

The influence of contrast media on serum osmolality, haematocrit and cardiac output

A comparative study in dogs

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Summary

Thirty-two mongrel dogs were used in a comparative study to assess the effect of normal saline solution, metrizamide and Cardioconray on serum osmolality, haematocrit and cardiac output. The study demonstrated that the higher the osmolality of the test substance, the greater the reduction in haematocrit and the higher the increase in cardiac output.

S Afr Med J 1985; 67: 468-470.

Cardio-angiographic ionic contrast media are usually of high osmolality. Thus Cardioconray (iothalamate sodium/iothalamate meglumine 2:1), which is used in neonates and children, has an osmolality of more than 2000 mOsm/kg water (vapour pressure method). The toxicity of ionic contrast media is usually attributed to the agent's hypertonicity.¹ According to Gavalaki *et al.*² the use of these agents in neonates is limited by the significant toxic effects. They also demonstrated that hypertonic media give rise to a compartmental fluid shift which could be dangerous.

Non-toxic contrast agents, of which metrizamide was the first to be employed, are used more widely now for neurological diagnosis.³ The osmolality of metrizamide with iodine concentrations of 190 mg/ml and 370 mg/ml is 261 mOsm and 600 mOsm/kg water respectively. In comparison with Cardioconray, therefore, it has a lower osmolality and thus theoretically should be less toxic.

The aim of this study was to compare the effect of normal saline solution, Cardioconray and metrizamide on the serum osmolality, haematocrit and cardiac output in mongrel dogs.

Materials and methods

Thirty-two mongrel dogs were divided into four groups: group 1 (control group) — 7 dogs given saline solution (osmolality 292 mOsm/kg H₂O); group 2 — 10 dogs to whom Cardioconray (osmolality 2000 mOsm/kg H₂O) was administered; group 3

— 10 dogs to whom metrizamide (osmolality 261 mOsm/kg H₂O) was given; and group 4 — 5 dogs in whom metrizamide with an osmolality of 600 mOsm/kg H₂O was employed. One dog in group 2 could not be used because of an anaphylactic reaction to the administration of Cardioconray.

The animals were given a general anaesthetic (sodium phenobarbitone). Four catheters (two arterial and two venous) were then introduced via a femoral cut-down and positioned in the pulmonary artery (No. 6 multipurpose balloon catheter), right atrium (No. 6 Goodale-Lubin catheter), left ventricle (No. 6 Cordis pigtail catheter), and right femoral artery (Teflon catheter). A bolus of the test agent (1.5 ml/kg) was injected into the right atrium and was repeated after 40 minutes. Blood samples were taken and the cardiac output (thermodilution method) was estimated at 1, 3, 5, 10, 20, 30, 41, 45, 50, 60 and 80 minutes. Serum osmolality (vapour pressure method with a Wescon 5100 Vapourpressure osmometer) and haematocrit values were estimated from the blood samples.

Statistical analysis

The *t*-test (two-sample test) was used to compare groups 2, 3 and 4 with group 1 (control group).⁴

Results

The osmolality, haematocrit and cardiac output values were expressed as a fraction of the baseline values before administration of the bolus of the test substance.

In all four groups the haematocrit decreased and the cardiac output increased 1 minute after administration of the bolus, while the osmolality changed only fractionally. The changes were very noticeable when the test agent administered had a high osmolality (Figs 1 and 2). The haematocrit reached a low level 5 minutes after administration of the first bolus in all four groups of animals. Thirty minutes after administration of the first bolus of test substance the haematocrit had not returned to the baseline value, but 40 minutes after the administration of the second bolus it did so, and even rose above the baseline value in groups 1 and 3 (Fig. 2). In all four groups the cardiac output fell below the baseline values. Figs 3 - 6 show the changes in cardiac output and haematocrit.

Discussion

When the effects of the various diagnostic agents are compared, it is noticeable that the substances with a high osmolality (groups 2 and 4) caused a statistically significant increase in cardiac output (Fig. 1), while the haematocrit decreased accordingly (Fig. 2). The change in osmolality was not statistically significant in any of the groups. The latter finding is at variance with the findings of Gavalaki *et al.*,² who found

