



ISCO3/MET/00/23 Rectal Insufflation

Index

Title.....	2
1.1. Brief background	2
1.2. Purpose	2
1.3. Scope	2
1.4. Acronyms, abbreviations and definitions	2
3. Procedure.....	3
3.1 Indications	3
3.2 Contraindications.....	3
3.3 Recommended doses intervals.....	4
3.4 Clinical evaluation.....	5
3.5 Preliminary operations.....	5
3.6 Main procedure.....	6
3.7 Side effects	6
3.8 Patients Follow-up.....	6
3.9 Effect Mechanism.....	7
4. Contingencies; Corrective Actions	7
5. References	7
5.1 SOP References	7
5.2 Other References	7
6. Documentation and Attachments.....	9
6.1 List of recommended medical disposables	9
7. Change History.....	9
8. Document Records	9



Title

ISCO3/MET/00/23 Rectal Insufflation

1.1. Brief background

The rectal administration of ozone is one of the oldest systemic and local forms of application. The biological effects of the Rectal Insufflations of Ozone (RIO₃) has been demonstrated extensively either experimentally or clinically. Furthermore, preclinical studies demonstrated its low toxicity. RIO₃ has been now extended to treat many diseases and is increasingly being used as a systemic therapeutic form. RIO₃ is already being viewed as an alternative to Mayor autohemotherapy (MAH). Using standardized clinical protocols, a therapeutic success can be reached with RIO₃. Handling the advantage and disadvantage of RIO₃, not as alternative to MAH but used properly (e.g. paediatric, geriatric, when MAH cannot be performed because i.v. is difficult due to unfavourable vein conditions, etc.), this method is a valid route of O₃/O₂ administration.¹ The RIO₃ is a systemic route. The gas is quickly dissolved in the luminal contents of the bowel, where mucoproteins and other secretory products with antioxidant activity readily react with ozone to produce reactive oxygen species (ROS) and lipid peroxidation products. These compounds penetrate the muscular mucosa and enter the circulation of venous and lymphatic capillaries.¹ This non-invasive technique can be used without risk in pediatric and elderly patients, and on patients with difficult veins' access for MAH. Generally, this is well tolerated and allows scaling doses similar to those used by MAH.

1.2. Purpose

The purpose of this SOP is to describe the procedure for Rectal Insufflations of Ozone (RIO₃).

1.3. Scope

This procedure specifies the technique, doses, volume of gas and frequency of application of ozone by rectal way.

1.4. Acronyms, abbreviations and definitions

G6PD	Glucose 6 phosphate dehydrogenase
MAH	Mayor autohemotherapy
RIO ₃	Rectal Insufflations of Ozone
ROS	Reactive Oxygen Species
SOP	Standard Operation Procedure
Total doses	Total amount, in micrograms, of ozone given per session, calculated as volume in mL multiplied by concentration in µg/mL



2. Responsibility

- Physician**
- Patients' Clinical records registration
 - Assessment of the indication, contraindications
 - Request the informed consent (ISCO3/QAU/00/21) and the privacy consent
 - Applications and monitoring
 - Recording all data on medical records
 - Prescription of investigations to assess the effectiveness of the treatment (e.g. biochemical or immunological assays)
 - Reporting any late complications
 - Patient follow-up
- Nurses**
- Accommodate the patients
 - Preparation of the clinical procedure
 - Supervision of patients, and vital signs control (temperature and pressure)
 - Detects and alerts the doctor to anomalies due to possible reactions
 - Notification of possible complications

A RIO_3 session should be done by a physician, adequately trained in ozone therapy. Also a trustworthy assistant, nurse, or paramedical professional, may do the procedure, provided this person is adequately trained for this work. It is the physician's responsibility to see that all steps of the procedure are done in the correct manner, in order to always avoid errors, accidents, and to prevent incidents.

3. Procedure

3.1 Indications

As a complementary systemic use, these generally comprise chronic inflammatory diseases or inflammatory symptoms,² asthma,³ Angiopathy,⁴⁻⁶ arterial circulatory disturbances,^{7,8} retinitis pigmentosa,⁹⁻¹¹ chronic inflammatory rheumatic disease,¹² virus-conditioned diseases,^{13,14} immune deficiency,¹⁵ fibromyalgia,¹⁶ alcoholics,¹⁷ cocleovestibular syndrome,¹⁸ complementary oncology.¹⁹ In addition, local diseases, such as: colitis,²⁰ proctitis, wounds²¹ or anal fissures.

