Lesson of the Week

Too much heparin: possible source of error in blood gas analysis

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Sodium heparin solution is widely used as an anticoagulant in blood gas analysis. Although alterations in blood gas measurements may occur when small sample volumes are diluted by heparin,[1 2] such errors are generally thought to be of theoretical rather than practical importance. We report on three patients in whom major alterations in blood gas measurements resulted from the use of excess heparin solution in the sampling syringe and discuss the clinical implications of diluting samples with heparin.

If heparin makes up 10% or more of the total volume of a sample for blood gas analysis important errors in the carbon dioxide pressure, bicarbonate concentration, and base excess will occur

Case reports

Case 1—A 67 year old woman with a long history of exertional dyspnoea was admitted as an emergency with a one week history of increasing dyspnoea. On examination she was extremely dyspnoeic with central and peripheral cyanosis. Results of initial arterial blood gas analyses were: pH 7·19, carbon dioxide pressure 4·8 kPa (36 mm Hg), base excess −14 mmol(mEq)/l, and oxygen pressure 7·6 kPa (57 mm Hg). These results were interpreted as metabolic acidosis with superadded mild type 1 respiratory failure. Thus she was given 100 mmol(mEq) sodium bicarbonate intravenously and started on 35% oxygen by Ventimask. Repeat arterial gas analyses six hours later showed: pH 7·44, carbon dioxide pressure 13·4 kPa (101 mm Hg), base excess +11 mmol/l, and oxygen pressure 5·3 kPa (40 mm Hg). The initial serum bicarbonate concentration, which had been estimated on a separate venous blood sample at the time of admission, was 24 mmol/l. The initial blood gas analyses showed profound reductions in pH, carbon dioxide pressure, and base excess, which were incompatible with a serum bicarbonate concentration of 24 mmol/l.[3] On further inquiry it appeared that in the initial arterial sample 1 ml of 1000 units heparin/ml had been used as an anticoagulant in a total sample volume of 4 ml. In a patient with severe carbon dioxide retention and respiratory acidosis, inappropriate and potentially harmful treatment was started because of a heparin induced error.

Case 2—A 51 year old man known to have chronic obstructive airways disease was admitted as an emergency with severe dyspnoea. Results of initial arterial blood gas analyses were: pH 7·08, carbon dioxide pressure 6·5 kPa (49 mm Hg), base excess −16 mmol/l, and oxygen pressure 6 kPa (45 mm Hg). As the sample volume was extremely small a repeat specimen was requested. Results were: pH 7·39, carbon dioxide pressure 7·7 kPa (58 mm Hg), base excess +8 mmol/l, and oxygen pressure 7 kPa (52 mm Hg). Here the initial results might have been interpreted as a mixed metabolic and respiratory acidosis rather than a compensated respiratory acidosis.

Case 3—An 84 year old woman was admitted as an emergency with symptoms and signs of cardiac failure. Results of initial arterial blood gas analyses were: pH 7·36, carbon dioxide pressure 1·3 kPa (10 mm Hg), base excess −16 mmol/l, and oxygen pressure 14·5 kPa (109 mm Hg), which were consistent with a compensated metabolic acidosis. As this sample (volume 2 ml) was noted to be dilute a repeat specimen was requested. Results were: pH 7·44, carbon dioxide pressure 3·9 kPa (29 mm Hg), base excess −2 mmol/l, and oxygen pressure 8·5 kPa (64 mm Hg). On further inquiry it became apparent that the first specimen had contained approximately 1 ml of 1000 units heparin/ml as anticoagulant, resulting in an apparent compensated metabolic acidosis.

In vitro effect of heparin on blood gas analysis

Venous blood samples for routine gas analysis were taken from 10 volunteers aged 22-30, none of whom had a history of respiratory disorders. Simultaneous samples were obtained using a Butterfly cannula inserted into an antecubital fossa vein and were drawn up into plastic syringes (Beckton Dickinson) containing 0·1, 0·2, 0·5, 1·0, 2·0, and 3·0 ml sodium heparin (1000 units/ml) respectively to a total volume of 5 ml. Samples were immediately mixed and gases estimated using a Corning 178 automated blood gas analyser. The samples with the lowest percentage volume of heparin (2%) were taken as the baseline, and appreciable deviations from these values were analysed using a paired Student's t test.

Results

The table shows the mean results for pH, carbon dioxide pressure, base excess, oxygen pressure, and actual bicarbonate concentration. Presumably because of buffering no appreciable

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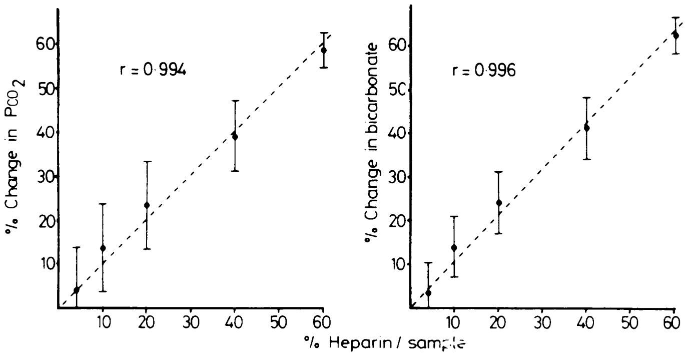
decrease in the pH was observed until 40% of the sample volume had been replaced by heparin. Both carbon dioxide pressure and bicarbonate concentration showed an inverse relation with the volume of heparin used. There was a close relation between the percentage change in each set of values for carbon dioxide pressure and actual bicarbonate concentration from baseline and the percentage volume of heparin in each sample (figure). This confirms that the fall in carbon dioxide pressure and bicarbonate concentration is caused by dilution. An appreciable reduction in carbon dioxide pressure and bicarbonate is therefore shown if 10% or more of the sample volume is heparin. A similar change in the base excess is also shown, but no appreciable changes in the oxygen pressure were seen, even with high dilutions of heparin.