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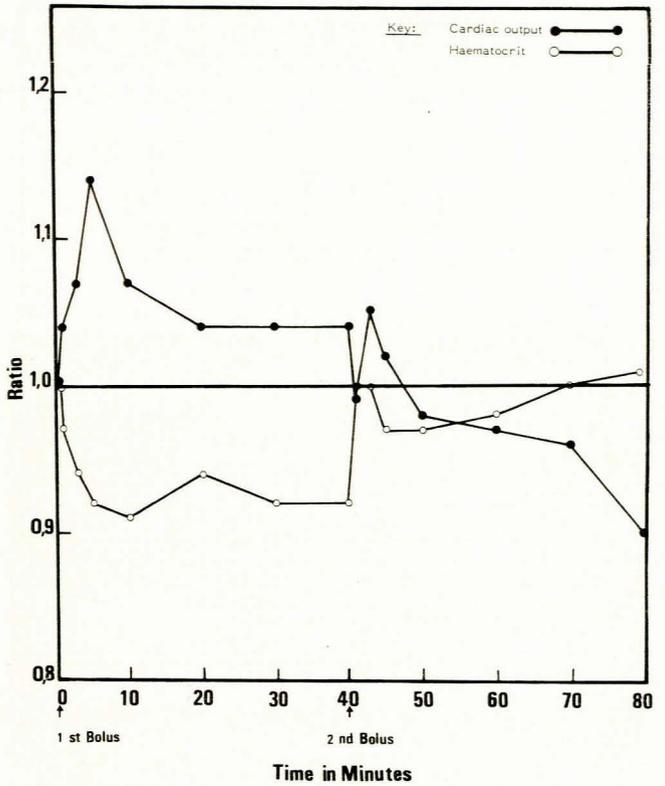
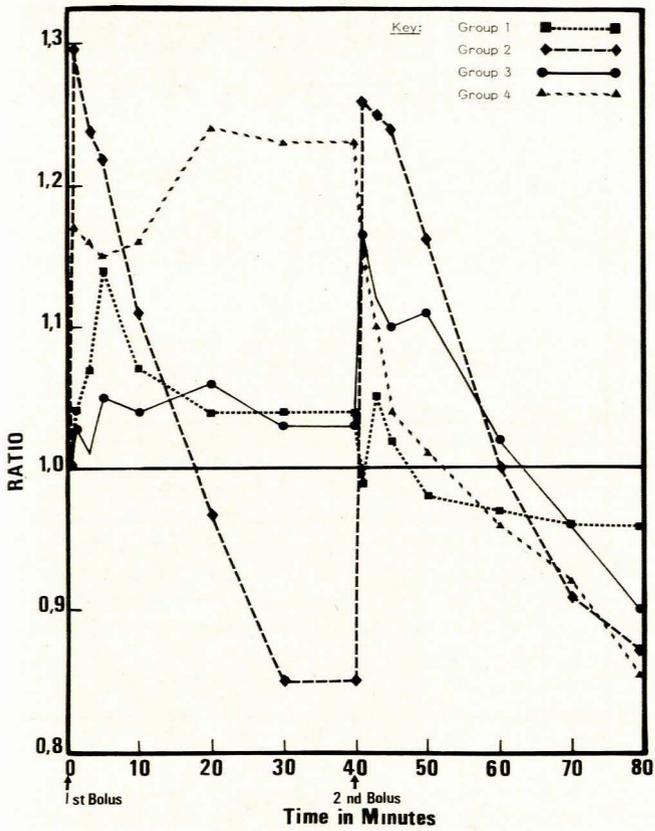


Fig. 1. Cardiac output in groups 1 - 4. Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for the appropriate group is shown at each point.

Fig. 3. Cardiac output and haematocrit in group 1 (normal saline). Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for cardiac output and haematocrit is shown at each point.