3.2 Contraindications

Absolute contraindication: Favism: Glucose-6-phosphate dehydrogenase deficiency (favism).*

Relative contraindications / special situations:

- ✓ Acute myocardial infarction
- ✓ Pregnancy in the first 3 months
- ✓ Uncompensated toxic hyperthyroidism - Basedow Graves status
- ✓ Thrombocytopenia less than 50.000 and serious coagulation disorders
- ✓ Severe Cardiovascular instability
- ✓ Acute alcohol intoxication



- ✓ Acute infarction of myocardium
- ✓ Massive and acute hemorrhage
- ✓ During convulsive states
- ✓ Hemochromatosis
- ✓ Patients receiving treatment with copper or iron.

* The prevalence of Glucose 6 phosphate dehydrogenase (G6PD) deficiency varies among ethnic groups with overall lower frequency in the Americas (3.4%), Europe (3.9%), and the Pacific (2.9%) as compared to sub-Saharan Africa (7.5%), the Middle East (6.0%), and Asia (4.7%).²² Test of G6PD is recommended prior to O₃ therapy in order to avoid complications).

Concentrations higher than 40 µg/NmL can hurt the enterocyte.²³

3.3 Recommended doses intervals

In chronic illnesses, the proper dosage of medical ozone produces temporary oxidative stress tolerance so patients require repeated cycles of ozone therapy (15-32 sessions, 2-5 per week, constituting one cycle). It is recommended to increase the dose in each consecutive cycle, repeated at a 3 to 4 month interval in the first year. If there is more than six months between each cycle, doses must be the same as in the first cycle. Beneficial results are reported following rectal dosing (low, middle and upper middle doses). High doses will only be used after two cycles of ozone therapy with an interval of three months each.²³

The range of dose is (10 – 35) µg/mL (Table 1 and 2).

The range of volume is (100 – 200) mL

Concentrations higher than 40 µg/mL can hurt the enterocyte.

Table 1. General dosages by rectal insufflations.

O ₃	High	Medium	Low	Remarks
C. (µg/mL)	30-35	20-25	10-15	Major concentrations of 40 µg/mL can hurt the enterocyte. The only exception is, in case of acute bleeding, in ulcerous colitis, begining with a high concentration of 60-70 µg/mL / and 50 mL Vol. Once the bleeding diminishes, reduce concentration.
V. (mL)	200	150	100	
Dose (mg)	6.0 -7.0	3.0-3.75	1.0-1.5	



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SOP: ISCO3/MET/00/23
Version: 1
Date: 05/02/2017
Page 5 of 9

Table 2. Pediatric dosages by rectal insufflations

Tab. 2 A. According to the oxidative stress

Weeks of treatment	Concentration O ₃ (µg/mL)		
	Oxidative stress		
	Low	Moderate	Severe
First	20	15	10
Second	25	20	15
Third	30	25	20
Fourth	35	30	25

Tab. 2 B. Volumes to be administered according to patient's age

Age of the patient	Volumes to be administered (mL)
28 days-11 months	15-20
1 -3 years	20-35
3-10 years	40-75
11-15 years	75-120

The dosage changes every five sessions. Cycles of 15-20 sessions are indicated every four-five months during the first year. Later the patient will be evaluated to determine the frequency of the cycles for the second year.

3.4 Clinical evaluation

A clinical and/or laboratory evaluation is necessary to establish a precise diagnosis and to permit comparisons between the patient's status before, during and after ozone therapy.

3.5 Preliminary operations

The patient must be fully informed in advance about the method itself, about all the steps of the procedure, about the desired effect(s) and also about the possible unwanted side effects. Also a written Term of Informed Consent should be read, understood and signed by the patient or the person responsible for the patient.

Device: must fit the standard requirement ISCO3/DEV/00/01

Syringes: Plastic-based devices, must meet the ISO 15747 standard: 2005 (This is the European Union regulation). All containers and devices used in O₃ therapy must be ozone-resistant and must not release phthalates.

Before administering rectal medicine, the door to the room should be closed to assure patient privacy. The patient should be encouraged to empty his or her bladder and bowels before the procedure. After removing lower garments and underwear, the patient should be positioned in bed



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SOP: ISCO3/MET/00/23
Version: 1
Date: 05/02/2017
Page 6 of 9

on his or her left side, with the top knee bent and pulled slightly upward, lifting the upper buttocks will enable visualization of his or her rectal opening. A waterproof pad should be placed under the patient's hips to protect the bedding, and a sheet should be draped over the patient to cover all of his or her body except the buttocks.

