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DOI: 10.1097/PAT.0000000000000218

Hazards of a floating separator gel: a case study

Sir,

Gel separator tubes are widely used to separate plasma (or serum) from the cellular components of blood, allowing sample storage in the primary tube.[1–3] The gel, typically a thixotropic polymer gel, has a density between that of plasma (1.026–1.031 g/cm^3) and the cells (1.092–1.095 g/cm^3)[1–3] (although gel density varies between tubes from different manufacturers).[4]

'Floating gel' is when the gel rises and sits at the top of the tube (i.e., above the serum or plasma component), after centrifugation. Although it is an uncommon occurrence, it poses great risks to both laboratory instrumentation and subsequently to the accuracy of patient results.

Floating gel is caused by a marked increase in plasma density[2,3] and has been reported in cases of sample contamination (with iodinated contrast media[3,5,6] or 'catheter locking' anticoagulant solutions[7]) and in multiple myeloma patients with very high paraprotein concentrations.[1,2,8] Two previous reports have described the floating gel problem and resultant analyser sampling probe occlusion,[1,5] but none have detailed the effects of iodinated contrast material contamination on patient results. Here, we report the outcomes of such a case which resulted in analyser malfunction and we also describe the spurious biochemistry results obtained.

A plasma sample, from a 69-year-old man who presented with acute myocardial infarction, gave a sample aspiration error alert on our Abbott Architect analyser (attached to an Abbott Accelerator Automated Processing System; Abbott, USA). Visual inspection showed an abnormally positioned gel separator (Fig. 1).

The sample had been collected in a BD Vacutainer PST II tube (heparin plasma, gel separator; BD, USA) and promptly centrifuged (at 2800 g for 10 min at 23°C in a swinging-bucket centrifuge). Further enquiry revealed the sample was drawn from a radial artery catheter, during an urgent coronary angiogram and percutaneous coronary intervention procedure. During this procedure, 180 mL of Visipaque (iodixanol; GE Healthcare, USA), an iodinated contrast agent, was administered intra-arterially via the same arterial catheter (and 5 mL of blood was discarded prior to sample collection).

The analyser sampling probe had entered and aspirated from the floating gel layer, contaminating several instrument components with gel, including the sampling probe, instrument mixers, cuvette and cuvette wash station. In response, the sampling probe had to be replaced and gel manually removed from the other components, resulting in 3 h of 'downtime' for the analyser and substantial delays in processing other specimens.

To investigate the biochemical effects of the iodinated contrast media contamination, an aliquot of the plasma sample was separated and tested (Table 1). All assays were performed on an Abbott Architect analyser except for osmolality which was measured using an Advanced Instruments Model 3250 Osmometer (Advanced Instruments, USA) and sodium, which was also measured by direct ion-selective electrode (ISE), on an ABL90 Flex analyser (Radiometer, Denmark).

Plasma iodine was measured in the sample on an Agilent 7700 Series instrument (Agilent Technologies, USA) and was extremely elevated at 49,470 mg/L (reference interval 0.04–0.09 mg/L), confirming iodinated contrast media contamination. The estimated density of the plasma was also found to be abnormally high at 1.047 g/cm^3, as measured on a refractometer (American Optical, USA; model number 10408)

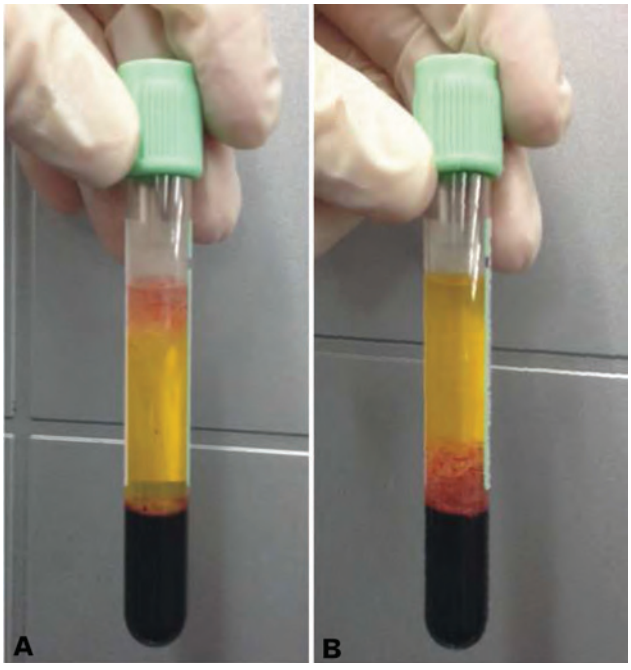

Fig. 1 (A) An image of the contaminated sample showing the floating gel, with (B) a normal sample for comparison.

