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INTEGRATIVE REVIEW ARTICLE

DISINFECTION OF AMPULES FOR INTRAVENOUS ADMINISTRATION: AN INTEGRATIVE REVIEW

DESINFECÇÃO DE AMPOLAS PARA ADMINISTRAÇÃO DE INJETÁVEIS: UMA REVISÃO INTEGRATIVA

DESINFECCIÓN DE AMPOLLAS PARA ADMINISTRACIÓN DE CONTENIDOS INYECTABLES: LA REVISIÓN

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ABSTRACT

Objective: to describe research studies on the efficacy of disinfection of ampules for intravenous administration in terms of microbial contamination. **Method:** integrative review with the guiding question << *What is the scientific literature production regarding the disinfection of ampules, for intravenous administration, in terms of microbiological contamination?* >>. For the selection of articles, we used the PubMed, CINAHL, LILACS and BEDEnf databases in the period from January to March 2013. **Results:** the sample consisted of four articles with quasi-experimental design, with moderate level of evidence; alcohol swab was used to prove the effectiveness of disinfection of ampules after their opening. The results were controversial, since part of the non-disinfected ampules showed no contamination of the contents. **Conclusions:** research studies with better methodological rigor are needed to recommend or abolish the disinfection of glass ampules using alcohol. **Keywords:** Drug Contamination; Disinfection; 2-Propanol; Injections.

RESUMO

Objetivo: descrever as pesquisas sobre a eficácia da desinfecção de ampolas para administração de injetáveis do ponto de vista da contaminação microbiana. **Método:** revisão integrativa com a pergunta norteadora << *Qual é a produção científica acerca da desinfecção de ampolas, para administração de injetáveis, do ponto de vista da contaminação microbiana?* >>. Para a seleção dos artigos, utilizaram-se as bases de dados PubMed, CINAHL, LILACS e BEDEnf no período de janeiro a março de 2013. **Resultados:** a amostra constituiu-se de quatro artigos com delineamento quase-experimental, com nível de evidência moderada; o álcool em forma de swab foi utilizado para comprovar a eficácia da desinfecção das ampolas após sua abertura. Os resultados foram controversos, uma vez que, parte das ampolas não desinfetadas não demonstrou contaminação do conteúdo. **Conclusões:** há necessidade de pesquisas com melhor rigor metodológico para recomendar ou abolir a desinfecção de ampolas de vidro utilizando álcool. **Descritores:** Contaminação de Medicamentos; Desinfecção; 2-Propanol; Injeções.

RESUMEN

Objetivo: buscar y describir los estudios sobre la eficacia de la desinfección de ampollas para administración de contenidos inyectables, considerando la seguridad microbiológica. **Método:** revisión integradora de la literatura con la cuestión orientadora << *¿Cuál es la producción científica relativa a la desinfección de ampollas, para la administración de productos inyectables, del punto de vista de la contaminación microbiana?* >>. Para la selección de los artículos, se utilizaron las bases de datos PubMed, CINAHL, LILACS y BEDEnf, entre enero y marzo de 2012, con descriptores de asunto y sin límite de tiempo. **Resultados:** la muestra consistió de 04 artículos con diseño cuasi-experimental, por lo tanto, con nivel moderado de evidencia. El hisopo en alcohol fue utilizado para probar la eficacia de la desinfección de las ampollas después de la apertura. Los resultados fueron controvertidos, ya que parte de las ampollas no desinfetadas no mostró contaminación del contenido. **Conclusiones:** dadas las limitaciones de los estudios, son necesarias investigaciones con mayor rigor metodológico para recomendar o abolir la desinfección de ampollas de vidrio con alcohol. **Descritores:** Contaminación de Medicamentos; Desinfección; 2-Propanol; Inyecciones.

