Ethylene oxide residues in Gelfoam

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Abstract— **As the increasing need to reduce medical costs, there was a demand for the sterilization of medical devices, either for reuse or for simple disinfection, for devices that had their packages open, but were not used. The ethylene oxide sterilization is widely used, especially when medical devices are thermal sensitive. Due to the high toxicity of ethylene oxide and byproducts , residues should be eliminated by an efficient device aeration after sterilization. The demand for sterilization does not always take into consideration the ethylene oxide sterilization possibility, as the oxide can modify the material characteristics, or even being of difficult aeration, what enables the residues accumulation. The present study deals with the feasibility of ethylene oxide sterilization of the product known as Gelfoam, classified as a surgical sponge. The results advise against Gelfoam ethylene oxide sterilization due to the great residues retention, above the limits established, and therefore can have human adverse effects.**

Keywords— **ethylene oxide residues, Gelfoam, sterilization.**

I. Introduction

There are several methods of sterilization used and disseminated in national and international market which can be physical or chemical. Among them there are the moist heat sterilization, plasma hydrogen peroxide, low temperature steam and formaldehyde, ethylene oxide, ionizing radiation and non ionizing radiationand sterilizing liquid chemical solutions. The ethylene oxide sterilization is one of the methods indicated for sterilization of thermal sensitive medical devices by using low temperature.

Ethylene oxide (EO) might suffer chemical reaction with other substances, such as liquids, it will derive in byproducts, such as ethylene glycol (ETG) and ethylene chloridrin (ETCH), as toxic as the gas itself. Ethylene oxide byproducts may be formed during the sterilization process, when the ethylene oxide gas contacts with water, especially at acidic pH, producing ethylene glycol, and, in the presence of chloride ions, forming ethylene chlorohydrin. This chemical reaction with ions, liquid, metals and other substances is also highlighted by Souza (1), as EO gas characteristic.

Whereas the toxicity is an ethylene oxide and byproducts feature, which may have different biological effects, it is important to ensure that residual levels are reduced by a suitable aeration process (2).

Absorbents materials are typically used to control bleeding in medical procedures. The absorbent called Gelfoam is a surgical sponge indicated for surgical procedures such as assisting in obtaining hemostasis, in the control of bleeding by ligature, Gelfoam is used where the conventional procedures is ineffective or impractical (3).

Gelfoam contains absorbable gelatin composed by pig skin, sterilized, bendable and able to absorb and keep many times their weight in blood. When implanted into tissues, Gelfoam is absorbed completely in four to six weeks, without formation of scar tissue. When applied to hemorrhagic areas of the vaginal mucosa, rectal, nasal or skin, Gelfoam liquefies completely within two to five days (3).

Gelfoam is available in packs of 6 sterile absorbable gelatin sponge, with dimensions of 80mm x 125 mm x 10 mm. As the procedure it didn't use all the sponges, some health services choose to resterelize the remaining sponges. So is frequent surgical services send Gelfoam to resterilization with ethylene oxide. A supplier of sterilization service to receive medical devices should assess whether sterilization is possible or not. It Should assess whether the sterilization by ethylene oxide won't alter the physical and chemical properties by chemical reaction of the raw material with ethylene oxide and byproducts.

Given this, there was concern about the sterilization of Gelfoam with EO, this technology which is different than dry heat, which is used when manufacturing. The presence of ethylene oxide residues in Gelfoam can cause adverse events not provided in the original product feature.

As is known, the composition of the material influences its ability to absorb, retain and liberate ethylene oxide. Also, the packaging materials vary in their properties allow penetration and dissipation of both the ethylene oxide gas as byproducts, mainly the ethylene chloridrin. The same situation is observed as the product density and density of transport packaging (4).

The penetration of the gas ethylene oxide and aeration of the medical device after EO sterilization depend on several factors, such as material composition, type of packaging, gas concentration, exposure time, temperature used during the sterilization cycle and quantity of moisture present in the medical device (5).

