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Effect of radiographic contrast media (Iodixanol, Iopromide) on hemolysis

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Abstract

Radiographic contrast media can lead to drastic changes of the morphology of erythrocytes. The change of the erythrocyte morphology is associated with a decreased deformability possibly resulting from distinctions in the loss of constituents of the membrane cytoskeleton. However, it is unclear whether there is an intravascular hemolysis as a consequence of the disintegration of the erythrocyte membrane.

The results of this study showed, that free haemoglobin increased from 16.8±10.0 mg/dl to 21.6±12.6 mg/dl after Iopromide application ($p=0.240$), while it slightly decreased from 20.5±10.3 mg/dl to 19.5±12.2 mg/dl after Iodixanol application ($p=0.547$). The slight decrease of free haemoglobin after application of Iodixanol differed significantly compared to the increase of free haemoglobin after Iopromide application ($p<0.05$).

This different response is thought to give evidence to the assumption that the erythrocyte membrane integrity was compromised leading to the release of free haemoglobin as an indicator of hemolysis as well.

Key words: Radiographic contrast media, Iopromide, Iodixanol, hemolysis, free haemoglobin

1. Introduction

Radiographic contrast media (RCM) exhibit great differences in their physicochemical properties [4] and can influence the morphology of erythrocytes and other blood cells to variable extent. Several studies revealed

enormous differences in the RCM-induced formation of echinocytes [2, 7-9, 11, 14, 15, 17, 20]. While after application of Iopromide in a concentration of 40% v/v 80.6±17.4 % of all red blood cells presented as echinocytes, after Iodixanol (also in a concentration of 40% v/v) 24.3±29.6 % echinocytes were found [8]. These differences could result from distinctions in the loss of constituents of the membrane cytoskeleton (e.g. Actin und band3), to a greater or lesser extent complete reformation of the spectrin network [6] and at a loss of binding elements needed to construe the membrane cytoskeleton and the membrane [6]. The clustering of band3, particularly, is discussed to reduce the deformability [12, 13, 16, 18], to lead to the abridgement of the lifespan and removal of erythrocytes by offering senescence signals [1].

However, it is not clear whether there is an intravascular haemolysis as a consequence of the demonstrated damage or disintegration of the red cell membrane. A direct result of haemolysis of RBCs would be the release of haemoglobin into the blood plasma leading to circulating free haemoglobin.

Therefore a study was started in order to answer the question if Iopromide 370 in comparison to Iodixanol 320 could have an influence on the release of free haemoglobin during a diagnostic coronary angiography.

2. Material and Methods

The study was performed as a part of a quality management project in the heart catheter laboratory in compliance with the Declaration of Helsinki/Somerset West [3]. The n = 20 patients enrolled in each group exhibited typical cardiovascular risk profiles (see Table 1). In each group merely two patients were acute smokers. Both groups did not discriminate regarding the outlined variables.

Table 1: Demographical and clinical data of both patient groups
(CAD: coronary artery disease; HLP: hyperlipoproteinemia)

RCM	Age [years]	male	CAD / myocardial infarction	hypertension	diabetes	HLP
Iodixanol 320 (*n*=20)	73.8±7.9	13	10/2	20	6	15
Iopromide 370 (*n*=20)	69.6±9.7	14	13/2	18	5	11

3. Results

Table 2 shows that the glomerular filtration rate (GFR, calculated according to the MDRD formula [10]), the left ventricular function, the total amount of RCM applied and the concentration of free haemoglobin that did not differ in both patient groups before the coronary angiography (two-sided t-test for unpaired samples: $p>0.05$ each). Whereas free haemoglobin increased in direction from 16.8±10.0 mg/dl to 21.6±12.6 mg/dl after Iopromide application ($p=0.240$), it decreased from 20.5±10.3 mg/dl to 19.5±12.2 mg/dl after Iodixanol application ($p=0.547$). The decrease of free haemoglobin after application of Iodixanol has shown significant differences concerning the increase of free haemoglobin after Iopromide application (two-sided t-test for unpaired samples: $p<0.05$).

Table 2: Glomerular filtration rate (GFR), left ventricular function (LVEF), total amount of RCM applied (RCM volume) and the concentration of free haemoglobin (fHb) before and after coronary angiography in patients suspected to suffer from coronary artery disease

RCM	GFR [ml/min]	LVEF [%]	RCM-volume [ml]	fHb [mg/dl] before Angio	after Angio
Iodixanol (*n*=20)	56.5±6.7	47.5±13.8	104.9±9.5	20.5±10.3	19.5±12.2
Iopromid (*n*=20)	59.8±1.7	50.7±19.0	102.4±7.2	16.8±10.0	21.6±12.6

4. Discussion

The results clearly demonstrate that the examined RCM influences the erythrocyte membrane in a different way and even can influence the erythrocyte integrity. After Iopromide application an intravascular increase of free haemoglobin happened in spite of the increase in blood volume due to a shift of interstitial fluid into the vasculature caused by the hyperosmolality of Iopromide (770 mOsmol/(kg H_2O)). This probably led to a certain dilution of free haemoglobin and to lower values of free haemoglobin concentration, consequently. The intravascular application of hyperosmolar RCM after a prior hydration therapy always carries the risk of an acute hypervolume load for patients suffering from heart insufficiency and from a reduction of kidney function and of RCM molecule elimination [19].

Iodixanol is isoosmolar and Iodixanol application leaves the intravascular blood volume practically unaltered. The slight decrease of free haemoglobin after Iodixanol application is thought to be a consequence of the infusion of electrolyte solution (and is in the range of the measuring precision). Equivalent volumes of electrolyte solutions accompanied the application of Iopromide as well as of Iodixanol. One patient in each of both groups (both suffered from diabetes mellitus and from reduced kidney function) received 1 l of electrolyte solutions also before coronary angiography.

An examination in vitro on the influence of RCM on human erythrocytes has worked out that the application of Iopromide induced a loss of actin and band3 to the extracellular space – assumed to be due to a loss in erythrocyte membrane integrity – and accompanied by a complete reorganization of cytoskeletal actin and the reformation of the spectrin network of the erythrocytic membrane cytoskeleton [5, 6].

After Iodixanol application to patients the concentration of free haemoglobin did not change at all. In contrast, after application of Iopromide a significant

increase of free haemoglobin was ascertained. This is thought to give evidence to the assumption that the erythrocyte membrane integrity was compromised leading to the release of free haemoglobin as an indicator of haemolysis as well.

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