World
Federation of
Ozone
Therapy

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Minimum requirements for both generating and handling ozone of medical grade

WFOT Scientific Advisory Committee

Recommendations on the choice of source of oxygen, generator of medical ozone-oxygen mixture and medical devices suitable for medical ozone therapy.

Introduction

Medical ozone is an oxygen-ozone mix with a range of ozone between 1 to 80 micrograms (µg) of ozone per millilitre (mL) of pure (medical) oxygen. Upper concentrations can be avalible for water, oil or cream ozonation. It is generated by a special device named medical ozone generator (MOG).

There is no worldwide regulation on the MOGs. In the European Union, the MOGs are considered Medical Devices under the generic regulation of the Directive 93/42 /EEC. It provides a broad concept of medical device: "any instrument, apparatus, plant, software, substance or other product, used alone or in combination (...) intended by the manufacturer to be used on humans for the purpose of diagnosis, prevention, control, therapy or attenuation of a disease, diagnosis, control, therapy, mitigation or compensation of an injury or handicap (...) ". Medical devices that can be placed on the market must be classified by the manufacturer according to the Directive 93/42 and are supervised by the Ministry of Health of each country.

However, this control on the devices collides with the real situation that registered and CE marked MOGs do not fulfil a minimum requirement on ozone generation accuracy, which is surprising and disappointing, due to the fact that ozone should be used with accuracy to obtain the desired clinical benefit.

Moreover, several small manufacturers worldwide have started to build MOGs with a very low quality and absolute lack of accuracy, although they have been approved by national regulations!

To try to solve this situation, the World Federation of Ozone Therapy – WFOT, with the help of its Scientific Advisory Committee, has developed this document. It will be used to ask the MOG manufacturers to fit the Best Technical Quality indicated by WFOT in order to achieve an international quality recognition of their devices, as WFOT has turned into a worldwide reference entity.

Moreover, as many of the auxiliary ancillary used for ozone application do not have a proper certification, a section related to ozone resistant disposable material has been included.

Gas feeding for obtaining medical ozone

Oxygen gas is considered in many countries a medical gas, and has specific regulations. Only medical oxygen should be used for medical ozone generators to avoid the risk of infection and production of other products apart from ozone (oxide and dioxide of nitrogen). Industrial oxygen cylinders are not suitable at all, as they don't fulfil the required pureness and asepsis. In Europe, their use for medical applications is forbidden.

Medical oxygen should fit the quality standard of the local Pharmacopoeia. If local Pharmacopoeia does not exist, the reference Pharmacopoeia could be:
- European Directorate for the Quality of Medicines (EDQM)[1]: not less than 99.5% V/V of O2.
- United States Pharmacopeia Convention[2]: not less than 99.5% V/V of O2.
- Russian regulation GOST 5573-78[3]:(not less than 99.8% V/V of O2.
- Japanese Pharmacopeia[4]: not less than 99.5% V/V of O2.

Some ozone generators using ambient air or oxygen concentrators are not suitable for medical use because,

1 https://www.edqm.eu/en/ph-eur-9th-edition accessed on 17/12/2016
2 http://www.usp.org/ accessed on 17/12/2016
3 http://www.russiangost.com/p-19487-gost-5583-78.aspx accessed on 17/12/2016
4 http://jpdb.nihs.go.jp/jp17e/ accessed on 17/12/2016

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even the Pressure Swing Adsorption (PSA) technology does not reach a sustained concentration of oxygen over 75%[5] and that leads to the production of substances different to ozone.

Material compatibility

For MOGs.

All materials used in pipelines, commuting and measuring devices inside an ozone generator must be ozone-resistant like: glass, quartz, fluoroplastic (PTFE also known as teflon®) silicone and austenitic stainless steel (300 series). Latex, rubber, polypropylene and other plastics, in pipelines or inner devices are not suitable[6].

These details cannot be verified, having to rely entirely upon the information given by the manufacturer. However, an international, respectable and commercially independent seal of certification is important to identify good quality MOGs.

The different techniques of ozone administration require ozone resistant medical devices.

Bagging and topical ozone administration.

Cups, bags and tubes should use ozone resistant material (teflon®, silicone, polycarbonate, …). Use certified products for ozone if possible.

Systemic indirect endovenous administration.

Sterile glass bottle are always suitable. Plastic bottles and plastic bags should be manufactured using only ozone proof material[6]. There are presently some devices EU certified for ozone therapy that have been tested by official laboratories.
The tubing used should also be ozone resistant when in direct ozone contact; they are usually made of free-ftalates PVC that are ozone resistant.

Ozone injections and systemic indirect intramuscular administration.

We still don't have 100% ozone resistant syringes. BBraun (B. Braun Medical Inc., Bethlehem (PA), USA) Omnifix and BD (Becton, Dickinson and Company, Franklin Lakes (NJ), USA) Plastipak use fair ozone resistant plastics (polypropylene) and medical silicone oil for lubricating, so it is suitable FOR SINGLE USE, even in the same patient. Reusing will increase the risk of release of plastic particles into the patient.

