大韓放射線醫學會誌 第21卷 第3號 pp. 351~356, 1985
Journal of Korean Radiological Society, Vol.21, No.3, 1985

Cardiovascular effects of Contrast Materials on Left Ventricular Angiography in Rabbits

— Comparing high osmolar and low osmolar contrast materials —

Kyung Mo Yeon, M.D., Man Chung Han, M.D., Chu Wan Kim, M.D.

Department of Radiology, College of Medicine, Seoul National University

抄 錄

左心室造影撮影에서 造影劑가 미치는 影響에 關한 實驗的 硏究

서울大學校 醫科大學 放射線科學敎室

延敬模·韓萬靑 金周完

토끼 20마리에서 meglumin salts of Ioxithalamate (Telebrix 30®)와 meglumin and sodium salt of Ioxaglate(Hexabrix®)를 左心室에 注入하여 滲透差異에 依한 心電圖 및 血流力學的 變化를 比較考察하여 보았다. 心電圖 및 血流力學的 變化는 造影劑 注入前, 注入中, 注入後 10分 까지 各各 記錄하였다. Hexabrix 注入群이 Telebrix注入群보다 左心室 擴張末期血壓, 左心室의 dp/dt, 左心室最高 收縮期血壓의 變化가 현저히 적게 나타났으며, 心電圖의 變化(PR prolongation, ST segment depression, T-wave inversion, Arrhythmia)에서는 현저한 差異가 없었다. 이러한 變化는 Hexabrix가 Telebrix보다 低滲透性인 때문으로 생각된다.

Introduction

The precise pathologic anatomy in complex congenital heart disease requires multiple injections of iodinated contrast materials into the cardiac chambers and/or great vessels.

In the presence of intracardial shunts, more large volumes of contrast material is often required. In neonates and infants the total volume of contrast material during single angiographic procedure is limited upto 3-4 ml/kg.

This limitation results from the deleterious effects of systemic hyperosmolarity caused by the contrast materials[1]and may be intensified in the neonate because of the relative immaturity of infants kidneys and delayed excretion of contrast materials[2].

We therefore tried to compare the EKG and left ventricular pressure change with those of high osmolar and low osmolar contrast agent in experimental model.

The purpose of the study is to determine and compare the effects of contrast materials on left ventricular hemodynamics.

Materials and Methods

Twenty rabbits, weighing 2-3 kg, were anesthetized with intravenously injected sodium pentothal (12mg/kg).

A catheter (Formocath polyethylene tubing, Becton Dickinson Co., 3F) was introduced via

이 논문은 1985년 4월 30일에 접수하여 1985년 5월 16일에 채택되었음.

the femoral artery into the left ventricle for pressure monitoring.

EKG and pressure monitoring were preformed simultaneously prior contrast material injection for ten seconds, during injection for 30 seconds and after contrast material injection for 10 seconds at 1, 2, 3, 4, 5, 7 and 10 minutes.

The following contrast media were injected into the left ventricle in each ten rabbits.

1) meglumin salts of Ioxithalamate (Telebrix 30®), 30g I/100ml, 1600mom/kg.
2) meglumin and sodium salts of hexaiodinated monocarboxylic acid (Hexabrix®), 32g I/100ml, 600mom/kg.

Each contrast media was injected in a volume of 3.2ml/kg for Telebrix 30® and 3ml/kg for Hexabrix® with forceful hand injection.

EKG and pressure monitoring was done by Heated stylus polygraph (Gilson Co.) with 50mm/sec speed.

During injection, single angiogram was made for proper localization of catheter tip (Fig. 1).

Analysed items were LVPSP (left ventricular peak systolic pressure), LVEDP (left ventricular end diastolic pressure), LV dp/dt, heart rate, P-R prolongation, ST segment depression, T-wave inversion and arrhythmia.

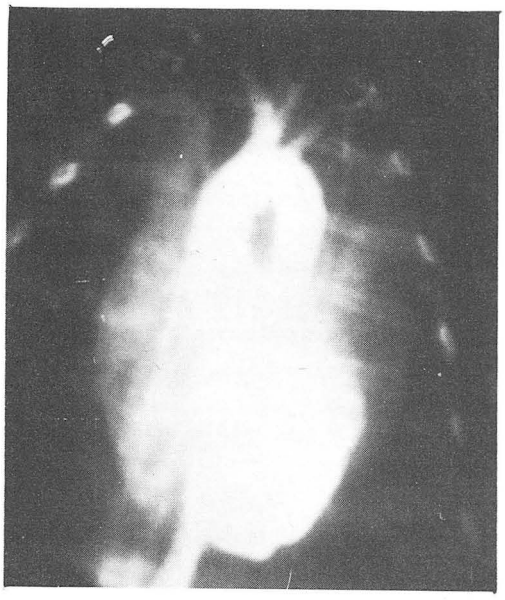

Fig. 1. Left ventriculogram for the localization of catheter tip.