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INTRODUCTION

Glass ampules have been widely used for storing drugs. Anesthesiologists, along with nursing technicians, are a significant part of the group of professionals who handle these materials routinely.¹

Ampules of drugs that are not stored in sterile packaging require a careful aspiration technique to ensure the maintenance of the aseptic chain.² There is a potential risk in contaminating the needle when performing the aspiration of the contents of ampules through the contact with its non-sterile neck. Furthermore, shards of glass, which theoretically could carry bacteria, may fall inside the ampule when it is open and, therefore, the anesthesiologist may administer these particles both intravascular and through the epidural and subarachnoid spaces.^{1,3-6} The possibility of bacterial contamination of the ampule contents while opening them has led to recommendations as to the disinfection of the neck of the ampule with alcohol^{7,8} and the use of antimicrobial filter needles in the process of aspiration.^{3-4,7,9} However, the efficacy and safety of these techniques are largely unknown and divergent.

The extent of the colonization of the exterior of the ampules depends on the variation of the conditions of manufacture and storage. A single study² on the bacterial colonization of the exterior of the ampules, fentanyl anesthetic in this case, found six positive cultures of body and label of 15 ampules (*Bacillus pycoides*, micrococci and coagulase-negative staphylococcus), although there was no positive cultures of the head or necks of ampules. By contrast, another research⁹ did not assess the initial colonization of bacteria on the outside of the ampules of fentanyl. Possibly, if the batch of ampules did not have bacterial contamination, or if it was minimal, this could explain the negative results of contamination of fentanyl assessed by the authors.

The ampules are repeatedly handled, stored in common areas and generally are not disinfected prior to their opening. Therefore, any contamination of the drug with glass particles, originating from the surface of the ampule, may be associated with microbial contamination.¹⁰ The effect of storage conditions showed to dramatically affect the extent of contamination of surfaces in ampules. A study compared the bacterial count of the surface of ampules of distilled water taken directly from their original packaging versus those stored for two days in

a hallway with wide circulation of people. There was an increased bacterial contamination from 3.2 to 169 colony-forming units per ampule.¹¹

We have to consider that there is in the market devices that are attached to the neck of the ampule in order to avoid injury in the hands of professionals.¹ In this case, their disinfection is unlikely when using this artifact, as they may be of individual use for each professional or of collective use. Yet, a study¹² showed that there was no significant difference in the number and size of the glass particles aspirated when comparing two methods of opening ampules, that is, manually or with the aid of an opener.

This study aims to describe research studies on the efficacy of disinfection of ampules for intravenous administration in terms of microbial contamination.

METHOD

The integrative literature review adopted was the research method, which includes the analysis and synthesis of research studies in a systematic way, contributes to the further development of the subject investigated, assists in decision-making and, therefore, in the improvement of clinical practice, and it is based on pre-existing research results, which has, as one of its main advantages, the ability to combine data from different research designs.¹³

The research question was << *What is the scientific literature production regarding the disinfection of ampules, for intravenous administration, in terms of microbiological contamination?* >> The literature review was conducted from January to March 2013, by electronic research using the databases: PubMed (biomedical and health sciences digital archives from the "US National Institutes of Health"), CINAHL (Cumulative Index to Nursing and Allied Health Literature) and LILACS (Latin American and Caribbean Center on Health Sciences Information) and BEDENF (Database of Nursing). The controlled keywords used in the PubMed database were: drug contamination and glass; drug contamination and glass and fentanyl; drug contamination and glass and fentanyl; glass and injections; drug contamination and drug packaging and equipment contamination; glass and 2-propanol; disinfection and glass and anesthetics. The uncontrolled keywords were: ampoule and drug aspiration. The same controlled and uncontrolled keywords were used for the CINAHL database. For the LILACS and BEDENF database, we used the same controlled keywords used for the PubMed

database, albeit in Portuguese, and the uncontrolled keywords used were: ampule, contamination and medication, also in Portuguese. To promote a wide search of articles, we used different crossings of controlled and uncontrolled keywords in each database. The search period of these databases was not delineated. We highlight that we also searched the references of selected articles where appropriate.

