



شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم



شبكة المعلومات الجامعية
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شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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توطئة للحصول على درجة الماجستير / الدكتوراه
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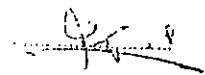
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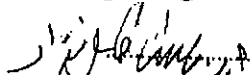
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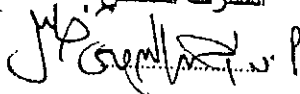
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NITRIC OXIDE
IN
ANAESTHETIC PRACTICE

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{ M.SC } OF
ANESTHESIOLOGY

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CP



DEDICATION

*I dedicate this work to my loving family, Misoon and
all my sweet friends for their help and assistance.*

Abstract

Nitric oxide (NO) is a unique molecule in the human body and is responsible for normal neurologic function, vasodilator tone and modulation of the inflammatory response. Massive endogenous release of NO appears to play a central role in sepsis and the systemic inflammatory response syndrome. Inhaled NO (1-80 ppm) can markedly attenuate pulmonary vasoconstriction and improve hypoxemia due to ventilation perfusion mismatch.

However, excessive doses of inhaled NO exacerbate acute inflammation and induce lung injury by the action of NO itself or its reactive metabolites. Thus far, its use has received FDA approval only for persistent pulmonary hypertension of the newborn (PPHN). However, on an investigational basis it can be used in lung and heart transplantation and LVAD insertion. Although prospective studies have not demonstrated that inhaled NO improves outcome in ARDS, its use as a component of an algorithmic approach has achieved an impressive survival rate. Other conditions in which inhaled NO shows promise include primary pulmonary hypertension, sickle cell Anemia and hypoxic chronic obstructive lung disease.

Key word:

Nitric oxide, Anaesthetic, ARDS, Pulmonary Hypertension, SIRS

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Introduction

The physiologic impact of nitric oxide (NO) was discovered upon the scientific community as recently as 1987, when it was determined that endothelium-derived relaxing factor (EDRF) and NO were one and the same. Hitherto, this small, highly unstable diatomic free radical was considered to be an atmospheric pollutant derived from the combustion of fossil fuel (i.e. automobile exhaust) tobacco or lightning ⁽¹⁾. Its concentration in the atmosphere is 10-100 parts per billion (ppb) ; in heavy traffic it is often more than 1.5 parts per million (ppm) and in the depth of a glowing cigarette it may reach 400 -1000 ppm ⁽²⁾.

NO is now recognized as vasodilator, a neurotransmitter ⁽¹⁾ and an immunomodulator which plays roles in cardiovascular, pulmonary, renal ⁽³⁾, gastroenterologic, urologic and neurologic disease states.

The last decade has seen an exponential growth in the scientific literature and knowledge of the multiple physiologic roles of endogenous NO and its therapeutic application by inhalation in the dose range of 1-80 ppm.

This essay will provide basic review of the pharmacology of nitric oxide, the normal physiological effects of endogenous NO, and role of deficient or excessive NO production in specific disease processes.

Finally, it will review the development of inhaled NO as a therapy for pulmonary disorders, including the adult respiratory distress syndrome and pulmonary hypertension. It will also discuss its use in current anesthesia to obviate when and how to use it ?

Endogenous synthesis of NO

Nitric oxide is synthesized from the amino acid, L-arginine, by a group of flavin-containing oxygenase enzymes commonly termed nitric oxide synthase (NOS) (Fig.1) ⁽⁴⁾. Endothelial cells were the first mammalian cells shown to release NO, a potent vasodilator. It is now accepted that various cell types can release NO and that at least three distinct isoforms of NOS exist.

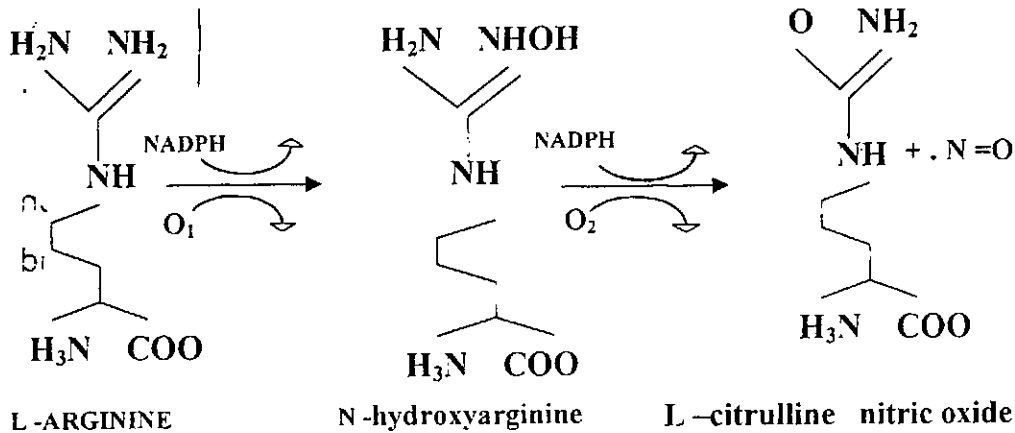


Fig.1: chemical reactions involved in the synthesis of nitric oxide. L-arginine is converted to L-citrulline and nitric oxide. The reaction is catalysed by nitric oxide synthase (NOS) in the presence of oxygen and the co-substrate nicotinamide adenine dinucleotide diphosphate (NADPH). NOS requires several cofactors including flavones and tetrahydrobiopterin.