THE EFFECT OF ACUTE CARBON MONOXIDE EXPOSURE ON THE BRAIN OF THE CONSCIOUS SHEEP

by

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Abbreviations

CO	carbon monoxide
cGMP	guanosine 3,5-monophosphate
COHb	carboxyhaemoglobin
Hb	haemoglobin
Hypoxia	hypoxic hypoxia
PO_2	oxygen partial pressure
PCO	carbon monoxide partial pressure
L/min	litres per minute
pH	-log [H ion]
mmHg	millimetres of mercury
ppm	parts per million
CSER	cerebral somatosensory evoked responses
CortSER	cortical somatosensory evoked responses
PaO_2	arterial oxygen partial pressure
IL482	Instrument Laboratories 482 CO-Oximeter
RHb	reduced haemoglobin
MetHb	met-haemoglobin
CaO	arterial oxygen content
CvO	venous oxygen content
mls	millilitres
Calc	calculated
HR	heart rate
$P_{et}CO_2$	end-tidal carbon dioxide concentration

Abbreviations (cont)

CBF	cerebral blood flow
$C_a[O_2]$	arterial oxygen content
$C_v[O_2]$	venous oxygen content
THb	total haemoglobin
nm	nanometres
mgs	milligrams
C_{red}	fractional concentration of reduced haemoglobin
C_{O2}	fractional concentration of oxyhaemoglobin
C_{CO}	fractional concentration of carboxyhaemoglobin
C_{met}	fractional concentration of met-haemoglobin
k	scalar constant
$[E]^{-1}$	inverse matrix
Sat_{COHb}	saturated carboxyhaemoglobin
Hct	haematocrit
g	grams
umol/min	micro-moles per minute

Abstract

The prevalent hypothesis of carbon monoxide toxicity is based on the combination of carbon monoxide binding to haemoglobin forming carboxyhaemoglobin (causing a fall in the bloods oxygen carrying capacity) and the reduction in the dissociation of oxygen from haemoglobin.

Although the relationship between inspired carbon monoxide concentration and the level of carboxyhaemoglobin level in the blood is well recognised, the relationship between carboxyhaemoglobin level, the oxygen status of critical organs such as the brain and heart and the progression of the acute symptoms is uncertain.

This thesis examines the relationship between carboxyhaemoglobin level and critical organ status, with particular reference to the brain, in eight chronically instrumented conscious sheep whilst being progressively exposed to carbon monoxide in the expired breath, to simulate an acute human poisoning.

In all sheep, the carboxyhaemoglobin levels at the end of the exposure to carbon monoxide was approximately 65 percent. Mean arterial blood pressure remained unchanged with the exception of two sheep, where carbon monoxide administration was stopped at 25 minutes due to a sudden onset of hypotension. Oxygen delivery to the brain was sustained throughout the administration of carbon monoxide due to a significant increase in cerebral blood flow. There was no evidence of metabolic acidosis or lactate production by the brain, suggesting the brain did not become hypoxic during the time course of the carbon monoxide exposure. Oxygen consumption by the brain decreased progressively, and the sheep showed behavioural changes which varied from agitation to sedation to narcosis. The mechanism of these changes was therefore probably unrelated to hypoxia, however, may have been due to raised intracranial pressure or a direct effect of carbon monoxide on brain function.

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