It is relevant to note that, in a first search with the keywords drug contamination and glass, we found an article that referred to the contamination of two anesthetics and related the event to the disinfection of ampules. Given this result, we found relevant to add keywords associated with anesthesia and anesthesiology.

Articles were selected by title and abstract according to the purpose of the study following the criteria of inclusion and exclusion. In the PubMed database, we pre-selected 142 references of articles; in CINAHL, 141 articles were identified; in LILACS, 78 articles; and in BEDENF, 21 articles, which amount to 382 articles and which resulted in a sample of 4 articles exclusive from the PubMed database, which were fully analyzed. It is interesting to note that the exclusion of the majority of articles was due to the repetition in the CINAHL database, mostly because they did not fulfill the purpose of the research, and, many of them, addressed the contamination of the contents of the ampules by fragments of glass, but without searching the contamination of the contents from the microbiological point of view. Moreover, after applying the exclusion criteria, the studies, almost entirely, addressed specific issues of medications without correlation with disinfection. For the extraction of the data, we used a data collection tool that has been validated and published.¹⁴ All studies obtained were evaluated by two researchers and, where there was disagreement, a third researcher performed the reading and confronted with the previous ones. For the analysis of the level of evidence and the research design of the studies included in the review, we used the concepts proposed by researchers in the field of nursing.¹⁵

For inclusion and analysis of the articles, we established the following inclusion criteria: articles that addressed the effectiveness of the disinfection of ampules in preventing contamination of their contents;

published in Portuguese, Spanish and English; and articles regardless of the research design employed. We excluded from this study the review articles of narrative literature, editorials, response letter and articles that addressed the contamination of drugs coming from their manufacture and physical contamination by shards of glass.

A summary of the data extracted from the articles included in the review was conducted in a descriptive manner enabling the reader to assess the quality of evidence (level of evidence) available in the literature on the subject researched and to identify knowledge gaps for the development of future research studies.

RESULTS

The four articles selected were published in the period 1991-2011, with most publications being from the 2000s. We found that all articles were published in English; of the countries of origin of publications, one was published in the America (California), one in Europe (Britain/Ireland), one was developed in Oceania (Australia) and one in Asia (Malaysia). In relation to the journals, there was some diversity, being them published in *Anesthesiology*, *Anaesthesia*, *Anaesthesia and Intensive Care*, and *Medical Journal of Malaysia*, respectively, all from the area of medicine. Regarding the type of study, the four (100%) articles had a quasi-experimental design, of the evaluation type (process analysis), therefore with moderate level of evidence (level III).¹⁵

In relation to the presentation of the results of the four scientific articles selected for this integrative review, there were 14 authors in total, with an average of 3.5 authors per article, all doctors, except for an article that involved a microbiologist.

Of the papers presented, two were jointly developed in hospitals and laboratories, one was exclusively developed in laboratory and another in a hospital institution.

Then, for the analysis of the studies, we proceeded to their description by considering: study, level of evidence, results and conclusions, which are presented in Figure 1.

