

The Effect of In-Vivo Intravenous Administration of Sodium Meglumine Diatrizoate On Some Haematological Parameters

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Abstract

Background: To investigate the in-vivo effects of intravenous administration of sodium- meglumine diatrizoate on some haematological parameters in a Nigerian population.

Methods: Blood samples were collected before and one hour after intravenous injection of sodium-meglumine diatrizoate from 50 subjects undergoing intravenous urography examinations who had no history of and laboratory confirmed diseases that may affect haematological parameters. Standard laboratory methods were used to assay the haemoglobin concentration (Hb), packed cell volume (PCV), total white blood cell (WBC) count and differentials and blood film for any morphological changes in the red blood cells (RBC). Comparisons were made between the mean values of these haematological parameters before and one hour post injection using paired t-test for any statistically significant differences,

Results: There were statistically significant reductions in the mean values of Hb concentration and the neutrophil count one hour post injection compared with their pre-test values ($p < 0.05$). The lymphocytes were also significantly increased post injection compared to the pre-test values whereas 70% of the erythrocytes were morphologically altered from their approximately 100% normocytic shape at pre-test.

Conclusion: Intravenous administration of sodium-meglumine diatrizoate causes in-vivo reduction in Hb concentration and neutrophil count in humans as well as poikilocytosis of the erythrocytes. Some of these effects have the potential of triggering or exacerbating crisis in a sickle cell anaemia subject which is endemic in our locality. Caution should therefore be exercised in the choice and administration of radiological contrast agents to sickle cell subjects. Preparations that are iso-osmolar with plasma and have less probability in precipitating crises should be preferred instead.

Keywords: Radiological contrast agents, haematological parameters, sickle cell

INTRODUCTION

Radiographic contrast agents are chemical substances which can alter the average atomic number or electron density of specific tissues and thus their x-photon absorption characteristics.¹ Its introduction into radiological imaging has helped to overcome the limitations imposed by poor inherent contrast of particularly soft tissues thereby enabling the demonstration of structures that would otherwise not have been possible with plain film radiography.

Ionic and non-ionic contrast agents are widely used in most contrast radiological examinations² but the type to be used depends on the part of the body or system to be examined.³ Iodinated contrast agents, especially those that are ionic, have been shown to be associated with adverse reactions⁴ and they constitute most of the contrast agents administered intravascularly for radiological investigations.⁵ These reactions which are initiated in the blood are dependent on the osmolality, chemotoxicity and ionicity of the contrast agents.⁶

Consequently, the effects of contrast media (CM) on haematological parameters have been the subject of much investigation. A change in plasma osmolality was observed when dog blood was mixed with sodium meglumine diatrizoate in-vitro and this resulted in deformability of the RBCs which increased with osmolality.⁷ An in-vivo study also using dog noted significant decrease in packed cell volume (PCV) and haemoglobin concentration following intravenous administration of a hyperosmolar CM.⁸ Human RBCs were observed to transform to either echinocytes or discocytes following an in vitro mixture of human blood and an ionic contrast agent, suggesting a potential for deformation.⁹

However, to the best of our knowledge there has been no in-vivo investigation of the effects of intravascular administration of radiological contrast agent on haematological parameters particularly in the locality.

This is important because the locality manages a good proportion of the global sickle cell patients who often present for contrast radiological investigations.

SUBJECTS, MATERIALS AND METHODS

A convenient sample size of fifty subjects, comprising 37 males and 13 females aged between 11 years to 60 years from referrals for intravenous urography investigation at a private radiological centre, Hansa Clinics, were enlisted into the study. Blood samples were collected only from those subjects who had no history of diseases that may affect haematological parameters and in addition gave consent for their blood to be collected for the study. Ethical approval was obtained to conduct the research and all other rules regarding the use of human for research were strictly adhered to.

Two millilitres of blood were withdrawn through any vein but mainly the ante cubital vein before and one hour after the administration of sodium meglumine diatrizoate from each subjects into a bottle prepared with EDTA as an anticoagulant. The haematological parameters, namely haemoglobin concentration (Hb) were assayed by the cyanmethaemoglobin method; the packed cell volume (PCV) by microhaematocrit method; and total white blood cell (WBC) count by Turks method. Blood films were stained by Leishmans' method for differential leucocyte counts. The morphology of the RBCs was further studied after the staining by viewing the slide microscopically. Morphological changes in the RBCs, for example poikilocytosis and anisocytosis were checked. Standard laboratory techniques as described by Bain¹⁰ were used for all the haematological investigations. All blood samples were analysed within one hour of collection.

Mean values of haematological parameters before and one hour after the injection of meglumine diatrizoate were compared using the paired sample t-test for any statistically significant differences.

RESULTS

Table 1 show the age and sex distribution of the subjects who participated in the study. 37(74%) males and 13(26%) females were enlisted and their ages range from 11 years to 60 years (mean =35.5years).

The mean values of the haematological indices before and after the injection of meglumine diatrizoate are shown in table 2.

The result of the paired t-tests show that only Hb g/dl concentration demonstrated significant difference

between the pre and post injection values ($p < 0.05$), whereas there was no statistically significant difference in the corresponding mean values for the PCV. The paired t-test indicates also that only the neutrophils and lymphocytes showed statistically significant differences between the pre and post injection mean values ($p < 0.05$).

Blood film microscopy reveals that before the injection of the contrast agent nearly all the cells were normocytic. One hour after the administration of CM 70% became morphologically altered and only 30% were normocytic. Fifty percent of the changes were variations in shape whereas the remainder were anisocytosis. The major poikilocytotic changes observed were echinocytes and pencil cells and the anisocytosis were mainly microcytes.