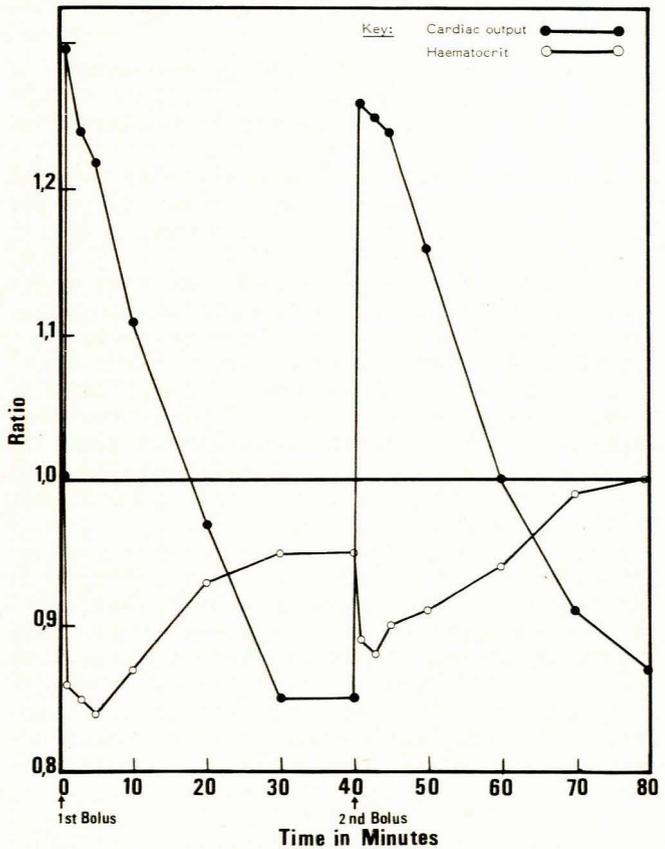
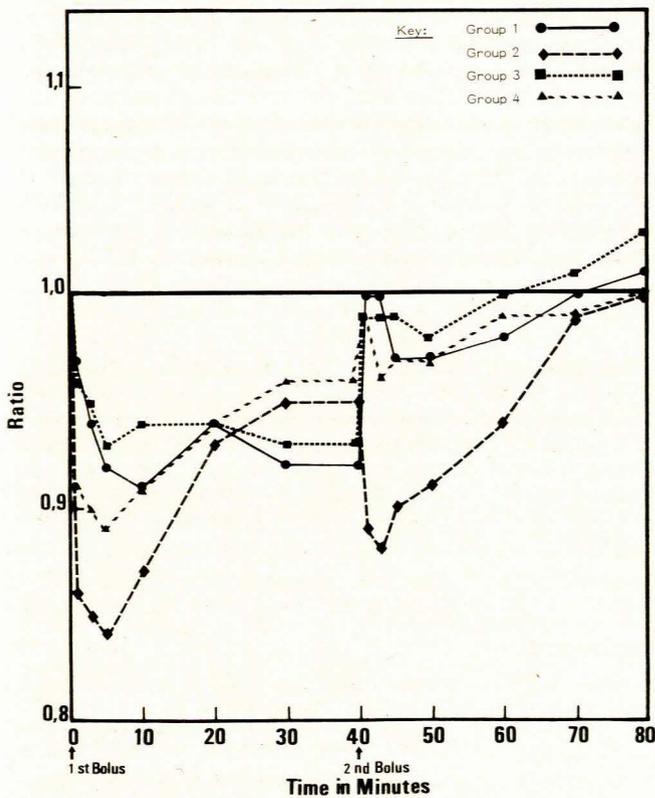


Fig. 2. Haematocrit in groups 1 - 4. Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for the appropriate group is shown at each point.

Fig. 4. Cardiac output and haematocrit in group 2 (Cardioconray). Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for cardiac output and haematocrit is shown at each point.

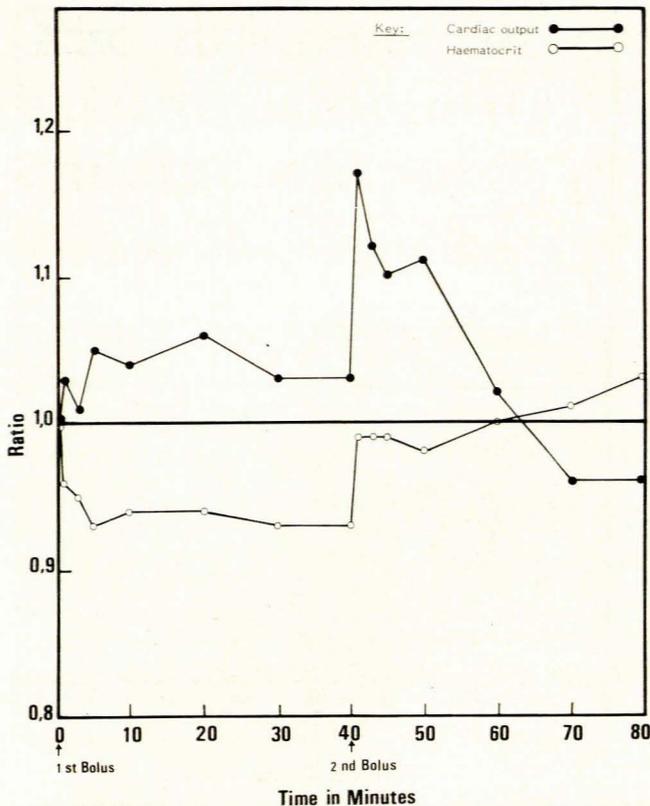


Fig. 5. Cardiac output and haematocrit in group 3 (metrizamide) (1 190/mg/ml). Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for cardiac output and haematocrit is shown at each point.

