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Editorial

MANAGEMENT OF DYSPNOEA DUE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Dyspnoea, an unpleasant sensation of difficulty in breathing is common symptoms of multiple pathologies. In chronic obstructive pulmonary disease (COPD) it is one of the most disabling symptoms. The underlying mechanisms generating this sensation are not clearly understood. The specific treatment of dyspnoea is still in the experimental stage. The severity of the sensation is related to the degree of airflow obstruction. Although much of the obstruction is not reversible with standard bronchodilator treatment, it is possible that commonly used drugs may have extrapulmonary actions, which reduce dyspnoea. Theophylline strengthens diaphragmatic contraction[1] and increases cardiac output[2], but the clinical significance of these observations has not been fully determined and properly documented.

Investigations are in the progress to elucidate the precise mechanisms, which produce the sensation of dyspnoea, in the areas of respiratory physiology, neurophysiology, pulmonary medicine and psychiatry. The perception of respiratory muscles effort appears to be quantitatively related to the intensity of the sensation of breathlessness[3]. Patients COPD also have reduced perception in the sensation of inspired volume during non-loaded breathing or of respiratory muscles force during inspiratory maneuvers[3]. This has led to the suggestion by Gottfried and colleagues[3] that these reductions in respiratory sensation are due to separate signals. The complex, multidimensional nature of these perceptions may explain the understanding of dyspnoea, which has remained elusive and indefinable.

The hypothesis that dyspnoea might be reduced by pharmacological alternations of signal processing in the central nervous system has attracted and fascinated a number of investigators. Benzodiazepine derivatives were initially reported to hold some therapeutic promise[4,5] however, subsequent studies[6,7] carried by Man and colleagues[8] have shown no significant benefit and considerable side effects with the use of these agents. Promethazine, a phenothiazine with antihistaminic and sedative properties, has also been reported to improve dyspnoea and exercise tolerance in normal individuals[8]. Patients with COPD may also benefit to a very modest degree by promethazine[9].

The effects of narcotics on respiratory drive are well known and recognized. The concept of

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Dyspnoea as a " pain equivalent" regulated by endogenous opiates is supported the observation that naloxone, an opiate antagonist, restores blunted ventilated load responses in COPD patients[10]. It has been suggested by Woodcock and associates[11] that narcotics may improve dyspnoea by decreasing oxygen consumption out of proportion to minute ventilation. Although acute administration of dihydrocodeine reduces dyspnoea by up to 20% long-term opiate treatment has variable effects on breathlessness and is associated with significant side effects notably increases in PCO_2, which probably outweigh the potential benefits.

Symptomatic drug treatment of breathlessness using benzodiazpines or systematic opiates is of a very limited value and associated with unacceptable adverse effects. Recently there has been much interest in the use of nebulized morphine for the relief of dyspnoea in COPD[12] and also in patients with malignant disease. It is simple and bloodless, delivers morphine directly into the pulmonary blood stream avoiding hepatic first pass metabolism and is reported to result in rapid analgesia[13] presenting with dyspnoea.

It may be particularly suitable for patients unable to take morphine by mouth who wish to avoid injections. It is also believed that nebulized morphine can relieve breathlessness associated with cancer and chronic chest diseases by a direct action on lung receptors[13]. One placebo-controlled trial showed a small increase in exercise endurance in patients with chronic airflow obstruction[12], while another study has not[14]. More recently, Masood and colleagues[15] used nebulized morphine in patients with severe chronic airflow obstruction and noticed that their studies did not support the hypothesis that nebulized morphine relieves breathlessness and altered sensation of breathlessness. The observed improvements in dyspnoea with these agents are modest at best and probably due to nonspecific sedation by these drugs. The concomitant reduction in minute ventilation is a potentially serious adverse effect in patients with marginal pulmonary function and the use of such drugs cannot be routinely recommended in patients with severe COPD.

It is therefore concluded that for achieving maximum therapeutic benefit in COPD patients it is essential to know the underlying mechanism of sensation of breathlessness. Since low dose nebulized morphine does not relieve breathlessness. The possibility remains that it may reduce breathlessness if given in still higher doses or to patient groups. Further studies using higher doses, more potent opiates or those, which because of their physical properties persist within the lung for longer, would be worthwhile.

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