Table 1: Sex and Age distribution of Subjects

Age group (years)	No.of subjects	Sex		percentage
		male	female	
11 - 20	6	5	1	12
21 - 30	10	8	2	20
31 - 40	6	4	2	12
41 - 50	16	11	5	32
51 - 60	12	9	3	24
Total	50	37	13	100

Table 2 Comparison of Mean Values of Blood parameters pre and post administration of meglumine diatrizoate N= 50

Parameter	Pre-injection mean	Post-injection mean	Difference	Paired T-test value
PCV (g/dl)	0.41 ± 0.04	0.40 ± 0.04	0.01 ± 0.02	0.81 p>0.05
Hb (g/dl)	13.50 ± 1.40	12.87 ± 1.53	0.64 ± 1.24	0.033 p<0.05
Mean cell Hb (g/dl)	32.75 ± 0.44	32.85 ± 0.37	-0.10 ± 0.31	0.163 p>0.05
Neutrophils(x 10 ⁹ /L)	49.10 ± 8.54	41.50 ± 11.81	7.60 ± 6.80	0.000 p<0.05
Monocytes(x 10 ⁹ /L)	1.50 ± 0.94	1.20 ± 0.67	0.30 ± 1.17	0.27 p>0.05
Eosinophils(x 10 ⁹ /L)	1.40 ± 0.11	1.40 ± 0.13	0.00	1.00 p>0.05
Lymphocytes(x 10 ⁹ /L)	47.80 ± 8.62	56.50 ± 11.43	6.35 ± 0.03	0.000 p<0.05
Total WBC(x 10 ⁹ /L)	5150.00 ± 443.04	5220.00 ± 438.41	-70.00 ± 439.00	0.48 p>0.05

DISCUSSION

The administration of hyperosmolar radiographic contrast agents has been associated with adverse reactions including allergy. Consequently, numerous investigations have been conducted to elucidate the mechanism of allergic reaction induction.^{11, 12, 13} However, its other effects on haematological parameters in-vivo in humans have been scantily investigated and none in the local population.

The results of the study show that there is no statistically significant difference in the mean values of the PCV before and one hour after the injection of sodium meglumine diatrizoate ($p > 0.05$). This result differs from that of Izci et al⁸ who noted a reduction in PCV 30 minutes following an in-vivo injection of a hyperosmolar ionic contrast agent in dog.

This study further demonstrated a statistically significant reduction in the mean values of haemoglobin concentration (Hb) one hour post injection with sodium-meglumine diatrizoate when compared with the pre-test values ($p < 0.05$). This finding confirms an earlier observation by Izci et al⁸ who used dog and measured mean value of Hb 30 minutes post injection. The reduction in the value of Hb post injection may be due to the dilution from the contrast media whereas the number of cells remains the same. The implication of this reduction in Hb concentration is that in patients who are anaemic, as is the case in sickle cell anaemia subjects, further depression in Hb may put more demand on the few normal cells and possibly precipitate undesirable conditions. This is in addition to the evidence that high osmolar radiographic contrast agents influence blood rheology and erythrocyte and platelet⁹ aggregation which may impair blood flow and precipitate or exacerbate crisis in the sickle cell anaemia subject.

Caution should therefore be exercised when administering hyperosmolar radiographic contrast agent on the sickle cell anaemia subjects. However, how soon the Hb returns to its pre-test value was not investigated. A statistically significant reduction was also noted between the mean values of the neutrophils before and one hour after the administration of the contrast agent. This is in conformity with the general statement of Cheesbrough¹⁴ that drugs and chemicals can decrease the number of neutrophils. Depending on the extent and the duration of the depletion of neutrophils, this may have serious implications in combating bacterial infection, particularly in sickle cell anaemia subjects who are highly susceptible to bone infections.

The mean values of the lymphocytes were significantly increased from their pre-test values one hour following

the injection of CM. This is consistent with earlier findings that CM elicits foreign body reaction and the production of antigen anti- body reaction. Though the mechanism of allergic reaction resulting from complications of the injection of hyperosmolar CM is not fully understood, histamine release mediated by basophils and mast cells have been reported.¹²

The mean values of the monocytes, eosinophils and total WBC count did not demonstrate any significant difference from its pretest values one hour post-injection. This pattern is similar to those of Izci et al⁸ who used dog.

Seventy(70%) of the RBC were morphologically altered one hour after the injection of CM compared to approximately 100% that were normal prior to the administration. The commonest deformities induced on the RBC were echinocytosis, pencil cell and micocytosis. Similar effects in in-vitro studies have been observed^{16,17} and the osmolality of CM has been identified as the cause of the deformity. This observation is definitely important in sickle cell anaemia subjects as deformation of the RBC has the potential of triggering a crisis or worsening it. Caution therefore needs to be exercised when such patients are to be investigated. Using preparations that are iso-osmolar with the plasma may be preferred as red blood cell deformability and aggregation have been observed to be highly inhibited^{16,17} in such conditions.

CONCLUSION

The intravascular in-vivo administration of sodium meglumine diatrizoate in human has been noted to cause a decrease in the haemoglobin concentration and poikilocytic and anisocytic changes of the RBCs. In our locality endemic with sickle cell disease caution should be exercised as both can trigger or exacerbate crisis. Preparations that are iso-osmolar with the plasma should be preferred to reduce the risk of precipitating crisis.

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