Medical Policy Manual Medicine, Policy No. 173

Hyperoxemic Reperfusion Therapy

Effective: September 1, 2023

Next Review: May 2024
Last Review: July 2023

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Hyperoxemic reperfusion therapy, also known as supersaturated oxygen infusion therapy, intracoronary hyperoxemic perfusion, and aqueous oxygen therapy, is a treatment where supersaturated oxygen is reinfused into a person's blood stream at the location of a cardiac injury.

MEDICAL POLICY CRITERIA

The use of hyperoxemic reperfusion therapy is considered **investigational** for all indications, including but not limited to acute myocardial infarction, cardiogenic shock, and stroke.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

None

BACKGROUND

Hyperoxemic reperfusion (HR) therapy, also known as supersaturated oxygen infusion therapy,

intracoronary hyperoxemic perfusion, and aqueous oxygen therapy, is a treatment where supersaturated oxygen is reinfused into a person's blood stream at the location of a cardiac injury is intended to reduce the damage to cardiac tissue in the event of a cardiac injury including cardiogenic shock, stroke, or myocardial infarction. HR therapy involves removing arterial blood followed by a supersaturation of oxygen which is then reinfused into the person's blood stream at the location of the cardiac injury. This is often a percutaneous procedure done in conjunction with a coronary artery stent placement.

REGULATORY STATUS

The FDA granted premarket approval (PMA P170027) for the TherOx Downstream® System manufactured by TherOx Inc in April of 2019.[1] According to the FDA PMA letter, the TherOx Downstream System is:

> Indicated for the preparation and delivery of SuperSaturated Oxygen Therapy (SSO2 Therapy) to targeted ischemic regions perfused by the patient's left anterior descending coronary artery immediately following revascularization by means of percutaneous coronary intervention (PCI) with stenting that has been completed within 6 hours after the onset of anterior acute myocardial infarction (AMI) symptoms caused by a left anterior descending artery infarct lesion.

EVIDENCE SUMMARY

Randomized Controlled Trials

The Acute Myocardial Infarction with Hyperoxemic Therapy (AMIHOT) I study included 269 subjects with acute anterior or large inferior myocardial infarction (MI) who were assigned to receive either hyperoxemic reperfusion therapy or normoxemic blood autoreperfusion.[2] The primary endpoints were final infarct size at 14 days, ST-segment resolution, and delta regional wall motion score index at three months. At 30 days follow-up, there was no significant difference in the incidence of the primary endpoints between the study groups. A post-hoc analysis showed that subjects who were treated with HR therapy for longer than six hours with anterior acute MI showed a greater improvement in regional wall motion, smaller infarct, and improved ST-segment resolution compared with normoxemic controls.

Stone (2009) published the AMIHOT II study including 301 subjects with anterior ST-segment myocardial infarction (MI) who were randomized to receive standard treatment or 90 minutes of HR with supersaturated oxygen perfusion combined with standard treatment.[3] The primary efficacy endpoint was infarct size and the primary safety endpoint was a composite adverse cardiovascular event score at 30 days. The authors reported the difference in infarct size (IS) was 26.5% in the control group compared with 20.0% in the HR group. In subjects with a left ventricular ejection fraction (LVEF) of less than 40%, IS was reduced from 33.5% in the control group to 23.5% in the HR group. For subjects with LVEF greater than 40%, these differences were not observed. There were no significant differences found between groups in terms of ST-segment measurement or cardiac biomarkers. There was no significant difference in adverse cardiovascular events after 30 days between the two treatment groups.

Nonrandomized Studies

David (2019) reported the outcomes of the IC-HOT trial, non-randomized, single-arm study which evaluated the safety of HR delivered to the left main coronary artery for 60 minutes in 100 subjects with anterior ST-elevation after coronary intervention.[4] HR therapy was administered to the left main coronary artery (LMCA) after stent placement in 100 participants with cardiac injury within six hours of the onset of symptoms. The primary endpoint was the 30-day composite of adverse clinical events compared to an objective performance goal of 10.7%. The composite adverse clinical events score at 30 days developed in 7.1% of participants. At four days, the median IS was 24.1% and at 30 days, the median IS was 19.4%. The authors concluded that supersaturated oxygen therapy was associated with

a favorable early safety profile. The study has significant limitations including a non-randomized design, an unmatched historical cohort, and the use of a safety endpoint and no efficacy endpoints. Larger randomized trials assessing the efficacy of HR are needed.

