

OPIOID INDUCED RESPIRATORY DEPRESSION

Essay

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List of Abbreviations

APSF	<i>Anesthesia patient safety foundation</i>
CNS	<i>Central nervous system</i>
CPAP	<i>Continuous positive airway pressure</i>
DOP	<i>Delta opioid peptide</i>
ETCO₂	<i>End tidal carbon dioxide</i>
GCF	<i>General care floor</i>
JCAHO	<i>Joint commission on the accereditation of healthcare organizations</i>
KOP	<i>Kappa opioid peptide</i>
MAOI	<i>Mono aminooxidase inhibitor</i>
MOP	<i>Mu opioid peptide</i>
NMDA	<i>N-methyl D-aspartate</i>
NOP	<i>Nociceptin orphanin FQ peptide</i>
NSAID	<i>Non steroidal anti-inflammatory drug</i>
OSA	<i>Obstructive sleep apnea</i>
OSAH	<i>Obstructive sleep apnea hypopnea</i>
PAG	<i>Peri-aqueductal grey area</i>
PCA	<i>Patient controlled analgesia</i>
Pco₂	<i>Carbon dioxide pressure in the arterial blood</i>
Po₂	<i>Oxygen pressure in the arterial blood</i>
SDB	<i>Sleep disordered breathing</i>
SG	<i>Substantia gelatinosa</i>

INTRODUCTION

Opioid analgesics remain the most commonly used drugs in the treatment of moderate to severe postoperative pain. The opioids that have been used for decades (such as morphine, methadone, and fentanyl) have become accepted treatments and are administered to patients by anesthesiologists under standard protocols.

Side effects related to opioid use have become well known and may be managed appropriately, with nausea, vomiting, sedation, and respiratory depression being associated commonly with postoperative analgesic doses. However, these side effects should not be trivialized. Postoperative nausea and vomiting is common and distressing to patients, and excessive sedation may contribute to increased morbidity and mortality. However, it is perhaps respiratory depression that remains the main hazard of opioid use, uppermost in the minds of nurses and physicians, because of the obvious risk of fatal outcome.

The first recorded human fatality from a morphine overdose dates from the 1850s. The Englishman Alexander Wood (1817–1884) performed one of the first injections of morphine to his wife who subsequently died from respiratory depression (*Macario and Pergolizzi, 2004*).

The toxic effects of morphine were noted earlier by Sertürner, the German pharmacist who was the first to isolate morphine from opium in 1806. In 1817, he published his discovery together with reports of the administration of the alkaloid to himself, three young boys, three dogs, and a mouse. One of the dogs died while he described the effect that morphine had on himself and his three young “volunteers” as near fatal (*Huxtable and Schwarz, 2000*).

Because of these side effects which is unpredicted and can occur postoperative where high trained medical care may become unavailable. Studies and researches have made to search for the ideal analgesic which can decrease the pain and protect the patient from its effect on heart and in the same time by pass the side effects.

AIM OF THE WORK

The aim of this study is to investigate the incidence, reversal and how to prevent and anticipate opioid induced respiratory depression.

CONTROL OF RESPIRATION

The nervous system normally adjusts the rate of alveolar ventilation almost exactly to the demands of the body so that the oxygen pressure (P_{O_2}) and carbon dioxide pressure (P_{CO_2}) in the arterial blood are hardly altered even during heavy exercise and most other types of respiratory stress (*Jordan, 2001*).

The respiratory center is composed of several groups of neurons located bilaterally in the medulla oblongata and pons of the brain stem. It is divided into three major collections of neurons: (1) a dorsal respiratory group, located in the dorsal portion of the medulla, which mainly causes inspiration; (2) a ventral respiratory group, located in the ventrolateral part of the medulla, which mainly causes expiration; and (3) the pneumotaxic center, located dorsally in the superior portion of the pons, which mainly controls rate and depth of breathing. The dorsal respiratory group of neurons plays the most fundamental role in the control of respiration (figure-1) (*Kara et al., 2003*).

A. Dorsal respiratory group of neurons:

The dorsal respiratory group of neurons extends most of the length of the medulla. Most of its neurons are located within the nucleus of the tractus solitarius, although additional neurons in the adjacent reticular substance of the

medulla also play important roles in respiratory control. The nucleus of the tractus solitarius is the sensory termination of both the vagal and the glossopharyngeal nerves, which transmit sensory signals into the respiratory center from (1) peripheral chemoreceptors, (2) baroreceptors, and (3) several types of receptors in the lungs.