Table 1 Biochemistry results showing the contaminated sample (B), with preceding (A) and subsequent (C) results on the same patient provided for comparison

Sample		A	B	C
Collection time		Day 1 01:55	Day 1 11:30	Day 1 13:00
Analyte	Reference interval			
Sodium, mmol/L	135–145	138	123	134
Potassium, mmol/L	3.5–5.2	4.0	5.4	5.5
Chloride, mmol/L	95–110	–	95	–
Urea, mmol/L	3.2–7.7	7.4	10.3	11.6
Creatinine, μmol/L	50–110	115	116	130
eGFR, mL/1.73 m^2	80–120	56	55	48
Sodium (direct*), mmol/L	135–145	–	131	–
Glucose, mmol/L	3.5–7.7	11.7	9.1	–
Osmolality, mmol/kg	280–300	–	313	–
Osmolal gap,† mmol/kg	≤10	–	31.6	–

* Direct ion-selective electrode (ISE) method used.
† Calculated using sodium measured by direct ISE.

using a previously reported equation relating specific gravity and protein concentration.[4]

The details of this case illustrate the hazards associated with iodinated contrast media contaminated specimens, including severe instrument malfunction (i.e., contamination with gel) and spurious laboratory results such as pseudohyponatraemia (123 mmol/L) and increased osmolal gap (31.6 mmol/Kg).

The interference observed in iodine contrast media contaminated samples has not previously been described, although potential dilutional,[6] aspiration[3] or other analytical errors[6] have been suggested.

The pseudohyponatraemia in this case could be attributed mainly to an increase in solid phase particles, as it largely corrected with direct ISE. Some dilutional effect may also have been present, based on the mildly low direct ISE sodium concentration (but additional markers of this, such as haematocrit changes, were not available). The osmolal gap was increased, suggesting contamination with unmeasured osmotically active substances, as was the osmolality (and although the manufacturer indicates Visipaque is isotonic, this effect on osmolality has previously been demonstrated).[5] The high plasma density (1.047 g/cm^3), due to contamination with Visipaque which has a density of 1.356–1.369 g/cm^3 (GE Healthcare), is consistent with previous studies showing floating gel occurring at plasma densities of ≥1.038–1.045 g/cm^3 in PST II tubes.[2,5]

Other reported analytical interferences that can occur with iodinated contrast media contamination, include falsely elevated cTnI, using the Opus Magnum cTnI assay (Behring Diagnostics) and an abnormal peak on capillary zone electrophoresis of serum proteins.[9]

Despite being spurious, the results in this case were otherwise biologically plausible and might have been accepted if other events (i.e., instrument error alerts) had not flagged the sample problem to laboratory staff (who subsequently noted they were significantly discordant from previous results). The biochemical findings were later confirmed with *in vitro* experimental data obtained by spiking blood, collected in PST II tubes from a healthy laboratory volunteer, with Visipaque (after discarding an equivalent volume of blood) and then centrifuging (Table 2).

Table 2 Biochemistry results from four blood samples, collected in PST II tubes (4.5 mL draw volume) from a laboratory volunteer, and spiked with increasing volumes of Visipaque

Volume of Visipaque added (μL)	0	50	100	200
Floating gel observed	No	No	No	Yes
Sodium, mmol/L	138	134	132	124
Sodium (direct*), mmol/L	141	139	137	131
Osmolality, mmol/kg	288	291	292	299
Osmolar gap,† mmol/kg	−6	0.8	5.9	25.6
Density, g/cm^3	1.029	1.032	1.034	1.040
Urea, mmol/L	6.4	6.3	6.1	6.1
Creatinine, μmol/L	82	78	77	73
Glucose, mmol/L	5.6	5.9	6.0	5.3

* Direct ion-selective electrode (ISE) method used.
† Calculated using sodium measured by direct ISE.

The analyser damage seen in this case, was more severe than previous floating gel cases, where only occlusion of sampling probes had occurred.[1,5] Although the cause of this is unclear, one suggested explanation is a defect of the analyser's sample detection mechanism (i.e., failing to differentiate between true sample and gel), resulting in continued sampling of the gel layer and more significant contamination. In this case however, the analyser did correctly detect the floating gel, prior to performing any assay. We speculate that gel from the sample may have adhered to the sampling probe and not been removed by the sampling probe wash station. The gel remaining on the probe could then have been transferred to the cuvette and other instrument components.

Iodinated contrast media contamination has previously been described in specimens collected from arterial lines in patients undergoing coronary angiography and PCI.[3,6] Collecting blood from indwelling lines is suboptimal and a potential source of contamination (or dilution).[10] Lines flushed with interfering agents should preferably be avoided or, if used, should be flushed with saline and sufficient volume of blood discarded, prior to collection.[6,10] In this case, although 5 mL of blood was discarded prior to collection, the line was not flushed after use of the contrast agent. Furthermore, the use of arterial blood samples for analytes other than 'blood gases' should be discouraged, as the concentration of some analytes (e.g., glucose) differs between collection sites.[11]

Delaying peripheral blood collection after administering iodinated contrast agents, for at least one distribution half-life (around 20 min)[5,6] or one elimination half-life (e.g., 2 h for Visipaque)[5] has also previously been recommended. In this case, repeat collection after 90 min showed resolution of the floating gel and biochemical abnormalities.

Visual inspection of samples after centrifugation is another way to detect floating gel samples, but is impractical in laboratories with a high degree of automation[1,3,4] and may be obscured by specimen labels.[1]

In conclusion, although uncommon, sample contamination with iodinated contrast media is an important cause of analyser malfunction and spurious results. If biochemical results are urgently required post use of a high volume of iodinated contrast media, clinical units should be made aware to use gel-free tubes and to take steps during collection to avoid contamination from an indwelling line.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: 10.1097/PAT.0000000000000219