Research Article

Comparison of Sterile Inhalation Water in Oxygen Humidifier Bottles with Tap Water And Investigation of Antibacterial Effects and Endotoxin Limits

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Abstract

In hospitals, medical air feeders and oxygen are used to create dry gas. Patients who need oxygen may experience upper respiratory tract problems due to inhalation of dry oxygen. Therefore, the airway must be humidified while the patient is receiving oxygen. This humidification process is carried out using sterilized water. Oxygen flowmeter is an instrument used in hospitals to adjust the level of oxygen gases. Sterile inhalation waters connected to these flowmeters are used in inpatient wards, intensive care units, operating rooms and all areas where oxygen needs to be administered to the patient. In this study, parameters that will affect water quality such as endotoxin limits, antimicrobial effects and heavy metals contained in untreated, non-sterile tap water and disposable sterile inhalation waters were compared with international norms such as ISO 22519 Standard and European Pharmacopoeia. As a result of the analyzes, it has been proven that the waters contained in the sterile inhalation system produced by Estaş comply with international norms.

In addition, it is foreseen that if sterile water cannot be used in hospitals, antibacterial, antiviral, antimicrobial negative effects will occur or if the same water is used more than once, cross-contamination will occur and different indications will occur. The use of sterile inhalation waters in accordance with the instructions for use reduces the risk of possible infection and ensures that the patient's saturation value reaches the desired level and provides ease of breathing. This solution aims to improve patient care conditions by reducing the risk of infection.

Keywords: *Inhalation Water, Disposable Sterile Inhalation water, Endotoxin Limit, Antibacterial Effects, Water for injection, Deiyonized Water,*

1. Introduction

Oxygen is given to many hospital and intensive care unit (ICU) patients. Worldwide demand for oxygen supplies has increased since the COVID-19 pandemic in 2021. Prior to the pandemic, many nations did not have such a high need for oxygen to meet their everyday needs (Karim et all., 2009). To meet the demand for oxygen, governments around the world are expanding their current infrastructure. Oxygen is a vital medication needed at every level of the healthcare system. Oxygen therapy is thought to be able to reduce 20–40% of pneumonia-related fatalities (WHO., 2021). In hospital settings, medical air is frequently utilized for neonatal environment management, aerosol medicine delivery, baby resuscitation, and mechanical breathing (Edwards et all., 2018). Before it is given, oxygen is often humidified to prevent harm to the tracheal mucosa. For this, oxygen nebulizers, prefilled disposable oxygen humidifiers, and reusable oxygen humidifiers are frequently utilized. According to the American Association of Respiratory Care's clinical practical guidelines, oxygen delivered through a nasal cannula should be humidified at a rate more than 4 L/min (Kallstrom., 2002). Long-term humidifier use, however, is linked to an increased risk of bacterial infection. There have been cases of microaerosols contaminating bubbling humidifiers with bacteria (Ahlgren, 1977, Rhame et all., 1986, Moiraghi et all., 1987). It has been noted that prefilled disposable oxygen humidifiers help to prevent bacterial contamination in wards (Koss et all., 1979, Seigel and Romo 1990, Cahill and Heath 1990, Golar et all., 1993, Malik et all., 2021). According to Moiraghi et al. (Moiraghi., 1987), the presence of contaminated water in oxygen humidifiers caused pneumonia deaths. The most likely causes of the contamination are contaminated oxygen being delivered from the wall outlet, infected respiratory equipment, and hospital staff handling the device with inadequately cleaned hands. It has been proposed that a black fungus present in the environment could be one of the causes of the elevated COVID-19 mortality rates (Malik et all., 2021). Mucormycosis is a potentially lethal disease that can be brought on by black fungus, particularly in those with compromised immune systems [Spellberg., 2005]. The poor quality of the water (piped and cylinder) used to humidify oxygen in the hospital setting causes black fungus to grow in the nasal tube. This fungus begins in the nose, travels to the eyes (Klotz et all., 2000), and ultimately the brain. It can paralyze nerves (Escobar., 1990), damage the eye permanently, and can trigger a heart attack (Naik et all.,2021-Jackman et all., 1992).

Within the scope of this study a disposable, sterile inhalation water equipment was produced. It is designed as a canister and contains deionised water. (water for injection). The device is used by connecting to the oxygen source with the oxygen humidity adapter. This device is classified as Class IIa, Annex-VIII Rule 2, Class IIa of the 2017/745 Medical Device Regulation, Annex-VIII Rule 2, as it is used to transport and store liquids or gases for the purpose of ultimately infusing them into the body. In addition, deionized water used in the device is produced by ESTAŞ. The purification system in deionized water production consists of many steps such as filters, reverse osmosis system, Ultraviolet sterilization and Endotoxin Filter. After the device's production has been ensured, the study's parameters endotoxin limits, antimicrobial effects and heavy metals contained in untreated non-sterile tap water and disposable sterile inhalation waters were compared with international norms such as ISO 22519 Standard and European Pharmacopoeia. No study has been found in which analyses were applied to both waters and compared for use in hospitals.