Results

Left Ventricular End Diastolic Pressure (LVEDP): Telebrix caused a $6.8 \pm 1.0\%$ increase within 10 secounds after injection (Fig. 2). At 3 minutes after injection, markedly decreased LVEDP and at 10 minutes after returned nearly normal status. Hexabrix caused an initial instantaneous increase in LVEDP at 5 seconds, and this was followed at 3 minutes by a decreased value ($1.3 \pm 0.9\%$).

Significant difference between Telebrix and Hexabrix was noted by the greater and more persistent increase in LVEDP with Telebrix.

Left ventricle dp/dt: Initial marked decrease was noted with Telebrix injection at 20 seconds and returned slowly preinjection level at 4-5 minutes. But decreased slightly with Hexabrix and returned rather rapidly at 1-2 minutes (Fig. 3).

Left Ventricular Peak Systolic Pressure (LVPSP): The systolic pressure showed a transitory decrease within 20 seconds after injection of Telebrix. After 1 minute, systolic pressure was above basal value.

But no systolic pressure decrease was

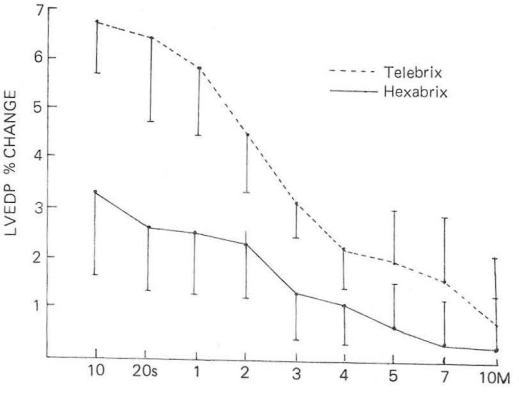

Fig. 2. Percent change of left ventricular end diastolic pressure after injection of contrast media. Mean and standard deviation are represented.

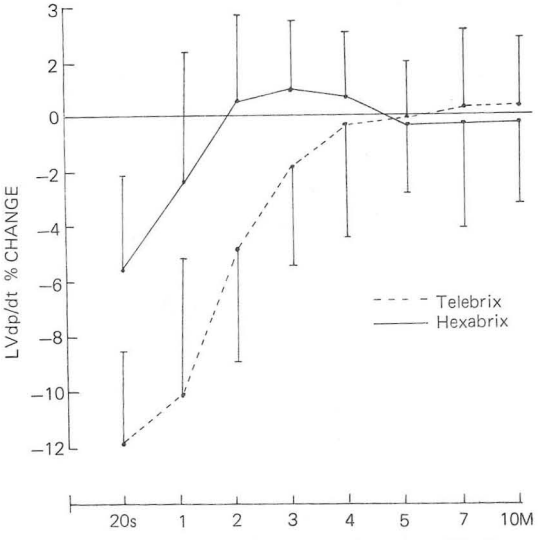

Fig. 3. Percent change of left ventricular dp/dt. Mean and standard deviation are represented.

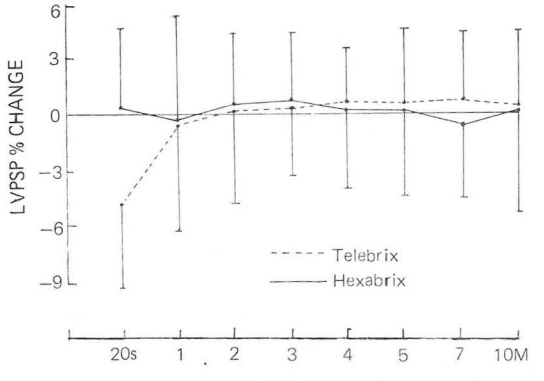

Fig. 4. Percent change of left ventricular peak systolic pressure. Mean and standard deviation are represented.

demonstrated in the group of Hexabrix (Fig. 4).

An example of sequential change of left ventricular pressure curve was demonstrated (Fig. 5)

Heart Rate: Heart rate decreased significantly at 30 seconds—1 minute after injection of Telebrix and Hexabrix although change was smaller with Hexabrix than Telebrix. The preinjection levels were reached within 3 minutes (Fig. 6).

EKG Changes: P-R prolongation, ST segment depression T-wave inversion and other arrhythmia were analyzed. P-R prolongation was peak at 5-20 seconds after injection with both contrast media and returned slowly preinjection levels after 5 minutes. No significant difference was observed between two contrast media (Fig. 7).

