Safety and efficacy parameters for medical ozone equipment according to current EU legislation

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Summary

The Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices obliges electro-medical machine manufacturers to certify machines according to updated safety and efficacy parameters compared to what was previously in force. Ultimately, the regulatory bodies have identified the certification companies that, according to the regulations in force, authorise the sale following the issue of a certificate. A periodic inspection (annual or biannual) will then be carried out to verify the safety and effectiveness of the equipment and the proposed treatment. Once an ozone generator has passed the checks, obtained the certification and its user manual has been properly explained to the purchaser, it is then the latter who will decide whether those specifications are sufficient for his or her way of therapy. Therefore, for the end user, the fundamental document is the user manual, which thus becomes the guide with which to operate that device. The purpose of this contribution is to highlight, by means of some specific patterns, the fundamental topics that should be observed by medical personnel using ozone for therapeutic purposes.

Keywords: Ozone generators vs proper dose concept; Safety; Regulation

Introduction

The Quality standards of common medicinal products in terms of starting materials, safety of use, stability and effectiveness are mainly beyond the skills of healthcare professionals. The same criteria cannot be applied in the case of therapeutic treatments with gaseous oxygen-ozone mixtures obtained through the use of special equipment, currently regulated at EU level by the Regulation 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices. The kinetics of ozone degradation make the extemporaneous obtaining of this gas at the time of the therapeutic act unavoidable.

In order to correctly approach a therapeutic treatment with ozone, the physician must have suitable instrumentation capable of defining concentrations and dosages for both systemic and infiltrative treatments. A comprehensive approach to patient eligibility, along with compliance with standard operational procedures is essential to normalize the safety of the practice of ozone therapy. In this respect, both the concepts of low dose and proper dose represent the achievement of the objectives of safety and efficacy of treatments, respecting the molecular relationships between substrates and molecules contained in the systems used [Viebahn-Haensler & León Fernández, 2021; Tricarico & Travagli, 2021]. The need for the clinician to ensure the greatest possible accuracy of dosage correlates with the hormetic response of the patient during treatment, resulting in time customisation in relation to patient feedback as a confirmation of the effectiveness of the therapeutic approach. A well-documented treatment report is important for promoting continuous evaluation of healthcare services, and leading to safer and better practice.

At this purpose, an ever-present issue concerns the question of how to express ozone and its derivatives. In fact, physicians habitually handle drug dosages in mass units, mainly mg or g. On the other hand, the possibility of dealing with ozone in the gaseous state mixed with another gas (mainly oxygen) or it is still in the gaseous state but solubilized in a liquid (water, buffer solutions) leads to having to clarify some aspects of the mode of expression of the concentrations units [Tricarico et al. 2020]. Briefly, concentrations of gaseous ozone in oxygen for medical use are

typically measured in units of the mass of ozone (i.e., μg or mg) per volume unit (i.e., cm3 or dm3, as well as mL or L, respectively). Moreover, the same concentrations may also be expressed as %. When these conditions occur, it is necessary to introduce conversion factors, mainly based on the molecular weight of ozone. Typically, conversion factors for ozone in oxygen are made assuming both pressure and temperature at defined conditions. On the contrary, if the ppm values are expressed, it should first be specified if they are ppmv (parts per million volume) or ppmw (parts per million weight). At this point and in accordance with the above, 1 ppmv O3 in O2 equals approximately 2 μg/dm3. On the other hand, when ozone is solubilized in a liquid, parts per million can be also expressed as milligrams of ozone per liter of a solvent (mg/L). This measurement is the mass of a chemical or contaminate per unit volume of water (note that ppm or mg/L on a lab report are equivalent).

All generators should have gold standard so that the therapist is put in the best possible position to make an informed choice of appropriate administration with regard to sensitive parameters such as, for example, reading the actual concentration to be used, the time to reach it, and compliance with tolerance with regard to average values.

Materials and methods

Identification of the minimum parameters to be indicated by manufacturers of ozone generators for medical use in the user manual for proper dose assessment.

Compilation of a pharmacological feedback evaluation form for the determination of the proper dose for medical use.

Results and discussion

A formal data model and standardized representation of parameters to be included for a correct evaluation of the proper dose support rigorous quality assessment. A proposal to achieve this is outlined in Table 1.

Table 1. Parameters to be included for a correct evaluation of the proper dose

Types	Qualitative assessment	Quantitative assessment
Modes of withdrawal	a. automatic syringe filling b. syringe connection with luer-lock mechanism c. automatic and immediate concentration setting	
Ozone concentration	Unit of measure	Tolerances (%)
Flux	Unit of measure	Tolerances (%)
Time	stabilisation of the ozone concentration in the mixture once the parameter is set	
Revision of Medical Devices	useful parameters for revision	Time intervals
Regulatory compliance	certificates, operational block after expiry	

On the other hand, a clinical feedback evaluation form for the determination of the proper dose for medical use is schematized in Table 2.

Table 2. Parameters to be included for a correct evaluation of the proper dose

Therapy start date: ..... Number of sessions scheduled:..... Type of administration .....

Blood chemistry tests if necessary, instrumental anamnestic evaluations if performed……
……..
……

- 1st session: date, procedure, dosage, concentration……..

Blood chemistry tests if necessary, instrumental anamnestic evaluations if performed……
……..
……

Possible side effects and adverse events: no / yes (which ones) and when they occurred .....

2nd session: history of the expected effects of the previous administration……

Blood chemistry tests if necessary, instrumental anamnestic evaluations, if performed……
……..
……

Evaluation of confirmation or modifications of the parameters of the previous administration……..
……

Possible side effects and adverse events: no / yes (which ones) and when they occurred .....

3rd session: history of the expected effects of the previous administration……

Blood chemistry tests if necessary, instrumental anamnestic evaluations, if performed……
……..
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Evaluation of confirmation or modifications of the parameters of the previous administration……..
……

Possible side effects and adverse events: no / yes (which ones) and when they occurred .....

End of therapy: history of the expected effects of the previous administration……

Blood chemistry tests if necessary, instrumental anamnestic evaluations, if performed……
……..
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Evaluation of confirmation or modifications of the parameters of the previous administration……..
……

Possible side effects and adverse events: no / yes (which ones) and when they occurred .....

Patient's signature: .....

Physician’s signature: .....

Conclusions

For the purposes of proper standardisation in both the treatment of pathologies and clinical research, it is necessary for practitioners to acquire knowledge and mastery of the equipment and procedures for administering ozone at the highest possible level. Furthermore, manufacturers of electro-medical equipment that generates ozone-oxygen mixtures must make every effort to produce devices that fully meet the demands of therapists. In collaboration with the scientific societies involved in the drafting of guidelines and/or good clinical care practices, considerable progress has been made. Nevertheless, much can still be done. The present Congress seems to us the ideal scientific context to open a reasonable reflection on this topic.

References

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