Results (mean (1 SD)) of blood gas analyses for pH, carbon dioxide pressure, base excess, oxygen pressure, and actual bicarbonate concentration

	Percentage volume of heparin per 5 ml sample					
	2	4	10	20	40	60
pH	7·37 (0·03)	7·37 (0·02)	7·37 (0·02)	7·36 (0·03)	7·34* (0·03)	7·31‡ (0·03)
Carbon dioxide pressure (kPa)	6·8 (0·7)	6·5‡ (0·7)	5·9§ (0·7)	5·2§ (0·7)	4·1§ (0·5)	2·8§ (0·3)
Base excess (mmol(mEq)/l)	+3 (1)	+3 (1)	0§ (1)	−3§ (1)	−8§ (2)	−13§ (1)
Oxygen pressure (kPa)	4·3 (1·1)	4·7 (1·2)	4·9 (1·2)	5·1 (1·5)	4·8 (1·3)	6 (2·5)
Actual bicarbonate (mmol(mEq)/l)	29 (2)	28† (2)	25§ (2)	22§ (2)	17§ (2)	11§ (1)

Conversion: SI to raditional units—Carbon dioxide and oxygen pressures: 1 kPa ≈ 7·5 mm Hg.
*$p<0·02$. †$p<0·05$. ‡$p<0·01$. §$p<0·001$.



Mean percentage change from baseline values of carbon dioxide pressure (Pco_2) and actual bicarbonate versus percentage of heparin per sample.

Comment

A recent report discussing potential sources of error in blood gas analysis considered the effects of temperature, delay in estimation, and air bubbles in the syringe[4] but did not mention dilution by excess anticoagulant. Over a short time we have had samples from three patients in which substantial alterations in blood gases occurred because of dilution by heparin. The abnormalities noted in these cases were a profound reduction in carbon dioxide pressure, bicarbonate, and base excess. Thus a type 2 respiratory failure with carbon dioxide retention may be erroneously interpreted as a type 1 disturbance with superimposed metabolic acidosis and inappropriate and potentially harmful treatment may be given.

When much of the early evaluation of techniques of blood gas measurement was done preheparinised vacuum containers were widely used,[5 6] but these have largely been abandoned, possibly because of the expense, and heparin solution must be added to a syringe before sampling. In general wards the responsibility for collecting arterial blood for analysis usually rests with an unsupervised junior houseman. There seems to be little uniformity in the amount of heparin used as anticoagulant, and the volume of sample sent to the laboratory is highly variable. In our experience blood gas samples taken by anaesthetists working in intensive care units are usually in 2 ml syringes. Samples sent from general medical or surgical wards, however, tend to be taken into 5 ml syringes, and the sample volume may vary from 0·5 ml to 5 ml.

Standard 2 ml or 5 ml plastic syringes have an effective deadspace (including needle) of 0·1 ml and 0·2 ml respectively. Given a full sample, filling of the deadspace with heparin solution (5% and 4% of the total volume respectively) would not result in an appreciable error (table). It is apparent from our studies that important alterations in blood gas results will occur when heparin solution comprises 10% or more of the final volume; thus smaller sample volumes are open to a greater risk of error by dilution, even when only the deadspace is filled with heparin.

Many junior doctors may be inadequately informed about the effect that excess heparin can have on blood gas estimation. We would recommend a maximum of 0·2 ml of 1000 units sodium heparin/ml in a 5 ml sample, or 0·1 ml in 2 ml sample, giving approximately 20 units heparin/ml blood, and any sample of a volume of 1 ml or less should be considered (technically) unsuitable for analysis.

References

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Is it advisable for people aged over 60 who are taking bran to supplement their diet?

There is no evidence that adding bran to a mixed Western style diet induces deficiencies of any mineral or vitamin. Experiments showing that bran induces negative balance of calcium, zinc, or iron have all been short term and probably in the long term, adaptation occurs, with reduced urinary excretion. Serum concentrations of iron, calcium, and zinc were no different in 68 people (some elderly) who had been taking bran 7-32 g/day for six to 48 months and in 43 people eating a similar Western style diet but without the addition of bran.[1] All the same, it is prudent to check that older people eating much bran (say, more than two tablespoonfuls a day) are indeed eating a sensible, mixed diet.—K W HEATON, reader in medicine, Bristol.

1 Rattan J, Levin N, Graff E, *et al*. A high-fiber diet does not cause mineral and nutrient deficiencies. *J Clin Gastroenterol* 1981;3:389-93.