Study/Level of Evidence	Objective	Results	Conclusions
Zacher, Zornow, Evans ⁵ Level III	To determine if the disinfection with alcohol of the neck of glass ampules intentionally contaminated with <i>Staphylococcus epidermidis</i> decreased the contamination of the contents of the ampules.	Three of the eight ampules of lidocaine and six of the eight ampules of propofol that were not disinfected with alcohol showed signs of bacterial contamination. The contents of all disinfected ampules remained sterile (p<0.001 vs. ampules of propofol without disinfection and p=0.20 vs. ampules of lidocaine without disinfection).	The data suggest that bacterial contamination of propofol and lidocaine may occur as a result of the opening of glass ampules. The disinfection of the outside of the ampule with alcohol immediately before the opening may decrease this risk.
Hemingway, Malhotra, Almeida, Azadian, Yentis ⁸ Level III	To investigate the incidence of contamination when glass ampules of opioids are opened, with or without disinfection with alcohol, for neuraxial anesthesia, and the effect of disinfection/non-disinfection with alcohol of ampules of distilled water, intentionally contaminated with coagulase-negative <i>Staphylococcus</i> , before their opening, with and without the use of 5µm filter needles for aspiration.	Of the 100 ampules analyzed, nine from the fifty (18%, 95% CI: 10-31%) without disinfection showed microbial growth compared with none of the fifty ampules (95% CI: 0-9%) disinfected (p = 0.04). In the second part of the study, most of the contamination occurred in ampules without disinfection, and this appeared to be reduced by the use of the filter, although the numbers were small. There was no significant microbial growth (<5 colonies) only for samples disinfected and aspirated with filter.	The authors suggest the disinfection of ampules with isopropyl alcohol and the use of filter needle when performing regional anesthesia. Although the effectiveness of the latter in preventing bacterial contamination is less certain.
Merriman; Paech; Keil ⁹ Level III	To determine, through a laboratory study, the extent of bacterial contamination of solutions of fentanyl from glass ampules stored and not sterilized using three different methods of aspiration: aspiration through a 5µm filter needle; aspiration through 5 µm filter needle after rubbing the neck of the ampule with alcohol swab; and, aspiration through a 5 µm filter needle added to an anti-bacterial filter.	There was no growth of bacteria in the samples inoculated directly in either blood agar plates or from the enriched culture broth for all 30 samples of the study.	They advocate the use of the complete aseptic technique and efforts to minimize the environmental contamination of ampules before use, since these are simple measures that can reduce bacterial contamination of the solution aspirated from ampules stored and not sterilized.
Roshaliza; Liu; Joanna ¹⁶ Level III	To determine the extent of the microbial contamination of the solution of fentanyl used for neuraxial injection performing the disinfection or not of the neck of the ampule with 70% isopropyl alcohol swab before opening them and aspiration of the solution of fentanyl using 21G needle or 5µm filter.	None of the samples of ampules disinfected or aspirated with straw filter grew microorganisms. Six percent of the samples of the ampule group that had not been disinfected had microorganisms when the fentanyl was aspirated using a needle, and the contamination increased to 16% when the aspiration was repeated two hours after exposure of ampules.	The disinfection of the outside of the ampules of fentanyl before their opening with 70% isopropyl alcohol swab or the aspiration of the contents using a 5µm filter proved to be equally effective to prevent bacterial contamination and should be practiced routinely when performing regional anesthesia, using the solution immediately without reuse.

Figure 1. Summary of studies included in the integrative review.

We described in details the studies analyzed in this integrative review, given that this form was considered the most appropriate for the reader's understanding and due to the scarcity of the sample allowing this kind of presentation of this review.

The first study⁵ sought to determine if disinfection of the neck of ampules with alcohol before opening them could influence contamination by bacteria of the content of the ampules. Glass ampules of propofol 1% (n=16) and lidocaine 1% (n=16) were intentionally contaminated with *Staphylococcus epidermidis* (approximately 10⁶ microorganisms in each ampule). Half of the ampules of each anesthetic were disinfected with alcohol swab before being

opened. All ampules were opened by one person who was unaware whether or not the ampules had received disinfection. The opening was performed with sterile gauze attached to the neck of the ampule. An aliquot of each ampule was pipetted in nutrient broth and incubated overnight at 37°C. These solutions were seeded in agar, incubated for 24h and then they were examined for bacterial growth. Three of the eight ampules of lidocaine and six of the eight ampules of propofol that were not disinfected showed contamination. The contents of all ampules that received disinfection before being open remained sterile (P<0.001). Seven (43.7%) of the non-disinfected ampules showed no contamination, and the

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disinfection of the ampules of lidocaine did not significantly reduce ($P=0.20$) the risk of such contamination. The data suggest that bacterial contamination of propofol and lidocaine may occur as a result of the opening of glass ampules without disinfection. They conclude that the disinfection of the outside of the ampule with alcohol immediately before their opening may decrease this risk

