that leakage cannot occur if the bottle is shaken or knocked over.

- To maintain the function of the ventilation filter, a re-injecting of larger amounts of liquid should be avoided with bottles held in an inverse position, as otherwise the filters may be blocked due to the moisture.

4. Summary

The newly developed '**Minispike Plus**' extraction cannula was tested in a clinical trial and under simulated conditions to evaluate hygienic safety. Compared to the conventional two-way-cannulas the new cannulas contain an additional particle filter and contact protection device with a top for the extraction cone that is easily closed. The investigations showed that the sterility of the multi-dose containers was maintained to a much larger degree than has been possible up to now.

From the point of view of hygienic standards it is quite safe to use the multi-dose containers with '**Minispike Plus**' cannulas for a duration of up to 4 days.

5. Literature

1. Alles,G. und F. Selenka: Die mikrobielle Kontamination von durchstichampullen bei mehrfacher Entnahme.
Hygiene und Medizin 14 (1989) 355-358

2. Kunz, B., W. Gräf und M. Günther: Refluxbedingte mikrobielle Kontaminations-risiken bei Durchstechampullen
Hygiene und Medizin 17 (1992) 17-22

3. Noble, W.C.: Microbiology of the Human Skin. Lloyd-Luke Ltd., London 1981

4. Ohgke, H., F.Muhr und J. Beckert: Mikrobielle Kontamination von Großampullen bei Mehrfachgebrauch.
Hygiene und Medizin 9 (1984) 476 - 478