For filtering purposes, when needed, several manufacturers (Merck-Millipore, Fisherbrand, ...) offer filters using PVDF (polyvinylidene difluoride) that is ozone resistant. The chassis is made of polyethylene, acrylic or PFTE (teflon®) so they can be used for a patient without problems. As for the rest of ancillary, we must be sure that they are built with ozone-resistant material.

Stopcocks are usually made of polycarbonate that is very ozone resistant. Please check this, as some manufacturers (BBraun, BD) are using now polyamide, that is very good for any known drug but not so good for ozone. However, it is good enough for a single use in any ozone technique.

Basic technical requirements for MOGs

Adjusting the ozone production.

Medical ozone generators must provide the exact values of the concentration of ozone in the oxygen-ozone mix form 1 to 80 µg/mL (even higher for other technics) with an error margin not above 10%[7].The measurement of actual ozone output can be made with different methods:
- Direct method, by single or double beam photometer system;

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5 http://ozonetherapy.org/medical-and-technical-requirements-to-the-options-of-ozone-generators-for-a-receipt-and-use-of-medical-ozone/ accessed on 17/12/2016

6 http://www.ozonesolutions.com/info/ozone-compatible-materials accessed on 17/12/16

7 Delgado, M. Ozone concentration measurements. State of the art. Revista Española de Ozonoterapia 2011;1(1): 87-92

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- Indirect method, by mathematical algorithm calculation;
- Hybrid method, by using both direct and indirect methods.

The photometer system measures directly the concentration of ozone in the mix. They use a mercury lamp or a LED lamp. The first ones may need more frequent calibration that the LED based systems. Anyhow, periodic revisions are needed following the manufacturer instructions.

The algorithm method determines the concentration by mathematical algorithm without direct contact with the gas. Oxygen flux and electric discharge in the generator tube are measured to calculate the ozone generated. The MOG calibration is checked by the manufacturer before selling, but periodic revisions are needed following the manufacturer instructions.

For all the MOGs, there should be an specific document from the manufacturer to control that the MOG is reviewed according to their instructions in case the devices are checked by the local health authorities.

For bag application, other parameters should be controlled:
- The gas flow rate or a specified amount of mix.
- The time of the procedure.

In this case, the MOG should have:
- Pressure meter in a range 0.01-0.5 bar with a relative error no more than 10%.
- Flow measuring device or metering device of mix with a relative error no more than 10%.
- Manufacturer calibrated constant flow with a relative error no more than 10%.
- Timer (optional, but advisable).

Ozone concentration and dosage should be able to be fixed by the user for any application.

The real value of ozone production (concentration and amount per time) and flow rate should be certified by an external laboratory and attached to the documents of the MOG.

The daily changes in the atmospheric pressure induce small changes in the density of the gas we get from the MOG. All of them are calibrated in the manufacturer location, so machines will not work as expected when conditions are quite different; the ozone generation will be right but when filling the bags or syringes, that are under atmospheric pressure, the ozone amount may decrease according the Boyle's law. This daily changes produce a negligible influence in the practice. However, doctors working usually under low atmospheric pressure due to highness (La Paz, Bolivia, f.i.) may have currently atmospheric pressure 30-40% below the standard at sea level, and should correct the ozone concentration by increasing it in a proportional way when using "open" administration procedures in which the content of the device, syringe, f.i., may be in contact with the air in the office, even for 1 second; the content (ozone-oxygen mixture) will tend to balance the pressure inside the device with the one in the office in a glance. You may loose 30-40% of the amount during this small lapse of time.

To avoid this question, some manufacturers have designed devices that use the normalized millilitre (NmL) to guarantee the right amount of ozone. Their MOG measure the temperature and atmospheric pressure of the environment and make automatic changes during ozone disposal.

The temperature of the operational environment can also influence but doctors usually operate under a narrow range of temperature, so the variation in density for this is negligible.

Others.

A syringe nozzle using standard measures (Luer taper - ISO 594-1:1986[8]) must be available, allowing easy attachment and detachment of a syringe with antibacterial filter to be filled, and will not allow any ozone to escape from the generator into the ambient air. Such nozzle must be easy to disinfect and must be protected against unwanted or accidental penetration of any solid or liquid contaminants when not in use.

8 http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=4693 accessed on 17/12/2016

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Legal requirements

The MOG must be conform to the requirements provided by the national regulation for medical devices of the manufacturer's country. For imported devices, the manufacturer should get a "Free Sales Certificate" (this document has different names according to the country), a document which certifies that the equipment complies with national regulations of the importing country. Warranty and customer support should fulfil national regulations.

Summary

According to this document, all MOGs should comply with the following:
- Use medical oxygen.
- Have a certification of an independent laboratory stating the materials used.
- Have a certification of an independent laboratory stating the ozone generation: concentration accuracy and amount per time production.
- Technical revision calendar program and control document.
- Fulfill legal requirements.