The incidence of contamination in the glass ampules used for neuraxial injections was investigated in another study⁸, and, it was also investigated if it was reduced by doing the disinfection of the neck of the ampules with isopropyl alcohol swab or using a needle filter. In the first part of the study, hundred ampules (7 of fentanyl and 93 of diacetylmorphine) were divided into two equal groups where half were disinfected with alcohol before having their contents aspirated. Swabs were collected from the residual contents inside the ampules, avoiding touching their neck, and then seeded and incubated. None (0/50) of the swab samples collected from the ampules that received disinfection showed microbial growth compared to eighteen percent (9/50) of those which were not disinfected ($p=0.004$). In the second part of the study, carried out in laboratory, hundred ampules of sodium chloride were contaminated with coagulase-negative *Staphylococcus* and divided into four groups: disinfected/not disinfected with alcohol and with/without the 5µm needle filter. The contents of the ampules were aspirated and the remaining aspirates were seeded and incubated as described above. The majority of the contamination occurred in the groups that received no disinfection, although the numbers were small; the use of filter needle seemed to reduce contamination, even though the results were not subjected to statistical analysis. Considering that the filter needle also reduces the risk of injecting glass particles (even if not contaminated), the authors suggest that the disinfection of glass ampules with isopropyl alcohol and the use of filter needle should be part of the routine of regional anesthesia.

The third study⁹ of this review, characterized as a laboratory pilot prepared to determine the extent of bacterial contamination of solutions of fentanyl from glass ampules stored and not sterilized, used three different methods of aspiration: aspiration through a 5µm filter needle; aspiration through a 5µm filter needle after rubbing the neck of the ampule with isopropyl alcohol; and, aspiration through a 5µm filter needle added to a 0.22 µm anti-bacterial

filter. Ten anesthetists properly dressed and simulating the practice of anesthesia in an operating room used each method once, in random order, to aspirate the solution of three different ampules of fentanyl. The study counted with the aid of assistants who opened the ampules initially using their preferred technique (bare hands or procedure gloves). To avoid potential reduction of skin bacteria by handling alcohol swab, the assistant was instructed to change the alternative technique (bare hands or procedure gloves) after handling a swab. The samples were subjected to bacterial culture on blood agar and enrichment broth for 48 hours, and the microbiologists were blinded to the anesthesiologists and aspiration techniques. There was no growth of bacteria detected in any of the agar plates inoculated directly into blood or from the enriched culture broth for all 30 samples of the study. This pilot study revealed no bacterial contamination of the solution of fentanyl, regardless of which of the three methods was used for aspiration.

Finally, the prospective study¹⁶ aimed to determine the extent of the microbial contamination of the solution of fentanyl used for neuraxial injection performing the disinfection or not of the neck of the ampule with 70% isopropyl alcohol swab before opening them and aspiration of the solution of fentanyl using 21G needle or 5µm filter. In Group A, fifty ampules of fentanyl were rubbed with 70% alcohol before opening and 0.5 ml of the solution was immediately aspirated using a syringe and 21G needle, and then the same content (0.5 ml) was aspirated using 5µm filter, and in this case without the needle. The same steps were repeated, after two hours, in the solutions that remained in the open ampules in the operating environment. In Group B, all the steps above were repeated but without disinfecting the ampules. The aspirated solutions were deposited on blood agar plates and incubated for 48 hours, and the staff of the microbiology laboratory was blinded as to the methods of aspiration. None of the samples collected from the ampules of Group A, disinfected and aspirated with 5µm filter or needle, had microorganisms. In Group B, the samples that were aspirated immediately and two hours after opening the ampules using 5µm filter did not recover any microorganism. However, in the same group, in 3 (6%) samples, microorganisms were recovered when fentanyl was aspirated using 21G needle and contamination increased to 8 (16%) when repeated after two hours, thus showing a statistically significant difference between

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the groups when the solution was aspirated with a 21G needle after two hours ($p < 0.001$). They conclude that the disinfection of ampules of fentanyl with 70% isopropyl alcohol swab before opening them and/or aspiration of the contents using a 5µm filter showed to be equally effective to prevent bacterial contamination of the solution of fentanyl and should be routinely performed in regional anesthesia.