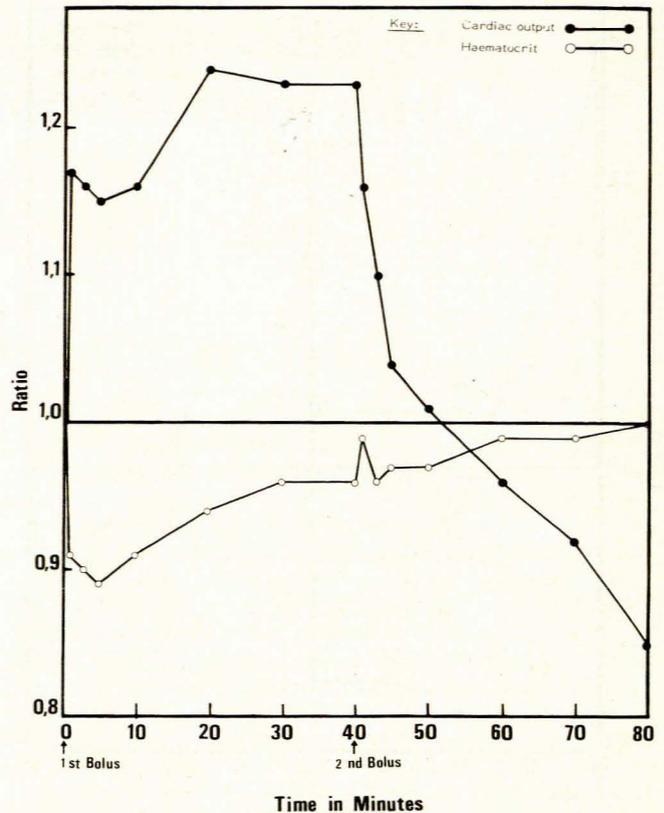


Fig. 6. Cardiac output and haematocrit in group 4 (metrizamide) (1 370 mg/ml). Fraction of control (pre-injection) levels 1 - 80 minutes after injection of the test drug. The mean ratio for cardiac output and haematocrit is shown at each point.

a significant increase in osmolality after the administration of a bolus of Cardioconray to neonates. The insignificant change in osmolality in the dogs is due to a rapid shift in compartmental fluid.

The increase in cardiac output after the first bolus of metrizamide in group 4 is probably not only due to the osmolality of the substance, because there was no increase after the second bolus (Fig. 6).

The findings of the present experiment confirm that hyperosmolar fluid causes a compartmental fluid shift,¹ i.e. intravascular overload and extravascular dehydration. It has been proved that hyperosmolar conditions can give rise to neurological manifestations, including cerebral haemorrhage.⁵ A further deduction is that this fluid shift must take place rapidly, since there was no statistically significant increase in osmolality in any of the four groups. Thus, a normal osmolality should not cause complacency as a severe fluid maldistribution could still be present.

In their study Gavalaki *et al.*² used furosemide to normalize the haematocrit and osmolality more rapidly. Their results suggest that this was good practice. On the other hand, their results pose the question whether or not the use of furosemide corrects the intravascular parameters only by getting rid of excess fluid while giving rise to extravascular dehydration. The present study has shown that a rapid increase in the intravascular compartment increases the preload with a resultant increase in stroke volume, leading to increased cardiac output.

Conclusion

From this study it would appear that: (i) the toxicity of contrast media can be attributed to their hypertonicity; (ii) a

normal serum osmolality during cardiac catheterization does not necessarily mean that there is normal distribution of body fluids; (iii) care must be taken during cardiac catheterization because the rapid fluid shift can give rise to acute cardiac failure in an already compromised patient; (iv) rapid cellular dehydration can cause fluid imbalance, leading to the possible danger of arrhythmias; (v) cardiac output increases because of acute volume expansion secondary to an osmotic fluid shift; and (vi) the non-ionic contrast media will be the contrast agents of the future in angiographic diagnosis.

We wish to thank Miss H. Weymar of the Cardiac Clinic, Tygerberg Hospital, for preparing the manuscript, as well as Mr M. C. de Jongh of the Department of Paediatrics for the preparation of the graphs. Thanks are also due to Mr G. Louw and the staff of the experimental theatre at the University of Stellenbosch for their assistance. Dr J. P. van der Westhuyzen, Chief Medical Superintendent of Tygerberg Hospital, is thanked for permission to publish.

REFERENCES

- Ekland A, Uflacker R. Effect of meglumine metrizamide on microcirculation. *Acta Radiol Diagn* 1978; 19: 969-976.
- Gavalaki E, Preston TD, Newman CGH. Effect of furosemide on hematocrit and plasma osmolality changes following angiography in children. *Cardiology* 1973; 58: 298-305.
- Engel I, Nitter-Nauge S, Adrew E, Levorstadt K. Amipaque: a new contrast medium in coronary angiography. *Radiology* 1977; 125: 317-322.
- Swinscow TDV. Statistics at square one. *Br Med J* 1976; 2: 291-292.
- Kravath RE, Aharon AS, Abal G, Finberg L. Clinically significant physiologic changes from rapidly administered hypertonic solutions: acute osmol poisoning. *Pediatrics* 1970; 46: 267-275.