



CONSENSUS CONFERENCE
LINEE GUIDA E BUONE PRATICHE
in OSSIGENO-OZONO TERAPIA

(Art. 6- L. 8 marzo 2017, n.24)

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Consensus Conference Roma

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PREMESSA

L'art. 6 della **Legge 8 marzo 2017 n. 24**, ha sancito l'improcrastinabilità della emanazione di Linee Guida da parte delle Società scientifiche accreditate presso il Ministero della Salute ai sensi della stessa Legge.

Ciò perché la Norma ha apportato un importante cambiamento in seno al Codice Penale che si è arricchito dell'**articolo 590-sexies** che prevede l'impunità per imperizia per i sanitari che, nello svolgimento della loro funzione, abbiano agito rispettando "*... le raccomandazioni previste dalle linee guida come definite e pubblicate ai sensi di legge ovvero, in mancanza di queste, le buone pratiche clinico-assistenziali...*".

Purtroppo le **Linee Guida italiane** valide ed utilizzabili -ai sensi di Legge- sotto il profilo della credibilità scientifica, in materia di ossigeno-ozono terapia sono praticamente inesistenti. Infatti, le così dette "Linee Guida" proposte da varie Società scientifiche, non rispecchiano i canoni imposti dal GIMBE (Gruppo Italiano Medicina Basata sull'Evidenza), dal GIN (Guidelines International Network) e dall'Istituto Superiore di Sanità, in modo particolare per quanto attiene al conflitto di interessi, per la composizione del Gruppo di Sviluppo delle Linee guida stesse e per le metodologie utilizzate.

La **Società scientifica Nuova FIO** (Federazione Italiana di Ossigeno-ozono) in regola con il disposto giuridico, dopo essersi accreditata presso il Ministero della Salute, ha sentito l'obbligo di ottemperare a quanto previsto in tema di **Linee guida e buone pratiche clinico-assistenziali**. Allo scopo si è data un regolamento interno, in linea con il precetto, al fine di produrre nel più breve tempo possibile le prime Linee guida, in tema di ossigeno-ozono terapia, valide secondo gli standard di riferimento.

Nel frattempo, sentito la cogente necessità e in accordo con il disposto giuridico, ha riunito il Comitato scientifico per rispondere ai quesiti relativi all'efficacia, alle applicazioni cliniche e ai rischi dell'ossigeno ozono terapia e

- dopo avere operato una attenta ricognizione di quanto in letteratura in tema di ossigeno ozono terapia (oltre 4000 lavori scientifici pubblicati);
- valutata la "Dichiarazione di Madrid sull' Ozonoterapia" (del 2010 e le revisioni del 2014 e 2015) prodotta dall'ISCO3 - International Scientific Committee of Ozone Therapy, composta da 38 associazioni nazionali e internazionali di ozono;
- valutato il Documento "Ozonoterapia basata sull'Evidenza" prodotto nel 2015 dalla WFOT - World Federation of Ozone Therapy, composta da 22 società scientifiche internazionali di ozono terapia;

Ha tenuto la **III Consensus Conference in tema di ossigeno-ozono terapia** in Roma il 9 maggio 2024.

Da questa sono emerse le seguenti **evidenze e raccomandazioni** che vanno comprese nell'alveo delle **BUONE PRATICHE CLINICO ASSISTENZIALI**

BUONE PRATICHE CLINICO ASSISTENZIALI IN OSSIGENO-OZONO TERAPIA

L'ozonoterapia è un trattamento medico che utilizza una miscela di Ossigeno e Ozono come agente terapeutico per trattare una vasta gamma di malattie. Il rationale di impiego si basa sul concetto che basse concentrazioni di Ozono possono rivestire importanti funzioni sulla cellula e numerosi sono stati i meccanismi d'azione dimostrati che confermano questa evidenza clinica.¹⁻¹⁰

1. UTILIZZO DELLA MISCELA DI OSSIGENO-OZONO

Per uso medico la miscela di Ossigeno-Ozono viene prodotta in concentrazione da una apposita apparecchiatura certificata in conformità con gli standard stabiliti, ad esempio all'interno dell'Unione Europea deve soddisfare le direttive CE. Il principio di funzionamento del generatore è quello di trasformare parte dell'ossigeno in ingresso in ozono medicale, in quantità tale da poterlo dosare in concentrazione variabile. La macchina deve essere obbligatoriamente provvista di fotometro, dispositivo per la quantificazione accurata dell'ozono prodotto.