DISCUSSION

Given the search for articles in the databases selected, we realized the scarcity of studies published that evaluated the efficacy of disinfection of ampules for administering intravenous injections. International studies that evaluated if the disinfection of ampules influences the contamination of their content are rare, and the national Brazilian ones are non-existent to date, although the national literature described in textbooks of Fundamental Techniques of Nursing and the like strongly recommends this practice, even without justification guided by evidence.

The knowledge and skills needed to prepare medications from ampules are taught early in the nursing curricula. A review of several books of Nursing Fundamentals and Basic Techniques revealed different perspectives on the disinfection of the neck of ampules before the aspiration of their contents.¹⁷⁻¹⁹ The differences identified in these textbooks, regarding this procedure, may not have been clearly researched and disseminated in the practice of nursing staff, which can lead practitioners to adopt different methods for opening ampules.

It is interesting to note that, of the authors of the articles from the sample, none were nurses, a fact that is at least intriguing, because, as previously mentioned, the practice of disinfection of ampules is strongly indicated in the nursing literature.

By contrast, we find that in the medical literature,^{5,8-9} specifically in the field of anesthesiology, the issue is searched from the point of view of both the glass fragments deposited inside the ampule when opening them and the microbial contamination; although, still with an incipient and directed production.

However, when we analyze the scientific literature²⁰⁻²² about the safe practice in the administration of intravenous injections, we realized that there are no specific recommendations of the major agencies as to the need or not to disinfect ampules before their opening. We also noticed that the

indication for disinfection is restricted to vials which have rubber covers that are perforated to aspirate drugs or immunobiologicals within them. In this case, the recommendation is to use 70% isopropyl or ethyl alcohol.

We note in our review that 43.75%, 82%, 100%, 94% and 84% of the ampules which were not disinfected with alcohol showed no contamination of their inside, respectively.^{5,8-9,16} It is worth noting that the rate of 43.75% was due to the intentional contamination of approximately 10^6 *Staphylococcus epidermidis* in the neck of each ampule and the negative rate of 82% was from the anesthetics administered on the spinal or epidural region in a unit of elective cesarean section, that is, simulating the actual practice. And, also, the negative rate of 84% was two hours after the opening of the ampules.¹⁶

Probably, the contamination of the contents of ampules occurs at the time of their opening, and, with it, broken glass possibly with bacteria attached to them fall within the ampule contaminating the solution.²³

The identification of fragments of glass contaminated with bacteria²⁴ led to the recommendation to use filter needles, although it has been known that their use does not totally eliminate the problem. A study⁵ identified that bacterial contamination by the introduction of fragments of glass to the drug solution can be minimized by disinfecting the neck of the ampule with alcohol before opening it. Microbial contamination can also occur when using ampules stored in dusty shelves, manipulated by non-cleaned hands, or handled with non-sterilized gauze, and with needles that come into contact with the outer surface of the ampule during the aspiration of the drug.²⁴ In turn, the rubbing of the neck of ampules before opening them had a negative effect on the prevention of contamination by particles of glass.²⁵

In the studies analyzed, we have observed that all of them used industrialized alcohol swab, usually isopropyl. However, they did not describe how they accomplished this disinfection and how long this procedure lasted.

Moreover, as for the disinfection of items or equipment, whether or not preceded by cleaning with soap and water, 70% w/v alcohol is indicated by means of friction on the surface of the product, leaving it to dry by itself, repeating 3 times the procedure, until completed the action time.²⁶ Henceforth, it seems unlikely that this practice is carried out in the daily opening of ampules for medication

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preparation. Thus, this practice should be investigated in view of the action of the alcohol on the elimination of microorganisms present in ampules and possible disinfection methods.