The aim of this study is to quantify the residues of ethylene oxide gas and its byproducts in samples of Gelfoam, forwarding samples which underwent the sterilization pro-

cess in EO, for the chemical testing laboratory for measurement of residues and subsequent comparison with maximum levels established by standards.

II. Method

The present study is a quantitative experimental approach performed by a provider of ethylene oxide sterilization services. The methodology consisted of residues ethylene oxide and byproducts quantification on Gelfoam samples. Measurements were made in outsourced laboratory and compared with acceptable limits, found in Brazilian Interministerial Decree No. 482 (6).

The samples were provided by an otorhinolaryngologic health service, they were cut out of their original size or whole units that were not used but removed from the original packaging. The samples had approximately 8 cm length and 2 cm width . The samples were individually packed in casing surgical paper and film, sterilized in ethylene oxide and sent to the specialized laboratory in gas chromatographic analysis to residues measure.

The equipment used for sterilization of the samples is subjected to annually qualification of physical and microbiological performance as well as the monthly preventive maintenance.

The physical parameters of the sterilization cycles in the study were 650 mg/l of ethylene oxide concentration, temperature of 55°C , relative humidity 60% and 180 minutes of products exposure time to these parameters. Products received at the end, one hour of mechanical aeration and further one hour of environmental aeration. The samples packed in polyethylene bags ziplock type and polystyrene (styrofoam) box, were sent to outsourced laboratory service for chromatographic analysis.

The Brazilian Interministerial Decree 482 of the Ministries of Health and Labour, in relation to aeration of products ethylene oxide sterilized, does not determine time or other conditions, but the executor of sterilization need to validate all stages, including aeration and residues shall not exceed the limits established by Decree 482.

To quantify the ethylene oxide residues and byproducts, three samples were sent to the outsourced laboratory performs the chromatographic analysis.

The classification of Gelfoam on the maximum residues limits of Decree No. 482 table, left doubts as to the acceptance criteria of maximum permitted of ethylene oxide and byproducts residues. The product is a correlate that comes in contact with blood and mucous and also a surgical sponge, so has different maximum acceptable limits, making difficult to interpretation of the data.

Statistical analyzes were performed with Minitab software (7).

III. Results and Discussion

The results obtained are shown in Table 1. Due to the difficulty of obtaining samples and testing costs, only three samples were tested. In order to analyze the measurements distribution the Figure 1 shows the data box plots, that shows different amounts of residues, predominantly ethylene glycol residues.

Table 1 – Ethylene oxide, ethylene chloridrin and ethylene glycol residues in Gelfoam samples

	Ethylene Oxide (EO ppm)	Ethylene chloridrin (ETCH ppm)	Ethylene glycol (ETG ppm)
Sample 1	< 8,4	193,1	883,3
Sample 2	< 10,4	176,6	617,9
Sample 3	22,5	143,7	779,4

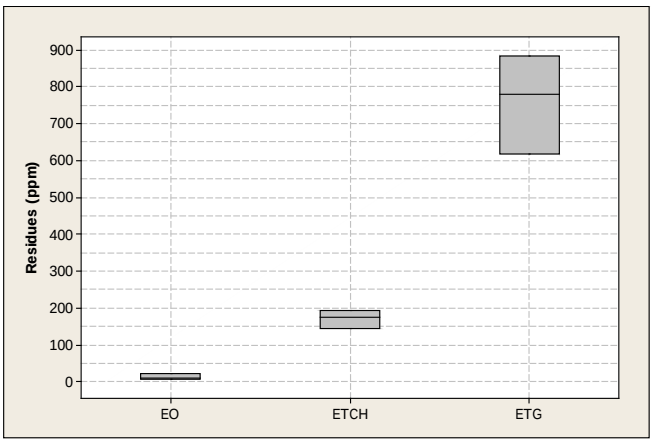

Figure 1 – Residues Boxplots of EO, ETCH e ETG in Gelfoam

Figure 2 shows the mean confidence intervals residues for 95% of substances measured EO, ETCH and ETG. Observed large differences in the amounts of residues found in accordance with the substance.

