Anaesthetic gas analysers: potential for confusion and errors if you live and work at moderate altitude

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In this issue of the SAJAA, Smith et al report on the effects of various end-tidal concentrations of nitrous oxide on the processed electroencephalogram (EEG) in the presence of approximately 1 MAC of sevoflurane. At low concentrations (10–60%), nitrous oxide had minor effects on 'state entropy' as measured by the M-entropy S/5 Module (GE Healthcare). However, at 70% there were statistically significant and clinically important decreases in entropy. Whereas previous studies have shown that nitrous oxide when given alone has few if any effects on EEG entropy, when administered with 1 MAC volatile anaesthetic agent, there is a threshold at which the effects of the volatile agent are potentiated by nitrous oxide. These findings are in accordance with other reports concerning studies of the clinical effects of combinations of nitrous oxide and oxygen.

Smith et al conducted their study in Pretoria, which is situated at an altitude of approximately 1 400 m above sea level and where the average ambient pressure is about 86 kPa. Like any drug, the effects of nitrous oxide depend on the number of molecules that are dissolved in the brain tissues and this is determined by the tissue gas tension[§] according to Henry's law. Brain tissue gas tension is in turn determined by blood nitrous oxide tension and this in turn is determined by the alveolar partial pressure of the gas. This phenomenon has important implications with regard to reporting the findings by Smith et al, because 60% by volume of nitrous oxide administered in Pretoria does not exert the same clinical effect as 60% nitrous oxide at sea level. Thus at sea level where the average ambient pressure is taken to be 101.3 kPa, the partial pressure of 60% nitrous oxide is 60.8 kPa; however, in Pretoria the partial pressure is only 51.6 kPa. That it is the alveolar partial pressure of nitrous oxide that determines its clinical effect was validated 28 years ago by James et al,[1] who demonstrated in conscious volunteers that the analgesic effects of nitrous oxide are decreased at altitude when administered in identical percentage-by-volume concentrations. The distinction between expressing gas concentrations in terms of volumes percent and partial pressures is important if the results of Smith et al are to be compared with those of other studies, which presumably were conducted at altitudes close to sea level. At sea level, percentage concentrations by volume are virtually equivalent to partial pressures expressed in kPa. For this reason, in order to avoid confusing readers, end-tidal nitrous oxide concentrations are expressed by Smith et al as volumes per cent at 1 400 m as well as at sea level.

These considerations are applicable to all inhaled gases and vapours including oxygen, carbon dioxide, anaesthetic vapours and nitrogen. Expressing gas analyser readings in terms of volumes percent can cause significant confusion.[2] Furthermore, there are implications concerning the use of anaesthetic devices at moderate altitude. The subject has been dealt with in detail elsewhere;[3] however, there exists a great deal of confusion in this regard, even among anaesthesiologists and service technicians who work at moderate altitudes such as in Gauteng. In addition, a significant number of cities and towns in sub-Saharan Africa are situated at moderate altitude; therefore, it is important that all who deal with gas-delivery and -measuring devices have a firm grasp of the underlying principles.

Our tendency to think of gas concentrations in terms of volumes per cent probably stems from the time when flowmeters were introduced early in the 20th century

[§] Because partial pressures of gases in solution cannot be measured directly, they are referred to as gas tensions. The tension of a gas in solution is the partial pressure of the gas with which it is in equilibrium and can be viewed as the tendency of a gas to escape from the liquid. It is thus the gradient that drives a gas across the blood-brain barrier.

and when the gas concentrations were assessed by devices that measured their proportions by volume, such as the Haldane apparatus for measuring carbon dioxide. When calibrated plenum vaporisers were introduced, their dials were calibrated according to conventional thinking, in volumes per cent, although in reality they deliver set partial pressures (see below). With the global acceptance of the SI units shortly after 1960, it was fortuitous that volumes per cent at sea level were numerically similar to partial pressures expressed in kiloPascals. The result was that there was no incentive to change the mindset of anaesthetists or of clinical researchers because most of the research (e.g. on minimum alveolar concentrations [MAC]) was being done in the UK, Europe and the USA, in cities that were close to sea level.

In a mixture of gases, each gas exerts a pressure as if it alone were present (Dalton's law of partial pressures). For example, in the earth's atmosphere, oxygen is present in a constant proportion of 21% by volume, regardless of altitude. The partial pressure of oxygen at sea level is therefore 0.21 x 101.3 = 21.3 kPa. At an altitude where the atmospheric pressure is 80 kPa (e.g. in Johannesburg), the partial pressure of oxygen is only 0.21 x 80 = 16.8 kPa. This relative decrease in oxygen partial pressure is the reason why sports teams that trained at sea level struggle at the altitude of Johannesburg, particularly in the second half of a strenuous game like rugby or soccer. It is important to recognise that it is the partial pressures of gases that exert their physiological effects. Thus, when a physician requests measurement of a patient's 'blood gases', the report is stated in units of partial pressure, that is, kPa or mmHg. In this instance gas volume per cent has no meaning. With regard to oxygen, it is the partial pressure of oxygen in the alveoli (therefore the blood oxygen tension) that determines whether haemoglobin will contain enough oxygen to oxygenate the tissues (the oxygen dissociation curve), and it is the tension of oxygen in the mitochondria of the cells that determines whether aerobic metabolism will take place. At an altitude of 3 000 metres, the atmospheric pressure is only 71.4 kPa (535.4 mmHg) and the partial pressure of oxygen is only 0.21 x 71.4 = 14.8 kPa (111 mmHg). This introduces the possibility of hypoxia, and therefore when flying an aircraft at altitudes greater than 3 000 metres above mean sea level, it is recommended that oxygen-enriched mixtures be breathed if the aircraft is not pressurised. Thus breathing a 50% mixture of oxygen at 3 000 metres will increase the inspired oxygen partial pressure to 0.5 x 71.4 = 35.7 kPa (267.8 mmHg). Airlines pressurise their cabins to an equivalent of 2 500 m where the ambient pressure is 76 kPa and the partial pressure of oxygen is 16 kPa.