Generalmente i generatori medicali sono dotati di tubi ad alto voltaggio (tubi Siemens) connessi in serie e collegati ad un trasformatore ad alta tensione controllato elettronicamente per generare un adeguato voltaggio. L'energia fornita consente la scissione della molecola di O_2 e la sua ricombinazione formando una miscela gassosa di O_2O_3 il cui rapporto sarà variabile in funzione del voltaggio applicato e del flusso di O_2 in ingresso. L'ossigeno in ingresso deve essere puro ed erogato da bombole medicali o da sistema centralizzato (vd. Ospedali e Case di Cura). La concentrazione di Ozono è indicata direttamente con il dato in $\mu g/ml$. Un distruttore catalitico consente di ritrasformare di nuovo l'Ozono in eccesso in ossigeno.

2. MATERIALI

Tutti i materiali impiegati devono essere monouso e resistenti all'ozono, certificati CE (nell'Unione Europea), registrati all'ente preposto. Si prediligono pertanto vetro, silicone, Teflon, siringhe siliconate, Etilene Vinil Acetato (EVA), PVC no dop (senza ftalato). I tubi e i guanti latex non possono essere impiegati perché a contatto con l'ozono si disintegrano rapidamente.

Si raccomanda che quando si eseguirà Ossigeno-Ozono terapia, si deve avere la dotazione di base per l'assistenza cardio – polmonare di base (BLS).

3. UTILIZZATORI

L'Ossigeno-Ozono terapia è una terapia medica e come tale può essere praticata esclusivamente da personale medico ed essere eseguita con assoluto rigore scientifico. Come ogni altra terapia medica (ad eccezione dell'anestesiologia e della radiologia) non è sottoposta né vincolata ad alcun conseguimento di specializzazione specifica post laurea. Nell'iter formativo professionale specifico è consigliabile – *ma non obbligatorio* – seguire un Master o Corso universitario di Perfezionamento monotematico o comunque contenente almeno

3 moduli di 3 CFU (Crediti Formativi Universitari) in Ossigeno-Ozono terapia Medica oppure altro corso accreditato, evitando corsi con evidente conflitto di interessi in quanto effettuati da strutture o soggetti con interessi commerciali.

4. VIE DI SOMMINISTRAZIONE

Le vie di somministrazione e di impiego, di seguito descritte, sono tutte state opportunamente testate e non si sono registrati effetti indesiderati con l'impiego dei dosaggi riportati. Accogliamo con favore il range terapeutico indicato dalle linee guida *Ozone Therapy International Library* ISCO3¹¹, *Levels of Evidence Working Group*, OCEBM¹², *Review on Evidence Based Ozone Therapy*, WFOT'S¹³, e dal contributo del dott. V. Bocci nel libro *Ozone a new medical drug*,¹⁴ e dei dottori A. Zambello e M. Bonetti nel libro *"Ozonoterapia: manuale pratico."*¹⁵²

Tranne che per la via inalatoria, da evitare per la tossicità bronco-polmonare, molte vie parenterali e topiche sono impiegate per somministrare ozono senza effetti tossici e partendo dal minimo dosaggio indicato.¹⁵

Per quanto attiene alle vie intra peritoneali e intra pleuriche sono disponibili allo stato attuale segnalazioni da parte di gruppi di studio¹²⁸. Sono anche disponibili segnalazioni, ma non studi clinici controllati, relativi alla efficacia della somministrazione intra peritoneale in caso di carcinosi da tumori ovarici. Ma per questa particolare via di somministrazione sono necessari ulteriori studi osservazionali e studi clinici controllati.^{16,17}

Le applicazioni cutanee (esempio ulcera diabetica) si effettuano con ozono in forma gassosa utilizzando dispositivi medici certificati CE costituiti da materiali resistenti all'ozono.^{18,19}

La via sistemica comprende diverse modalità:

- **VIA VENOSA:** vengono prelevati, in flaconi sterili, in vetro o sacche di plastica ozonoresistente, in conformità con i regolamenti dell'Unione Europea, tra i 100 mL ed i 250 mL di sangue venoso dal paziente. In questi flaconi deve essere presente anticoagulante⁵⁰. Ad esso viene poi miscelata una concentrazione di ozono che varia, preferibilmente, tra i 10 µg/mL e gli 60 µg/mL. Questa miscela viene poi ri-somministrata immediatamente nella vena del paziente, senza interrompere il circuito.
20-21-22
- **VIA MUSCOLARE PROFONDA (glutea):** vengono prelevati 10 mL di sangue venoso in una siringa sterile da 30 cc già caricata con la stessa quantità di miscela ossigeno-ozono alla concentrazione massima di 40 µg/mL e reintrodotta, previa opportuna miscelazione, intramuscolo nel gluteo.²³
- **VIA RETTALE:** il gas viene somministrato mediante un catetere attraverso l'orifizio anale nell'ampolla rettale. Il volume consigliato per questa pratica va fino ai 200 mL con concentrazione di ozono tra i 20 µg/mL ed i 50 µg/mL. Si consiglia adeguata preparazione.^{14, 24}

La via periferica comprende diverse modalità:

Per quanto riguarda le **vie di somministrazione periferiche**, l'ozono viene somministrato più frequentemente attraverso infiltrazione. Si utilizza una siringa sterile monouso, riempita con la miscela solo alcuni istanti prima dell'utilizzo. Questo perché l'ozono degrada rapidamente, fino a scomparire del tutto trasformandosi nuovamente in ossigeno. In questo caso, la somministrazione diverrebbe del tutto inefficace, sebbene innocua. Tale via comprende:

- INTRAMUSCOLARE PARAVERTEBRALE con possibilità di essere effettuate lungo tutta la lunghezza della colonna vertebrale.^{25,26} Sono consigliate concentrazioni da 5 a 30 10-25 µg/mL di ossigeno-ozono con un volume tra i 2 e 4 mL per il tratto cervicale e dorsale, e tra i 4 e 10 mL per il tratto lombare.²⁷
- INTRADISCALE viene effettuata, a livello cervicale e dorsale tra i 4 e i 10 mL, con supporto radioguidato, spesso con paziente sedato. Per la lombare si consiglia singola infiltrazione, ripetuta solo se necessario non prima di due, tre settimane. Si consiglia, per la discopatia lombare, 5-10 mL di O₂-O₃ ad una concentrazione di 25-35 µg/mL. Per la discopatia cervicale, si indica, 2-3 mL di O₂-O₃ ad una concentrazione di 25-35 µg/mL.^{28,29}
- INTRAFORAMINALE per l'infiltrazione cervicale, si indica, un volume di 3-4 mL ad una concentrazione di 10-20 µg/mL. Per quella lombare, si utilizza la stessa concentrazione ad un volume di 7-10 mL.³⁰
- INTRARTICOLARE si utilizza una concentrazione tra 10 e 30 µg/mL con un volume dipendente dalla dimensione dell'articolazione trattata.³¹
- USO TOPICO CON SACCHETTO DI OZONO, indicata nelle lesioni cutanee con concentrazioni che vanno da 10 ad 30 µg/mL a seconda della gravità della lesione per una durata di 10-20 minuti previa indicazione dell'arto con fisiologia.³²
- SOTTOCUTANEA può essere indicata a fini cosmetici nella panniculite fibro-edematosa, in cui si consigliano volumi limite di 100 mL totali per seduta ed un volume di 1-2 mL per punto con concentrazioni di 8-10 µg/mL con ago di 0.4 mm (27 G). Si consiglia l'associazione con Terapia sistemica per una maggior efficacia.³³
- INSUFFLAZIONE IN FISTOLA, con una concentrazione di O₂O₃ di 10-80 µg/mL.¹⁴
- INSUFFLAZIONE VESCICO-URETRALE E VAGINALE di 50-100 mL di O₂O₃ direttamente in uretra o vescica alla concentrazione di 10-30 µg/mL.^{34,35 132}
- APPLICAZIONE AURICOLARE con una concentrazione di 10-25 µg/mL per 5 minuti.^{36,38}
- VIA NASALE Ponendo grande attenzione a non far inalare la miscela che viene somministrata in apnea. Una dose massima di 60 mL di O₂-O₃, ad una concentrazione di 10-12 µg/mL.³⁹
- MICRODOSI DI O₂-O₃ NEI TRIGGER POINTS E NEI PUNTI DI AGOPUNTURA si consiglia infiltrazione intramuscolare di 3-5 mL di O₂-O₃ con concentrazione di 6-9 µg/mL, oppure per quanto riguarda l'agopuntura si indica l'infiltrazione di 0.1-0.3 mL (massimo 1 mL) con concentrazioni di 6-9 µg/mL.⁴⁰
- VIA TRANSDERMICA A MEZZO DI SAUNA OZONIZZATA, APPLICAZIONE TOPICA DI ACQUA, OLIO E CREME OZONIZZATE. L'ozonizzazione di acqua distillata viene effettuata in ambiente ambulatoriale mentre gli olii devono essere prodotti in laboratori semi-industriali.^{41,131}
- APPLICAZIONI ODONTOIATRICHE⁴²⁻⁴⁴

