

# Hypoxia and stroke

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## Introduction

Hypoxia after acute stroke is common, underdiagnosed and undertreated. Partial oxygen pressure falls with age, with values well above 12 kPa at the age of 20, about 11 kPa at 50 years and just above 9 kPa in 70 year old subjects. The normal range of oxygen saturation is  $97 \pm 2\%$  in younger adults, but in healthy older people the mean is slightly lower at 95% [1, 2].

## Prevalence

Sulter *et al.* reported that 63% of stroke patients had at least one episode of hypoxia, defined as a saturation of less than 96% for more than 5 minutes [3]. In a recent local study we found that the mean oxygen saturation in awake stroke patients was 94.5%, which was about 1% lower than in controls. It might be argued that a 1% difference is not clinically relevant, even if statistically significant. However, the S-Shape of the oxygen dissociation curve means that small falls in arterial oxygen pressure do not result in any changes in saturation. Thus any drop in saturation signifies that arterial oxygen pressure has already fallen considerably. This does not necessarily apply to single bedside assessments of oxygen saturation, since most oximeters have a 2% margin of error for each measurement. But even here a persistent change in saturation, which represents multiple individual assessments, is reliable since random errors even out over repeated measurements.

## Effects of hypoxia

The effects of severe and prolonged hypoxia are obvious, but the relationship between mild hypoxia and outcome has been addressed by a number of studies [1]. Silva *et al.* reported that hypoxia doubled the risk of early deterioration after stroke. There is also evidence to link nocturnal desaturations to functional outcome with lower Barthel scores at 12 months in those with frequent nocturnal desaturations. Sandberg *et al.* demonstrated an association between nocturnal desaturations,

delirium, mood and low ADL. In a group of 185 stroke patients followed over 5 years Moroney *et al.* found that patients with hypoxic ischaemic events such as heart failure, seizures, pneumonia, sepsis, myocardial infarction and arrhythmias during the post stroke hospital admission were more likely to be diagnosed as having dementia than patients without such events. Although mild hypoxia is associated with adverse outcomes, there is no direct evidence for a causative link. However, until more is known, it is sensible to assume that preventing hypoxia is a reasonable and safe strategy.

## Causes of hypoxia

To prevent and treat hypoxia after stroke adequately, it is important to be aware of its causes. These include aspiration, positioning of the patient, medical complications, sleep apnoea, changes in the central regulation of respiration, and stroke related weakness of respiratory muscles.

Stroke patients are at risk of aspiration because of reduced oropharyngeal sensation and impaired cough response. Dysphagia can be demonstrated in up to 50% of stroke patients within the first week. Some are clearly symptomatic, but aspiration is silent in the majority. Oxygen desaturation of more than 2% after a water swallow test is a good clinical indicator of aspiration [4]. The extent and duration of desaturation is affected by food consistency and may be more prolonged with solid aspiration. Aspiration of secretions is common in patients who are nil by mouth, and airway protection is particularly important in this group.

There are several reasons to think that oxygenation after stroke should be affected by body position. Upright position is likely to reduce aspiration. In the presence of diaphragmatic weakness, oxygenation should be better when upright than when supine. Data from clinical studies are contradictory. Elizabeth *et al.* demonstrated a 1% difference in oxygen saturation between the supine and propped up positions. In the largest study published so far, Rowat found a higher oxygen saturation in sitting than in lying. Amongst the supine positions, lying on the right was associated with better oxygenation

no matter whether the patient had right or left hemiparesis [5]. In contrast, Chatterton did not show a difference in oxygen saturation when patients were sitting in a chair, sitting propped up in bed, or lying good side down and bad side down at a 45 degree tilt. However, there was no supine group in the latter study. On the balance of current evidence, sitting and propped up in bed positions appear to be preferable to lying supine.

Complications such as pneumonia, pulmonary emboli, fluid overload and arrhythmias are common and treatable causes of hypoxia after stroke. Since such complications are unlikely to be present on admission, it is important to continue monitoring oxygen saturation, even in patients with normal oxygenation on presentation.

Sleep apnoea has been variously cited as occurring in 44–95% of patients after stroke, and is easily missed without oximetry. It is usually defined as more than 10 desaturations per hour of sleep, and may be obstructive, central, or mixed [6]. While the typical sleep apnoea patient in the community is male, overweight and snores loudly, many patients with sleep apnoea after stroke have none of the typical characteristics. In stroke patients airway collapse may not be due to the anatomical shape of the neck and oropharynx, but due to centrally mediated changes in upper airway tone [6].

When considering the effects of the stroke on the central regulation of respiration [7], impaired airway protection and reduced respiratory drive spring to mind since apnoea is the usual cause of death in patients with brain stem strokes and transtentorial herniation. It is less appreciated that hyperpnoea is a common sequel of stroke. The cortex has an inhibitory function on respiration, and cortical damage therefore leads to an increase in respiratory rate. Hyperventilation is strongly associated with poor outcome. Cheyne-Stokes respiration may be seen in up to 50% of stroke patients at some point in their illness. It is most common in bilateral cortical lesions, but may also occur with unilateral lesions, infratentorial lesions and without any cerebral pathology, particularly in subjects with cardiovascular disease. Although it is usually seen as a harbinger of death, especially in large strokes and with cerebral oedema, it also occurs in clinically stable conscious patients. Lesions in the brainstem slow the respiratory rate, and lesions in the medulla oblongata cause apnoea.