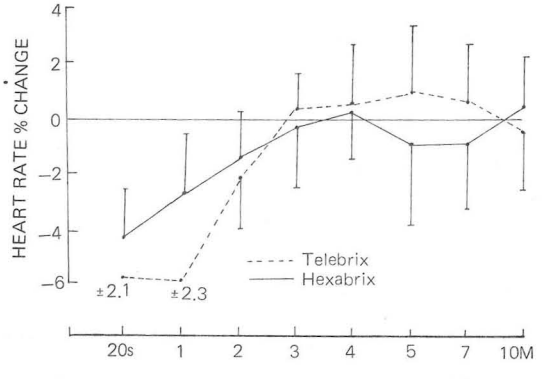

Fig. 6. Percent change of heart rate. Mean and standard deviation are represented.

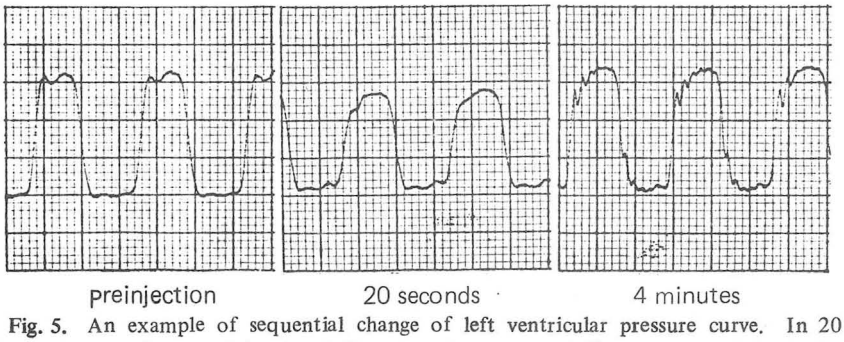

Fig. 5. An example of sequential change of left ventricular pressure curve. In 20 seconds after injection, left ventricular peak systolic pressure and dp/dt decreased significantly and normalized at 4 minutes later. Left ventricular end diastolic pressure increased at 20 seconds after and reached baseline at 4 minutes later.

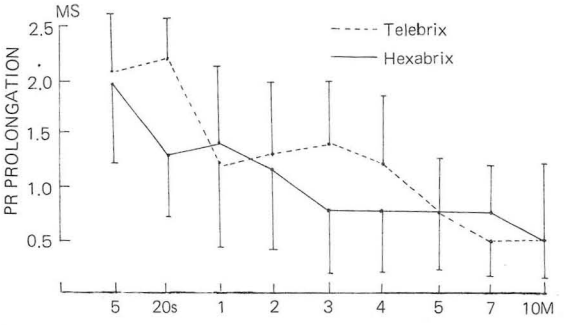

Fig. 7. PR interval prolongation. The unit is millisecond. Mean and standard deviation are represented.

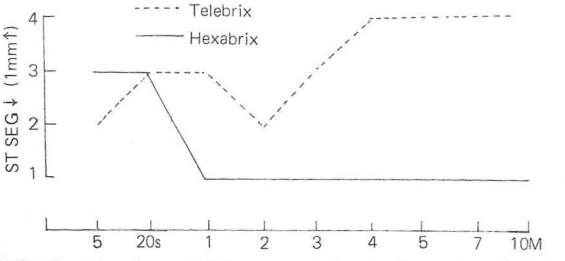

Fig. 8. Number of ST segment depression more than one mm.

Total number of ST segmental depression was similar with both contrast media but mild, transient changes were showed by Hexabrix and deep, persisted changes by Telebrix (Fig. 8).

We cannot find out any significant difference of T-wave change between two contrast media.

A case of ST segmental depression was demonstrated (Fig. 9).

The incidence of arrhythmias was shown in Table
1. The most frequent arrhythmia was ventricular premature beat. These arrhythmias appeared early phase (during injection—5 seconds) and soon recovered. No significant differences in the incidence of arrhythmia were seen following ventriculography with two contrast media.

Discussion

Intravascular contrast media are essential for diagnostic radiology. Without a safe intravascular contrast media, diagnostic

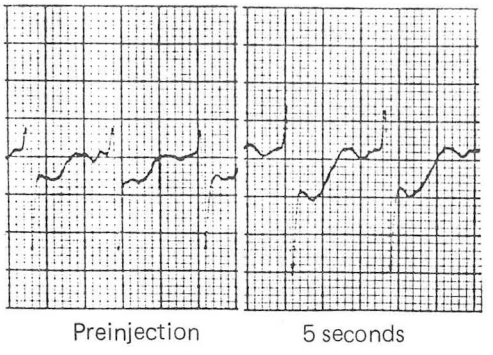

Fig. 9. An example of ST-segmental depression more than 2mm at 5 seconds later.