Given the doubt about the correct interpretation of the product to establish the maximum acceptable values arranged in the Decree No. 482, Gelfoam was analyzed in three categories of exposure to the surgical area: correlate which comes in contact with blood; correlate which comes in contact with mucous membranes and as a surgical sponge itself. The comparison of results is presented in Table 2.

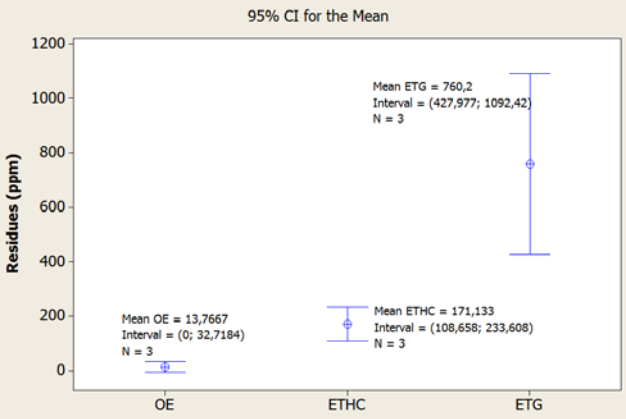

Figure 2 – Confidence intervals residues of EO, ETCH and ETG in Gelfoam

Table 2 - Results of ethylene oxide residues and by-products in Gelfoam samples rated as acceptable limits

	Mean 95% CI for EO- ppm samples – (Max Lim)	**Mean 95% CI for ETCH- ppm samples – (Max Lim)**	**Mean 95% CI for ETG- ppm samples – (Max Lim)**
Surgical sponge	(0 – 32,7) 3 - (25)	(108,7 – 233,6) 3 - (250)	(428 – 1092,4) 3 - (500)
Correlate with blood	(0 – 32,7) 3 - (25)	(108,7 – 233,6) 3 - (25)	(428 – 1092,4) 3 - (250)
Correlate with mucous	(0 – 32,7) 3 - (250)	(108,7 – 233,6) 3 - (250)	(428 – 1092,4) 3 - (5000)

IV. Conclusions

Considering Gelfoam as surgical sponge that is implanted and absorbed by the region that will be submitted to hemostasis, the results are within the expected compliance of ethylene chloridrin residues. The residues levels of ethylene oxide and ethylene glycol samples showed most than expected results considering the mean 95% confidence interval.

Considering Gelfoam a correlate that comes in contact with blood, it has contact with hemorrhagic region and is absorbed by the body: the results of this classification are all above acceptable limits, considering the mean 95% confidence interval.

Considering Gelfoam a correlate which also comes in contact with mucous membranes: the results are within compliance for residues of ethylene oxide, ethyle chloridrin and ethylene glycol with residues below the maximum limits, considering the mean 95% confidence interval.

The results of chromatographic analysis indicated that Gelfoam, sterilized with ethylene oxide, has residues above the limits recommended by the Decree No. 482/1999, demonstrating that the product is not compatible with ethylene oxide, given the fact that the original sterilization factory is heat dry, it produces no toxic residue. The raw material is porous and wet, it may produce and retain large quantities of unwanted toxic residues. By laboratory evidence Gelfoam classified only as a correlate that comes in contact with mucous could have reliable indication of sterilization by ethylene oxide residues present within acceptable limits. But the product does not only come into contact with mucous membranes, but also with blood, contraindicating sterilization method of the present study.

However, the sterilization of Gelfoam in ethylene oxide has been frequently performed. The lack of information about the presence of toxic residues in the product as well as the lack of registries of adverse events for its use take health services to adopt this practice.

The recommendations of the manufacturer of non resterilize Gelfoam and discard the product if the package has been violated must be followed. It also here the recommendation for using packaging with fewer units, for not to induce users to reuse the remaining units.

Because of the number of samples is small the results cannot be considered definitive, but show strong evidence, especially for the large quantity of residues found in the samples, often well above the maximum limits established by Decree No. 482.

Conflict of Interest

The authors declare that they have no conflict of interest.

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