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Efficiency in endotoxin removal by a reprocessing protocol for electrophysiology catheters based on hydrogen peroxide plasma sterilization

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Abstract

Electrophysiology and ablation cardiac catheters, which come in contact with blood during clinical use, are required to be non-pyrogenic (<20 endotoxin units (EU)/device). This study aimed to quantify the residual endotoxin load in reprocessed devices as a mandatory step to guarantee safe reuse. We monitored the pyrogenic status of the device ($n = 61$) in three fundamental steps of the reprocessing protocol: after clinical use, after decontamination-cleaning treatments and after complete reprocessing, including sterilization by hydrogen peroxide gas plasma. Finally, a depyrogenation test was produced for evaluating the depyrogenation efficiency of the sole hydrogen peroxide sterilization treatment.

Results showed that standard clinical use did not represent a source for endotoxin contamination, while the use of tap water and manual cleaning processing could increase the pyrogenic load in a significant way. The introduction of the sterilization by hydrogen peroxide gas plasma resulted in effective reduction of the endotoxin contamination and in safe reprocessing of 15 of 15 clinically used catheters. In addition, tests conducted on in vitro spiked catheters showed that initial pyrogenic loads of 40, 80, 200 EU/device were reduced to less than 11 EU/device. Depyrogenation testing demonstrated efficiency in endotoxin reduction of more than 62 times (1.8 log). These results show the determining role of hydrogen peroxide gas-plasma sterilization in the reduction of pyrogenic load on medical devices. Considering actual hygienic requirements at single-use device reprocessing, hydrogen peroxide gas-plasma sterilization can be considered as an efficient treatment at non-lumen cardiac electrophysiology catheter reprocessing.

Keywords: Endotoxin; Pyrogen; Plasma sterilization; Electrophysiology catheters; Reuse; Reprocessing

Introduction

Reprocessing and reuse of single-use cardiac catheters are widespreading practices throughout the world because of the increasing incidence of cardiac diseases

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requiring catheterisation and high cost of single devices (Blomstrom-Lundqvist, 1998; Conseil d'Evaluation des Technologies du Québec (CETQ), 1994; Mickelsen et al., 2001; Robert Koch Institute recommendations (RKI), 2001).

Reuse of disposable devices, besides concern about functional reliability and physical integrity alterations (Avitall et al., 1993; Bentolila et al., 1990; Lerouge et al., 2000; Tessarolo et al., 2004), includes the risk of infection, toxicity, and pyrogen residues too (Aton et al., 1994; Favero, 2001; Ferrell et al., 1997; Heeg et al., 2001; Jacobson et al., 1983).

Electrophysiology and ablation cardiac catheter come into contact with blood during clinical use and are to be non-pyrogenic. Considering that the reprocessed catheter has to conform with all hygienic requirements like new devices, a validated endotoxin test should be performed to prove non-pirogenicity of reprocessed catheters.

A useful recommendation to minimize endotoxin contamination is to process, package, and promptly sterilize the item to reuse in order to limit the time of bacterial contamination and growth (Kundsin and Walter, 1980). In fact, sterilization is intended to kill bacteria adhered to the device, thus minimizing the risk to infect the host. Sterilization, however, does not necessarily eliminate the killed bacteria and the sterile device may harbour bacterial residuals as the lipopolysaccharide (LPS) complex located on the outer wall of Gram-negative bacteria. This biologic complex may lead to rise fever, changes in white cell count, hypotension, intravascular coagulation, and is recognized as responsible of pyrogenic phenomena (Williams, 2003). Therefore, considering that conventional sterilization by steam or ethylene oxide does not destroy the LPS (Kundsin and Walter, 1980), and does not alter the pyrogenic activity of endotoxic fragments (Sweadner et al., 1977), the absence of endotoxins should be ensured before the catheter is sterilized (Nottebrock, 1999).

A recently introduced sterilization technique, based on hydrogen peroxide gas plasma as sterilizing agent, was approved by the Food and Drug Administration (FDA) and nowadays this non-thermal treatment is a widespread technique to sterilize temperature-sensitive medical devices. Previous studies underlined the suitability of this technique for medical devices and disposable cardiac catheter reprocessing in a safe and effective way without potential harmful residuals (Bathina et al., 1998; Penna et al., 1999; Penna and Ferraz, 2000; Vickery et al., 1999). The characterization of the sterilization process, based on an effective sequence of chemical and physical reactions including ionized species, free radicals, and UV radiation, may also suggest a potential for endotoxin reduction as argued by some authors (Lerouge et al., 2001; Moisan et al., 2001).

This study faced the problem of pyrogenic risk at reusing single use non-lumen cardiac catheters for electrophysiology and ablation procedures. We aimed at assessing the suitability for an experimental reprocessing protocol and the efficiency of hydrogen peroxide sterilization to guarantee a non-pyrogenic-regenerated catheter after both standard clinical use and worst-case contamination obtained by in vitro endotoxin spiking.

Materials and methods

We monitored the device pyrogenic status in three fundamental steps of the reprocessing protocol: after clinical use, after decontamination-cleaning treatments, and after complete reprocessing including sterilization by hydrogen peroxide gas plasma. Moreover, a depyrogenation test was performed in order to evaluate the depyrogenation efficiency of the sole hydrogen peroxide sterilization treatment.

With this purpose, 61 cardiac electrophysiology and ablation non-lumen catheters produced by the major worldwide manufacturers (Medtronic Inc., MN, USA; Bard Inc., NJ, USA; Biosense-Webster Inc., CA, USA; St Jude Medical Inc., MN, USA) were collected during 2 months of local cardiology department activity (S. Chiara Hospital, Trento, Italy) after clinical use. Catheters' number, type, and manufacturer are reported in Table 1.

The whole study was carried on by using the *Limulus* amebocyte lysate (LAL) gel–cloth assay following recommendations by US and European Pharmacopoeias. A lot of reagents from Cape Cod having a sensitivity of 0.125 endotoxin units (EU) per ml (Pyrotell®, lot #S02-235, Associates of Cape Cod Inc., MA, USA) was used for the entire study. The nominal sensitivity was proved in respect of control standard endotoxin (CSE) (lot #89, 0.5 μg/vial, Associates of Cape Cod Inc., MA, USA) following the manufacturer's indications.

We firstly developed and validated a suitable, efficient and reproducible method to elute endotoxins from the device polymeric surface and, secondly, we applied this methodology to real samples.

According to both US and European Pharmacopoeias, the limit for non-pyrogenic medical devices was fixed at 20 EU per device (FDA, 1987a).

A retrieval method, optimized to maximize endotoxin recovery efficiency, was assayed on 15 catheters spiked with a known amount of CSE units. LAL test by gel cloth was performed on different dilutions of the eluate to obtain the average percent ratio of endotoxins recovery. This ratio was subsequently considered at defining proper dilutions for LAL test and actual quantities of EU in elution of real samples. Devices were tested for the limit value of non-pirogenicity