Oxygen analysers respond to changes in oxygen partial pressure (not percentage), but unfortunately their displays are almost invariably labelled '%'. If one were to calibrate an oxygen analyser at sea level and then transport it to Johannesburg it would no longer read '21%' in air but 0.21 x 80 = '16.8%'. The measurement is correct, but the labelling is incorrect. It is wrong to recalibrate the instrument to read '21%' as this can delude the anaesthesiologist into thinking that he/she is administering 20% more physiologically active oxygen to the patient than reality. In order to calibrate an oxygen analyser at altitude, one must have an idea of the expected ambient pressure. If, for example, the ambient pressure is 85 kPa, after exposing the transducer to air, the reading should be set to 0.21 x 85 = 17.9 '%'. After exposing it to pure oxygen the calibration should be set to 85 '%' (not 100%).

The advent of gas and vapour analysers has revolutionised the administration of inhaled anaesthetics and it is now possible to titrate anaesthesia to precisely targeted end-tidal concentrations. Most gas analysers work according to principles that depend on the physical activity of the gas, namely its partial pressure: This applies to analysis by infrared absorption spectrometry (carbon dioxide, volatile anaesthetics and nitrous oxide), paramagnetism (oxygen) and Raman scattering (volatile agents) but not mass spectrometry. Many monitoring units measure ambient pressure and provide the user with a choice to display gas concentrations in terms of either partial pressures or volumes per cent. This has had the unfortunate effect of surreptitiously introducing further confusion with regard to the administration of anaesthesia at altitude. At sea level it is immaterial which option anaesthesiologists choose; however, at altitude the clinician must have a clear concept of what the display implies. If the display is in kPa, he/she would be correct in assuming that the gases are exerting the same clinical effects as would happen at sea level. If, however, the display is in terms of volumes per cent, he/she may be misled into thinking that the end-tidal concentrations are exerting the same effect on the patient as at sea level. If, for example, the end-tidal displays are 60% nitrous oxide and 1.5% sevoflurane by volume, these would be adequate to prevent awareness at sea level. However, in Johannesburg the exhaled partial pressures are only 48 kPa of nitrous oxide and 1.2 kPa of sevoflurane, which may introduce the possibility of patient awareness. This consideration is of special importance in the light of

the findings of Smith et al who have demonstrated the threshold effect exerted by 60 kPa of nitrous oxide in potentiating the anaesthetic effects of sevoflurane as measured by EEG entropy. It behoves anaesthetists working at altitude to ensure during their pre-anaesthetic machine-checking procedures that they know which units are being displayed by their gas analysers. Moreover, equipment suppliers and service technicians should inform users about the monitor displays and their calibration procedures. Equipment manufacturers should be persuaded to modify their displays to register measured quantities in both units separately and simultaneously, namely in kPa as well as in volumes per cent at ambient pressure, thereby eliminating the possibility for confusion in the minds of the users. Failure of manufacturers to do so may have medicolegal implications in the event of a claim for awareness.

Older gas analysers that do not take ambient pressure into account present a potential hazard if the service technician is not aware of the differences in readings at sea level and at altitude. For example, when calibrating a capnograph, the technician may use a pressurised cylinder containing a mixture of gases of which carbon dioxide forms a 5% proportion. On releasing the calibration gas at the inlet of the capnograph, the gas enters the device at atmospheric pressure and the carbon dioxide will exert a partial pressure comprising 5% of ambient pressure. The technician then needs to know the ambient pressure and to set the capnograph accordingly, in other words to read 0.05 x 80 = 4 kPa in Johannesburg. If this procedure is not followed and the gas analyser is set to read 5 '%', if a patient undergoes controlled ventilation to maintain end-tidal carbon dioxide concentrations of 4.5 '%', there will be hypocapnia as the real end-tidal partial pressure will be 3.6 kPa. By the same argument, such a device will also overread anaesthetic vapour partial pressures if the correct calibration procedure is not followed.

Traditional tapered tube flowmeters with bobbins have been replaced by digitised devices in many modern anaesthetic machines; however, it is not clear whether these devices also mix the fresh gas supply according to proportional volumes. It is not of great importance if the gas analysers, for example the fresh gas oxygen analyser, have been calibrated correctly.

Vaporisers can be thought of as saturated vapour pressure diluters (with the exception of the desflurane vaporiser, which is a special case). Saturated vapour pressure is, for practical purposes, independent of barometric pressure. Thus, vaporisers will deliver a constant partial pressure regardless of altitude and the dial setting can (and should) be read as partial pressure, not concentration. Since these devices are usually calibrated using a Raleigh refractometer using the refraction of polarised light, calibration at altitude remains accurate. As with the flowmeters, this is relatively unimportant as long as the anaesthetic measuring devices are properly calibrated to measure partial pressures.

In summary, a gas in solution exerts its effects by means of partial pressure, causing the gas to dissolve. All modern monitoring systems actually measure partial pressure, not concentration. It is time to abandon the archaic use of concentration and adopt the modern paradigm of partial pressure for all measurements of anaesthetic gases.

References

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