After placing a bedpan within quick access, the nurse should explain the procedure to the patient. This explanation should include the importance of breathing slowly through the mouth to enhance relaxation of the rectal sphincter and to avoid oppositional pressure. The patient should be made aware that there may be an urge to push the medicine out, but that he or she should try to hold it for at least 10–15 min after instillation, as most rectal medications need time to be absorbed.

3.6 Main procedure

The nurse should wash his or her hands and put on gloves. The foil wrap should be removed from the rectal catheter. External lotions, ointments or creams can be applied directly, using a gloved finger or a (10 · 10) cm gauze pad. Prior to administering the tip of the catheter, or applicator should be lubricated with a water-soluble lubricant. To insert a rectal catheter, the lubricated, tapered end of the catheter should be placed at the rectal opening and gently pushed into the rectum. The catheter should be pushed continually toward the umbilicus until the full length of the nurse's gloved index finger has been inserted into the rectal opening (i.e., about 7.5 cm, for an adult patient). When inserting a rectal catheter into children, the catheter should be pushed about 2.5 cm beyond the rectal opening, or up to the first knuckle of the nurses' index finger. When inserting a rectal catheter into infants, the little finger should be inserted one-half inch (1.25 cm) beyond the rectal opening. The buttocks should be released and the finger removed. Gently administer the ozone over approximately 5 min period while the patient is laying on his/her side.

3.7 Side effects

When ozone was administered by rectal insufflation, cases of bloating and constipation were reported.^{19,24} Is also reported slight irritation and transitory flatulence¹⁶ and mild, short-term irritation.¹⁵

If the concentration used causes irritation or discomfort, consider lowering the concentration used or discontinuing treatment until irritation subsides.

According to clinical trial more than 46 984 rectal applications has been done in 716 patients, number applications varies between 1 and 40 treatments per year, only in two case, there was described slight transient flatulence immediately after rectal ozone insufflation.²⁵

3.8 Patients Follow-up

Patients may be followed and re-evaluated from time to time, from the clinical / subjective point of view and/or with laboratory and/or image examinations.



3.9 Effect Mechanism

At low doses, systemically applied ozone in the form of RIO_3 acts as a bioregulator, ozone intermediary (H_2O_2 , 4-hydroynonenal, etc.)²⁶ induce a signal transduction via the oxidation of glutathion or cysteine residues and the corresponding nuclear factors, resulting in a regulation of the antioxidants via Nrf2 information,^{26,27} or an immunomodulation via NFkB.²⁵

For rectal administration, there were 6 controlled studies, 2 randomized,²⁵ with 227 ozone patients, 6 studies without a control group comprising 484 ozone patients. The indications agree with the classic indications of ozone therapy, as a rule associated with a chronic inflammatory process; the type of application also corresponds to the classic and standardized application forms.

For RIO_3 all studies show statistically significant clinical and/or pharmacological improvements, without adverse effects or adverse reactions.²⁵

4. Contingencies; Corrective Actions

In case of side effects follow the instructions of ISCO3/CLI/00/01 "Fist Aids in ozone therapy (Inhalator exposition and accidental over dose)" and report the side effect using ISCO3/REC/00/03 "The ISCO3 Safety Information and Adverse Event Reporting Program Form".

5. References

5.1 SOP References

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ISCO3/DEV/00/01 Guidelines and Recommendations for Medical Professionals Planning to Acquire a Medical Ozone Generator.
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SOP: ISCO3/MET/00/23
Version: 1
Date: 05/02/2017
Page 8 of 9

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SOP: ISCO3/MET/00/23
Version: 1
Date: 05/02/2017
Page 9 of 9

6. Documentation and Attachments

6.1 List of recommended medical disposables

Siliconated Luer lock syringe or glass syringe of 50 mL or 60 mL
Gloves and disinfectant solution
Rectal catheter No. 8, 10, 12, 14, 16, 18, 20
Water soluble Lubricant

7. Change History

SOP no.	Effective Date	Significant Changes	Previous SOP no.
ISCO3/MET/00/23	25/11/2016	Draft.	First version
	05/02/2016	Final version	First version

8. Document Records

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