We highlight that the contents of the ampules may be contaminated with alcohol used to disinfect them, due, in part, to the non-standardization of the volume of alcohol used to humidify the cotton, the pressure used to break the ampule and the drying time after disinfection. Accordingly, there is evidence of contamination of the contents of the ampules with alcohol during their opening, a fact that has been implicated in causing neurological sequelae such as meningitis.²⁷

Sanitizers can become contaminated during inadequate techniques of manufacture or transport (intrinsic contamination) or during handling or use in health-care settings (extrinsic contamination).²⁸

A study²⁹ described a pseudobacteremia by *Bacillus* sp. resulting from contamination of the alcohol swab and used to perform disinfection of blood culture bottles. The authors demonstrated that this organism remained viable for at least 28 days after soaking the cotton in 70% ethyl alcohol. However, they believe that the microorganism originated from the cotton and not from the alcohol, because microbiological tests performed in five packages of cotton, without use from different units in the hospital, recovered the same microorganism from blood cultures.

Another study³⁰ detected by genotyping a pseudoepidemic of *Bacillus cereus* where the source was 70% ethyl alcohol used as an antiseptic in different hospital units. The origin of the contamination was the 95% ethyl alcohol, which was used for the manipulation of the 70% one and which was stored at the plant that supplied the alcohol and at the hospital pharmacy which received it.

In Brazil, it is common practice to use alcohol wipes to perform the disinfection of ampules and serums before opening them, and not industrialized swab, as demonstrated in the studies analyzed. Still, many Brazilian institutions use alcohol stored in plastic oilers, which does not guarantee that the concentration of the alcoholic solution is the same as indicated on its label after several days of use and handling, given its high volatility. However, it is important to note that alcohol, as a disinfectant, is characterized as low-level, i.e., it destroys vegetative bacteria, some fungi and viruses, but not mycobacteria or spores. Its use is for

the disinfection of items such as pressure devices or surfaces such as beds, as long as there is no presence of organic matter.²⁸

Another important point to be noted in the Brazilian reality is the fact that, in order to make savings, the cotton used to perform the disinfection of ampules or injections is handled by nurses with bare hands, or, to facilitate the use, it is not uncommon to see these professionals using spatulas to form balls of cotton, that is, for that end, it is necessary to take a piece of cotton and roll it on a spatula in constant movements of rotation against the bare hand. It is no wonder that this practice, besides being inadequate, can contaminate this cotton with various microorganisms from the hands. To make matters worse, the cotton can be stored in an unsecured way, being exposed to various environmental conditions for several days.

A recent Brazilian study,³¹ in order to investigate the practices of prevention of hospital infection related to anesthesia performed by anesthesiologists, found that only 24 (30%) of them reported performing disinfection of the ampules with alcohol for use in the neuroaxis. On the other hand, they did not describe whether the disinfection was performed using cotton or industrialized swab, or how to perform this procedure.

It is worth pointing out that only one study⁸ used glass ampules containing sodium chloride, which were intentionally contaminated in order to verify the effect of disinfection with alcohol in the contamination of the solution. It is inferred that the anesthetic medications were preferably used for microbiological testing because of their easy contamination during handling⁹ and the consequences, such as infection of the neuroaxis, being easier to correlate with the contamination of the anesthetic used.

It is essential to describe some methodological observations of the studies analyzed. In one study⁵, the sample was too small and not probabilistic; there is no clarity on which was the technique used to open the ampules; they did not describe how the disinfection was performed and how long it lasted; as well as if the opening of the ampules was conducted in a controlled environment using laminar flow hood. A curious fact in this research is that, even though they were not disinfected, almost half of the ampules showed no contamination of their contents.

In another study⁸, the authors did not describe the time to disinfect the ampules and reported that the assistants from the operating room often did not sanitize their

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hands to open them. As for the microbiological analysis, the samples were collected by inserting a swab into the ampule, after aspiration by the anesthetist, which may have caused external contamination. Also, they state that they did not consider the different ways of disinfecting the ampules, the time elapsed to become contaminated again after the disinfection or the time required for drying after disinfection.