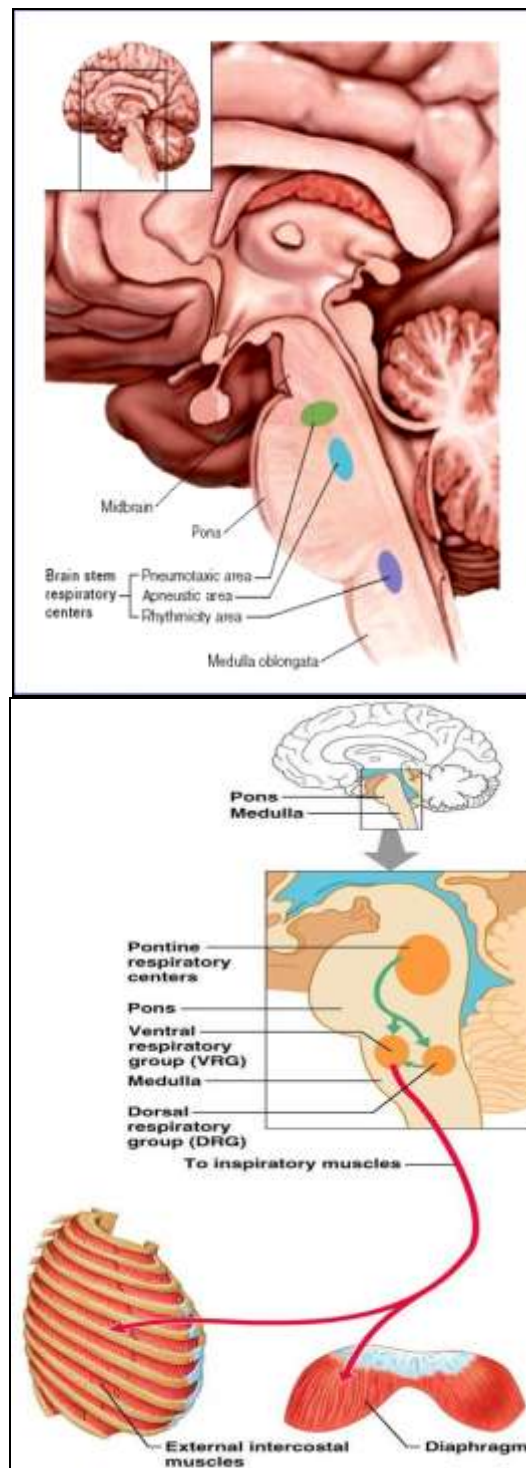


Figure (1): The respiratory center (Semenza, 2004).

Rhythmical inspiratory discharges from the dorsal respiratory group:

The basic rhythm of respiration is generated mainly in the dorsal respiratory group of neurons. Even when all the peripheral nerves entering the medulla have been sectioned and the brain stem transected both above and below the medulla, this group of neurons still emits repetitive bursts of inspiratory neuronal action potentials **(Richerson, 2004)**. The basic cause of these repetitive discharges is unknown. In primitive animals, neural networks have been found in which activity of one set of neurons excites a second set, which in turn inhibits the first. Then, after a period of time, the mechanism repeats itself, continuing throughout the life of the animal. Therefore, most respiratory physiologists believe that some similar network of neurons is present in the human being, located entirely within the medulla; it probably involves not only the dorsal respiratory group but adjacent areas of the medulla as well, and is responsible for the basic rhythm of respiration **(Feldman et al., 2003)**.

Inspiratory “Ramp” Signal:

The nervous signal that is transmitted to the inspiratory muscles, mainly the diaphragm, is not an instantaneous burst of action potentials. Instead, in normal respiration, it begins weakly and increases steadily in a ramp manner for about 2 seconds. Then it ceases abruptly

for approximately the next 3 seconds, which turns off the excitation of the diaphragm and allows elastic recoil of the lungs and the chest wall to cause expiration (*Motorola et al., 2000*).

Next, the inspiratory signal begins again for another cycle; this cycle repeats again and again, with expiration occurring in between. Thus, the inspiratory signal is a ramp signal. The obvious advantage of the ramp is that it causes a steady increase in the volume of the lungs during inspiration, rather than inspiratory gasps (*Jordan, 2001*). There are two qualities of the inspiratory ramp that are controlled, as follows:

1. Control of the rate of increase of the ramp signal, so that during heavy respiration, the ramp increases rapidly and therefore fills the lungs rapidly.
2. Control of the limiting point at which the ramp suddenly ceases.

This is the usual method for controlling the rate of respiration; that is, the earlier the ramp ceases the shorter the duration of inspiration. This also shortens the duration of expiration. Thus, the frequency of respiration is increased (*Hilaire et al., 2003*).

B. Pneumotaxic center:

A pneumotaxic center, located dorsally in the nucleus parabrachialis of the upper pons, transmits signals to the