2. Materials and Methods

Within the scope of the study, a device that will primarily be used to humidify oxygen was designed and produced, then deionized water was produced inside, and then the endotoxin limits, antimicrobial effects and heavy metals contents of deionized water and tap water were analyzed and interpreted. For this purpose, the device produced is classified as Class IIa, Annex-VIII Rule 2, Class IIa of the 2017/745 Medical Device Regulation, Annex-VIII Rule 2, as it is used to transport and store liquids or gases for the purpose of ultimately infusing them into the body.

The bottle and humidity adapter of our product are non-invasive and do not come into contact with the patient. However, sterile inhalation water comes into contact with mucosal membranes together with oxygen. The water contains no additional solutes, is typically available in a plastic container of various sizes, and may be provided with an adaptor for connecting to the inhalation therapy device. After application, it cannot be reused. It is manufactured for single use and cannot be re-autoclaved. The device design was made, the canister and plastic band were supplied by the supplier company and the sterilization processes were carried out within ESTAŞ. Figure 1 shows the system designed by ESTAŞ and produced by the supplier. The deionized water in the device is produced in the production line and the filling processes are carried out.

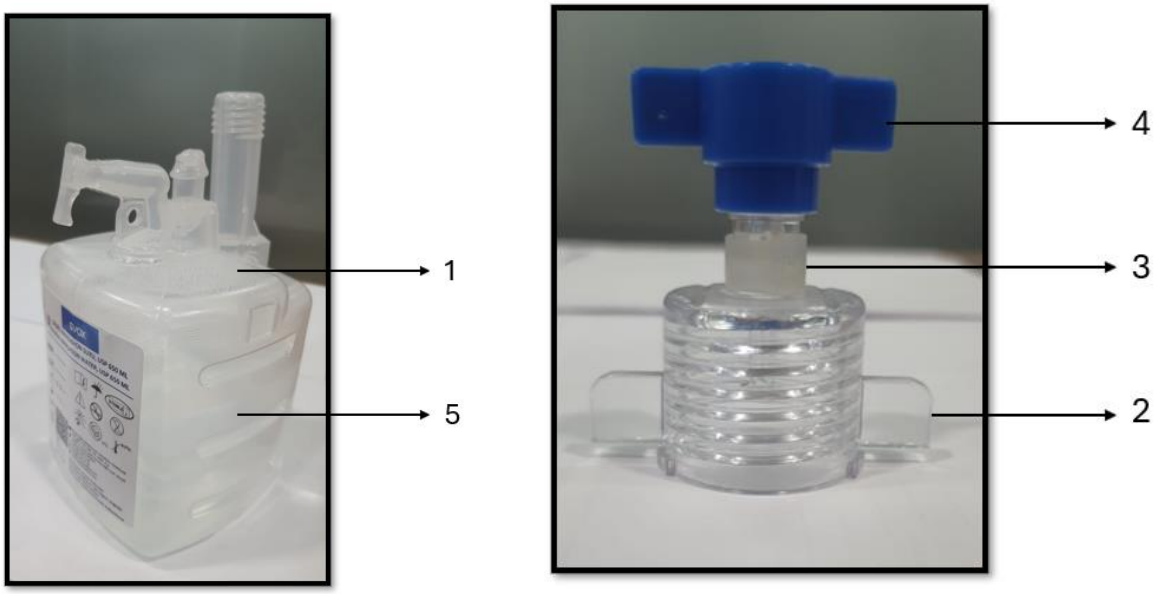

Figure 1. Product system visual.

Table 1. Product System Parts – Contact – Raw Material and Biocompatibility Evaluation:

Comp. Code	Component Name	Raw Material Info	Sterility Information	Contact	Product Code
1	Bottle	PPR (Random Polipropilen)	-	No contact.	RES-IS-01
2	Humidifier Adapter Part-1	PC (Polycarbonate)	Ethylene Oxide	. No contact.	RES-IS-03
3	Plastic Band	PVC (Polyvinyl chloride)	Ethylene Oxide	No contact.	RES-IS-02
4	Humidifier Adapter Part-2	POM (Polyoxymethylene)	Ethylene Oxide	No contact.	RES-IS-04
5	Deionized (Injection) Water	Water for Injection	Steam Sterilization	Sterile inhalation water comes into contact with mucosal membranes together with oxygen.	RES-IS-06

PPR (Random Polypropylene) was used for the bottle part (RES-IS-01) during product production. The humidifier adapter consists of three separate parts; PC (Polycarbonate) was used for the transparent connection part (RES-IS-03), PVC was used for the plastic band part (RES-IS-02) and POM (Polyoxymethylene) was used for the blue connection part (RES-IS-04) in the Table 1.

After the device production, disposable sterile inhalation water and tap water were sent to an external laboratory for endotoxin limits, antimicrobial effects and heavy metals contents and were analyzed and interpreted. The device that was produced is a new device and there are no previous or similar generations of the device within our own organization.

3. Results

The device was successfully produced and the analysis results of sterile inhalation water and tap water endotoxin limits, antimicrobial effects and heavy metals are given in Table 2. The results are the parametric values specified in Annex-1 and Annex-2 of the Regulation on Water Intended for Human Consumption No. 25730 for deionized water, and the conformity assessment was made according to these values.