Table I. The incidence of arrhythmias

Arrhythmia	Telebrix	Hexabrix
VPB	6	9
Vent. tachycardia	1	1
AV block	0	1

radiology would lose much of its contribution to clinical medicine. The major side effects of contrast media are allergic, chemotoxic, osmolar and hemodynamic effects[3,4]. The underlying cause of allergic (anaphylactic shock) effect is not known and no antibodies to contrast media have ever been detected. The adverse reaction may vary from mild to fatal. These reactions are not dose dependent and several death have been reported after one ml test dose.

Conventional contrast media are salts which in solution dissociate into anions (the iocinated ion) and cathions (sodium or meglumine).

These iodinated anions have a markedly low clinical toxicity but cathions have an appreciable toxicity, high concetrations of sodium are more toxic to the brain and myocardium and cause more peripheral vasodilatation[5, 6, 7].

With osmolar effect, erythrocytes become smaller, deformed, shrunken and their internal viscosity increase. Incrased viscosity may lead to the local peripheral resistance. Hyperosmolar solution damages the endothelial cell.

There is a direct relationship between the ex-

tent of capillary endothelial damage and the osmolarity of the fluid[4]. On the other hand, damage to the blood brain barrier[3] depends on the osmolarity as well.

Contrast media causes vasodilatation which depends on the osmolarity, and the feeling of warmth and pain[8] during arteriography is due to this local vasodilatations. Vasodilatation reduces systemic peripheral resistance and therefore lowers the systemic blood flow.[9]

Hyperosmolar contrast media raises the osmolarity of the plasma which results osmotic hypervolemia and adds strain on the left ventricle.

The contrast materials we used are meglumin salts of Ioxithalamate (Telebrix 30®) which has high osmolarity (1600 mosm/kg) and meglumin and sodium salts of hexaiodinate monocarboxylic acid (hexabrix®) which has low osmolarity (600 mosm/kg).

Current intravascular radiological contrast media are salts and produce solutions of very high osmolarity 5 to 8 times that of tissue and plasma (300 mosm/kg).

Volumes of contrast media used for each injection in this study (3ml-3.2ml/kg) are greater than the amount used clinically but multiple injection is needed and the total amount is about same. Left ventricular pressure changes are due to a sudden increase in left ventricular volume by the rapid injection of contrast media and direct myocardial depressant effect of the contrast media and peripheral vasodilatation.

The elevation of left ventricular end diastolic pressure may be secondary to the volume expansion resulting from the hypertonicity of the contrast media, myocardial depression, or both[10].

Hyperosmolarity is a major factor in the myocardial depressant effects of contrast materials.

An experimental study shows high concentration of Na^+ and perhaps other single valence cations do exert a profound negative inotropic action[11].

Thus, excess Na^+ is the major factor causing the negative inotropic actions of contrast media and hyperosmolarity has no role in this regard.

The decline in heart rate during injection and delayed return in heart rate during injection and delayed return to baseline level is cholinergic effect.

Occasionally, direct stimulation of the parasympathetic pathway may occur during injection. This produces a vasovagal reflux with resulting hypotension and bradycardia.

The sequence of hemodynamic changes after injection of contrast media is hypotension due to peripheral vasodilatation and direct myocardial depression followed by alteration in baroreceptor activity. This phenomenon produce sympathetic activation and parasympathetic withdrawal.

Thus, heart rate, left ventricular contraction and vasodilatation return to preinjection level.

The EKG changes such as P-R interval prolongation, ST segment depression, T-wave inversion mean ischemia of conduction system and myocardium.

Contrast materilal has a direct inhibitory effect on the sinoatrial node. A similar inhibitory effect has been observed on conduction through the bundle of His and purkinje fibers[12]. Infusion of ionic contrast material into SA nodal and AV nodal arteries caused a progressive decrease in heart rate or increase in the PR interval. A similar inhibitory action was shown for other hyperosmolar solutions[13, 14].

Since hyperosmolarity is a dominant factor in causing, this effect, the low osmolar contrast media induced much smaller changes in these parameters.

Conclusion

This study shows remarkable change of left ventricular end diastolic pressure and left ventricular dp/dt with high osmolar contrast material (Telebrix 30®) but mild change with low osmolar contrast material (Hexabrix®).

Evidence from these experiments indicates that low osmolar agent has less severe hymodynamic and electrophysiologic effects on cardiovascular function.

Low osmolar contrast media is expected to reduce the risk of significant complications in clinical angiography.

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