Weakness of respiratory muscles on the hemiparetic side may also be considered as a cause of hypoxia after stroke, but there is little evidence that it plays a major role. Cortical stroke results in weakness of voluntary, but not involuntary, action of the intercostal muscles and the diaphragm on the affected side. Clinical manifestations of this would be reduced breath sounds on the affected side on deep inspiration and an elevated hemidiaphragm on the chest X-ray. Since only voluntary, but not automatic, respiratory movements are reduced,

this should not affect baseline oxygenation, but may make the patient more prone to infection on the affected side.

### Prevention and treatment

In the management of hypoxia after stroke it is important to realise that respiratory suppression is a very late, and pre-terminal event in stroke. If a conscious stroke patient is hypoxic, the most likely cause is reversible and peripheral rather than central. Oxygen supplementation may be required, but should not be the only or the main treatment strategy. Airway management and mechanical removal of secretions is of primary importance in all patients with a reduced level of consciousness, dysphagia and/or inadequate cough. Further issues to pay particular attention to are positioning of the patient, avoidance of sedative medication, prevention of aspiration, and treatment of complications and concomitant medical conditions. The role of mechanical ventilation after stroke remains unclear, but is likely to have a limited place in the management of stroke patients.

National and international stroke guidelines unanimously stress that hypoxia must be prevented and, if present, treated vigorously. The level of oxygen desaturation at which treatment should be started is, however, not defined. For a more general patient population the American College of Chest Physicians and the National Heart and Lung Institute recommend oxygen supplementation if the oxygen saturation falls below 90%. Perfusion increases in the healthy brain in response to hypoxia, thus compensating for lower oxygen saturation of the circulating blood. This adaptation does not occur in the ischaemic brain, where blood flow is limited or absent, making stroke patients more vulnerable to the effects of hypoxaemia. I would argue that any fall of oxygen saturation should be taken seriously in patients with cerebral ischaemia, and that treatment should be started early. Since the mean oxygen saturation for older people is 95% [2], this value may be a reasonable cut off point for initiating therapy.

Very little is known about the best management of Cheyne-Stokes respiration after stroke. In a small uncontrolled case series Nachtmann found that oxygen supplementation at a rate of 2 l/minute lead to normalization of the respiratory pattern and an improvement in oxygen saturation in 5/5 cases. In the same study he reports similar improvements of oxygenation and respiratory pattern in 7/7 patients treated with a 250 mg theophylline infusion over 1 hour [8].

The gold standard treatment for obstructive sleep apnoea is nocturnal CPAP ventilation via a facial mask. This treatment is, however, poorly tolerated after stroke and, given the high prevalence of sleep apnoea, not practical for the majority of sufferers. Oxygen supplementation has been suggested as an alternative.

## C. Roffe

Frohnhofen *et al.* tested the effectiveness of oxygen supplementation in stroke patients with sleep apnoea unwilling to try CPAP ventilation and report a reduction in the number of central and mixed apnoeas, but also a small increase in the duration of each apnoeic episode. Overall, however, the mean and lowest nocturnal oxygen saturation increased, and desaturations and the time spent with a saturation below 90% were reduced. Furthermore, oxygen treated patients performed better on cognitive tests after one week of treatment [9].

If oxygen treatment is thus effective in most types of post stroke hypoxia, and if hypoxia is often missed, it might be argued that it should be given routinely to all stroke patients. This question was addressed in a recent study of 292 patients with acute stroke who were randomized to receive 3 l oxygen/min via nasal cannulae or no routine oxygen [10]. There was a small, but statistically non-significant, excess of deaths in the oxygen group. When patients were stratified for initial stroke severity (taking a Scandinavian Stroke Scale score of 40 as a cut off), oxygen treatment was associated with higher mortality in mild strokes and a trend towards less deaths in severe strokes. In their discussion the authors relate the increased mortality in oxygen treated patients with mild stroke to a possible hyperoxia related increase in free radical generation. Other conceivable explanations include a risk of infection due to oxygen administration sets and reduced early mobilization. In view of the findings of this study routine oxygen supplementation to all stroke patients cannot be recommended.

## Conclusion

In conclusion, hypoxia in stroke patients is commonly intermittent and more likely to occur at night. Continuous or regularly repeated monitoring is thus required for diagnosis. Oxygen treatment is effective in improving most types of hypoxia after stroke, but other measures such as airway management, positioning, prevention of aspiration and prevention and treatment of other medical complications should also be considered. In view of the potential adverse effect of oxygen treatment,

routine oxygen supplementation of all strokes cannot currently be recommended. In the absence of direct experimental evidence, a cut off point for oxygen saturation of less than 95% would be a reasonable level at which treatment should be commenced. Further research is required to characterise the patient groups who may benefit from oxygen supplementation and the relationship between oxygen supplementation, oxygen saturation and outcome.

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