Addendum: Si segnala che sono iniziate ad emergere evidenze cliniche sull'Ozonoterapia periferica delle patologie che interessano le tube Eustachio^{37,240}. La NUOVA FIO si impegna ad approfondire ulteriori nuove evidenze sulla valutazione scientifica dei risultati della miscela gassosa in tali regioni.

5. DOSI E VOLUMI

Per uso medico vengono utilizzate, a seconda della via e della modalità di somministrazione, dosi di ossigeno-ozono a basse concentrazioni. Le dosi raccomandate per ciascun impiego sopra considerato non ha fatto registrare danni o fenomeni di tossicità, infatti, alle dosi terapeutiche i meccanismi di protezione antiossidante dell'organismo sono sufficienti a controllare la produzione di radicali liberi -neutralizzandone l'azione nociva- e favorendo la reazione antiossidante che è alla base del meccanismo d'azione della terapia. Nella somministrazione per via sistemica è necessario definire il volume di sangue da prelevare. Di norma, è ritenuto accettabile un prelievo del 2% - 4% di sangue autologo, prendendo in considerazione il peso del paziente da trattare e considerando effetti o ricadute emodinamiche e ipovolemiche.

6.a CONTROINDICAZIONI ASSOLUTE

La somministrazione di ozono è controindicata ^{45-51 55,56}

- In **Associazione contemporanea con altri farmaci** nella stessa siringa o flacone per l'effetto ossidante della miscela.
- **Deficit di glucosio-6-fosfato deidrogenasi (G6PD)** nella somministrazione sistemica.
- **Vie di somministrazione intravenosa e intra-arteriosa** direttamente dalla siringa al torrente circolatorio da evitare.

6.b CONTROINDICAZIONI RELATIVE NELLA SOMMINISTRAZIONE SISTEMICA

- **Allergie al Citrato ed altri anticoagulanti.**

6c. RACCOMANDAZIONI NELLA TERAPIA SISTEMICA

Anamnesi positiva per epilessia. Alcune esperienze hanno testimoniato il possibile scatenarsi di una crisi in concomitanza con la somministrazione.¹¹⁻¹⁴

1 - **Gravidanza.** Nonostante non esistano studi scientifici che ne controindichino l'utilizzo ma, al contrario, sono riportate esperienze positive dell'ossigeno ozono terapia per il trattamento di alcune patologie legate alla gravidanza, l'utilizzo dell'ozono terapia sistemica può essere sconsigliato da un punto di vista medico-legale per evitare un contenzioso -oggi- dall'esito dubbio.⁵²⁻⁵⁴

2 - **Sport agonistico.** Sebbene non esistano studi scientifici che ne controindichino l'utilizzo poiché l'ozono

esercita una benefica funzione antiossidante, le attuali normative in materia di doping ne vietano l'uso per via sistemica.