Chen (2021) published a one-year follow up study to the IC-HOT trial where clinical outcomes were compared with a propensity-matched control group of patients with anterior ST-elevation MI. Supersaturated oxygen therapy was associated with lower composite endpoint of all-cause death or new-onset heart failure (HF) or hospitalization for HF after one year. There were no significant differences at one year between treatment groups in the rates of reinfarction or target vessel revascularization. This follow-up study suffers from the same limitations as the David study described above.

Trabattoni (2006) published a non-randomized trial comparing 51 subjects with acute MI who received HR therapy for 90 minutes or standard therapy.[5] Subjects were treated at 12 hours or less after onset of symptoms by percutaneous coronary intervention. The authors reported participants in the HR group showed a significantly shorter time-to-peak creatine kinase release, a shorter creatine kinase half-life period, and a higher rate of complete ST-segment resolution. At three months post treatment, the HR group showed a significant improvement of mean left ventricular ejection fraction and wall motion score index. This study is limited by a small sample size and a non-randomized study design.

Section Summary

There are a limited number of published high-quality studies evaluating the safety and efficacy of HR therapy for the treatment of individuals with MI. The IMIHOT trial showed no significant difference in primary endpoints between treatment and control groups and the IC-HOT trial has significant study design limitations. Additional well-designed studies with appropriate comparators and long-term results are necessary to establish the clinical utility and efficacy of HR therapy in individuals with MI.

PRACTICE GUIDELINE SUMMARY

No clinical practice guidelines were identified addressing the use of hyperoxemic reperfusion therapy for any indication.

SUMMARY

There is not enough research to show that hyperoxemic reperfusion (HR) therapy improves health outcomes for people with any indication, including but not limited to acute myocardial infarction, cardiogenic shock, and stroke. No clinical guidelines based on research address the use of HR therapy for people with any indication. Therefore, HR therapy is considered investigational for all indications, including but not limited to acute myocardial infarction, cardiogenic shock, and stroke.

REFERENCES

1. Approval FP. FDA Premarket Approval (PMA) TherOx Downstream System. [cited 7/10/2023]. 'Available from:' https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P170027.
2. O'Neill WW, Martin JL, Dixon SR, et al. Acute Myocardial Infarction with Hyperoxemic Therapy (AMIHOT): a prospective, randomized trial of intracoronary hyperoxemic

reperfusion after percutaneous coronary intervention. *J Am Coll Cardiol.* 2007;50(5):397-405. PMID: 17662390
3. Stone GW, Martin JL, de Boer MJ, et al. Effect of supersaturated oxygen delivery on infarct size after percutaneous coronary intervention in acute myocardial infarction. *Circ Cardiovasc Interv.* 2009;2(5):366-75. PMID: 20031745
4. David SW, Khan ZA, Patel NC, et al. Evaluation of intracoronary hyperoxemic oxygen therapy in acute anterior myocardial infarction: The IC-HOT study. *Catheter Cardiovasc Interv.* 2019;93(5):882-90. PMID: 30265429
5. Trabattoni D, Bartorelli AL, Fabbiocchi F, et al. Hyperoxemic perfusion of the left anterior descending coronary artery after primary angioplasty in anterior ST-elevation myocardial infarction. *Catheter Cardiovasc Interv.* 2006;67(6):859-65. PMID: 16649231

CODES

Codes	Number	Description
CPT	0659T	Transcatheter intracoronary infusion of supersaturated oxygen in conjunction with percutaneous coronary revascularization during acute myocardial infarction, including catheter placement, imaging guidance (eg, fluoroscopy), angiography, and radiologic supervision and interpretation
HCPCS	None	

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