Water analysis reports are used by water treatment system users and public health authorities (Shaikh and Birajdar., 2024). These reports evaluate the chemical, biological and physical properties of water. Analysis is important to determine whether water contains any contaminants. Water analysis reports determine whether water meets the standards that regulate its quality.

Deionized water is a substance used in many sectors and its quality control must be meticulously ensured. Especially in the health, pharmaceutical, cosmetic and food sectors, deionized water is an integral part of production processes. Deionized water is high purity water that does not contain impurities such as ions, minerals, microorganisms and organic substances. It is distinguished from tap or natural source water by being free of all foreign substances. It is usually produced by methods such as distillation, reverse osmosis and deionization. Bacteriological tests are performed to detect the presence of bacteria that can cause disease in water. These tests specifically target coliform bacteria, fecal coliforms and E. coli.. According to the study results, no bacterial contamination or bacterial growth was observed in either water sample. However, these analyses are not for any hospital or patient use, they are only data obtained as a result of preliminary studies. It is anticipated that the results may vary if these waters remain in the hospital environment for a long time.

Bacterial endotoxin determination is of critical importance, especially in sterile and parenteral (injectable) drugs, medical devices and biotechnological products (Bergheim et all., 2024). Endotoxin can be expressed as a component of the outer membrane of gram-negative bacterial cells. In short, it is a lipopolysaccharide found in the cell wall of gram-negative bacteria. It is

found in environments where gram-negative bacteria live, such as water and air, and continues to exist even if the bacteria die. It is imperative for patient safety that products are free of endotoxin, because endotoxin contamination can lead to life-threatening risks such as sepsis and toxic shock. Therefore, the LAL test is an important part of quality control and legal requirements in the production process. Conductivity measurement in water is a test performed to determine the amount of ions in water. The more dissolved ions water contains, the higher its conductivity. Low conductivity is important, especially in pure water and dialysis water, for the detection of ionic impurities. Conductivity is measured in microsiemens (µS/cm) and the conductivity value of pure water should be less than 1 µS/cm. High conductivity can compromise product quality and the safety of production processes. When the results of this study are examined in Table 2, the most important difference between sterile inhalation water and tap water is endotoxin and conductivity values. It is understood from the analysis results that the sterile inhalation water produced by Estaş does not contain endotoxin and is of the recommended water quality according to ISO22519 standards. When the tap water results are examined, it is seen from the results that the water contains endotoxin. It is imperative for patient safety that the products do not contain endotoxin, because endotoxin contamination can cause life-threatening risks such as sepsis and toxic shock.

Table 2. Investigation of sterile inhalation water and tap water endotoxin limits, antimicrobial effects and heavy metals parameters.

Parameter	Unit	Results (sterile inhalation water)	Results (tap water)	Analysis method	Limit
Hardness	mg/L $CaCO_3$	<1	327	SM 2340 C	<1
Endotoxin	IU/ml	<0.25	>0.25	Gel-Clot Method	<0.25
Microbial Contamination	kob/ml	0	0	TS EN ISO 6222	< 10
Escherichia coli Detection	kob/100 ml	0	0	TS EN ISO 9308-1	<1
Total Coliform Bacteria	kob/100 ml	0	0	TS EN ISO 9308-1	<1
Detection of Pseudomonas aeruginosa	kob/100 ml	0	0	TS EN ISO 16266	<1
Determination of Calcium (Ca) Content	mg/L	Not detected	126.8	SM 3010 B, SM 3120 B	-
Determination of Lead (Pb) Content	µg/L	Not detected	Not detected	SM 3010 B, SM 3120 B	≤10.0
Determination of Magnesium (Mg) Content	µg/L	Not detected	19.39	SM 3010 B, SM 3120 B	-
Determination of Potassium (K) Amount	µg/L	Not detected	Not detected	SM 3010 B, SM 3120 B	-

Conductinity	µS/cm-1	2,01	568,0	TS 9748 EN 27888	< 1,3
pH	-	6.84	7.54	TS EN ISO 10523	6.50<-<9.50

In such a case, the importance of using sterile disposable inhalation water in oxygen humidification bottles in hospitals becomes evident.

4. Discussion and Conclusion

In hospital settings, it is necessary to use distilled water continuously before using it in oxygen therapy devices. It is not recommended to use tap water in humidifiers, even after boiling, because after a while; impurities (micro metals and minerals/salts) start to accumulate and cause serious health problems even after the valuable life-saving oxygen therapy is used. In low and middle income countries globally, oxygen purity can be a major problem that requires the earliest local interventions. Countries where malaria, sepsis, pneumonia and other diseases are common should also prioritize areas where oxygen therapy is required on a large scale.

For all the reasons mentioned, in cases where oxygen is needed, it should be disposible, specific to the patient, and external tap water supplementation should definitely not be used in terms of endotoxin limits. After this study, it is planned to carry out the recommended tests of sterile inhalation water in the hospital environment and after patient use and to evaluate the results in the field of application.

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