3 - **Pazienti in terapia con Dicumarolici.** Si raccomanda di monitorare più frequentemente l'INR in corso di terapia sistemica con ozono.^{11,13}

4 - **Malattia di Basedow Graves e stati di Iperitiroidismo.** Allo stato attuale in letteratura è difficile reperire lavori scientifici adeguati che dimostrino gli eventuali effetti collaterali dell'ozono terapia in pazienti affetti da l'ipertiroidismo, tiroiditi autoimmuni o simili.¹³

7. APPLICAZIONI CLINICHE

La qualità delle prove è stata valutata in base al tipo di fonte (meta-analisi e revisione sistematica di trials clinici randomizzati) e altri fattori come validità statistica e rilevanza clinica.^{11-14, 57} I livelli di evidenza sono stati adattati dalla U.S. Preventive Service Task Force e dal Centro per la Medicina Basata sulle Evidenze

Le patologie sensibili al trattamento con ossigeno-ozono possono essere classificate in tre categorie secondo la Medicina Basata sulle Evidenze (EBM). I livelli di evidenza selezionati nell'ozonoterapia sono stati classificati come:

Impieghi con Evidenza di tipo A:

Basata su revisioni sistematiche con trials controllati randomizzati, revisioni sistematiche con omogeneità di studi di coorte oppure revisioni sistematiche con omogeneità di studi caso-controllo.^{58- 91, 134, 135, 138-144-145-147-151}

- **Malattie della colonna vertebrale: ernia discale, protrusioni discali, discopatie, sindrome delle faccette articolari.**
- **Gonartrosi e condromalacia rotulea.**

Impieghi con Evidenza di tipo B:

Basata su trials controllati randomizzati individuali, studi di coorte o di caso-controllo.^{50, 92 - 102, 118, 133,136 - 142 -150, 160, 178, 179, 183 - 197, 188, 194, 224, 228, 232, 241-255}

- **Fibromialgia**
- **Ischemie degli arti**
- **Malattie infettive cutanee acute o croniche causate da batteri, virus e funghi**
- **Neuropatia causata dalla chemioterapia**
- **Patologie ortopediche: osteoartrite localizzata, tendinopatie, sindromi canalicolari degli arti**
- **Piede diabetico**
- **Sindrome di Bastrup**
- **Spondilolisi**
- **Spondilolistesi**

- **Stenosi canalare**
- **Ulcere cutanee e ustioni**
- **Mielopatia spondilogenica**
- **Articolazione Temporo Mandibolare (ATM)**

Impieghi con Evidenza di tipo C:

Basata su opinioni di esperti
 senza valutazioni critiche esplicite, case report, fisiologia, ricerche di laboratorio,
 epidemiologia descrittiva.^{13,103-132-137-139-140-141-143-146-148, 256-265}

- **Asma bronchiale**
- **Astenia correlata al cancro.** L'ozonoterapia, associata alla terapia convenzionale, può diminuire gli effetti collaterali della terapia oncologica, accelerare e migliorare i risultati. Pertanto, l'ossigeno-ozono è da considerarsi terapia di supporto. Inoltre ai dosaggi impiegati nella terapia infiltrativa l'ozono non può indurre mutazioni oncogene
- **Demenza senile, M. Alzheimer**
- **Endometriosi e patologie croniche ginecologiche**
- **Malattia infiammatoria cronica dell'intestino**
- **Malattie autoimmuni:** sclerosi multipla, artrite reumatoide, malattie infiammatorie croniche intestinali, sindrome di Raynaud
- **Malattie del fegato: epatite A, B, C**
- **Malattie polmonari quali enfisema, fibrosi polmonare, sindrome da distress respiratorio acuto, BPCO**
- **Morbo di Parkinson**
- **Oftalmologia:** retinopatia diabetica, degenerazione maculare senile, retinite pigmentosa, glaucoma cronico, maculopatia secca
- **Panniculopatia edemato-fibrosa (cellulite)**
- **Patologie interessanti le Tube di Eustachio**
- **Sclerosi Laterale Amiotrofica (SLA)**
- **Sclerosi Multipla**
- **Sepsi grave e disfunzione multi organo**
- **Sindrome da fatica cronica**
- **Trattamento della carie ed altri disturbi a livello dentale, parodontopatie**

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