In another study analyzed⁹, the authors did not describe the disinfection time and how they performed them, as well as how the ampules were opened. On the other hand, they used measures to ensure optimal detection of bacteria, including the addition of enriched broth and blood agar, and preliminary tests excluded the possibility of an inhibitory effect of the solution of fentanyl on bacterial growth. Finally, they recognize that although the sample was small (n=30) they believe that it was properly designed, allowing the simulation of the clinical practice in the institution, since the inability to recover the bacteria in any of the three groups was minimized.

Finally, some points should be highlighted in the last study¹⁶. The microorganism with higher frequency of isolation was *Staphylococcus sp* (6 samples). The authors do not describe how the disinfection of the ampules was performed, the friction time and how to do it; they report that disinfection was performed and the ampules dried before their opening, however they do not mention this time; they performed the disinfection and after the "drying" of the ampules they opened them with their bare hands, i.e., they did not use the swab to support the breaking the neck, which may suggest that the possible microbial recovery could come from the hands of the assistant who opened the ampules.

Still related to this study, there is evidence that, from the ampules that were not disinfected, 47 (94%) showed no contamination of their contents when aspirated with 21G needle and, after two hours that the ampules remained open, 42 (84%) did not recover microorganisms.

While in one study⁸ it was shown that there was bacterial growth of the aspirated contents of ampules which were not disinfected with alcohol swabs and which used 5 µm filters, in another study a divergent fact occurred using the same methodology and it did not recover any organism¹⁶. We highlight that, theoretically, a 5 micrometer filter is not capable of filtering microorganisms by itself, because the size of bacteria ranges from 0.5 to 1.0 micrometers. The authors of

the last study¹⁶ presuppose that the filter probably withheld microorganisms that were aggregated and also those that were attached to the glass particles. However the authors did not cultivate the glass particles that were filtered to confirm their hypothesis.

It may be preferable to use medications in containers which need not be broken as glass ampules, such as, for example, the packaging of drugs in plastic little bottles; however, this polymer is not inert and may be subject to degradation and oxidation and eventual interaction between parenteral drugs and plastic components, which hinders the widespread use of this material in the manufacture of such containers¹. Multi-dose vials are also part of this strategy for reducing the risks; however, these containers can produce particles of rubber, chemicals, or others, which may be as contaminant as the glass ones. Thus, before recommending the replacement of glass ampules for other types of containers, additional studies need to be performed.⁴

It is important to note that the process of administering medications, briefly, starts at the time of prescription, goes to the pharmacy for separation and distribution and ends with the preparation and administration by nurses, nursing staff or other professional, such as physicians. In this context, the broad overview of the medication system is of fundamental importance to the professionals whose daily life includes dealing actively in one of the stages of preparation and administration of medications and thereby ensure a responsible and safe care to the patient.³¹ Within this aspect, we highlight the microbiological safety at the moment of opening ampules.

CONCLUSION

We can conclude that national studies related to the subject proposed, indexed in the databases searched, are nonexistent, and scarce in the international databases searched.

Regarding the design of study, all had a quasi-experimental design, of the evaluation type (process analysis), therefore with moderate level of evidence (level III).¹⁵

All studies searched used anesthetics, which does not represent the daily practice of the majority of injections stored in ampules. This fact is noteworthy, as most of the injected medications are not anesthetic.

The alcohol used was of the swab type, which does not occur in the Brazilian reality for the opening of ampules. Some of the ampules that were not disinfected showed no

contamination of the contents, a fact at least interesting and subject for research with other drugs or solutions.

In general, the studies are methodologically weak and incomparable due to the methodologies employed and the culture techniques used. Therefore, they are inconclusive to recommend or not the disinfection of glass ampules with alcohol, although, it is a widespread practice and suggested by the authors of the studies analyzed.

It is clear the need for further controlled studies to prove the efficacy of alcohol to disinfect the ampules intended for the application of intravenous injections, as well as the standardization of the material and the method to disinfect and open the ampules.

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