

## Paired Comparison of Iopamidol and Iopromide in Hepatic Arteriography<sup>1</sup>

Young Ho Choi, M.D.<sup>2</sup>, Jin Wook Chung, M.D., Guk Myung Choi, M.D., Chang Jin Yoon, M.D., Keon Ha Kim, M.D., Seung Gyu Moon, M.D., Hyo-cheol Kim, M.D., Jae Hyung Park, M.D.

**Purpose:** To compare the clinical efficacy of iopamidol 370 and iopromide 370, as used in hepatic arteriography, in terms of their safety, patient tolerance, and image quality.

**Materials and Methods:** Between February and April 2001, 30 patients (M:F=27:3; mean age, 57 years) with hepatocellular carcinoma underwent hepatic angiography in which iopamidol 370 was used for transcatheter arterial chemoembolization (TAE). Sensations of heat or pain following contrast injection, a patient's distress or discomfort levels, and any side effects of the contrast media were monitored, and afterwards patients were asked whether they were aware of any differences between iopamidol 370 and iopromide 370, which had been used in hepatic angiography for previous TAE prior to February 2001. Three experienced independent radiologists assessed the diagnostic efficacy of the contrast media in terms of overall image quality, which was statistically analysed using Wilcoxon's signed ranks test.

**Results:** No patient experienced sensations of heat or pain during angiography, or showed any objective distress or discomfort, though two suffered mild nausea during angiography with iopamidol 370. None was aware of any difference between iopromide 370 and iopamidol 370. In terms of overall image quality, the diagnostic efficacy of contrast media in all patients was 'good' to 'excellent', with no significant difference between iopromide 370 and iopamidol 370 ( $p > 0.05$ ).

**Conclusion:** In hepatic arteriography, the clinical efficacy of iopamidol 370 is comparable with that of another nonionic contrast medium, iopromide 370, in terms of safety, tolerance, and image quality. Iopamidol 370 is thus a useful alternative medium.

**Index words :** Contrast media, efficacy study  
Contrast media, comparative studies  
Contrast media, angiography

The development of contrast media for angiography has always been directed toward substances with in-

creased tolerance and good radio-opacity. Since the first nonionic contrast agent was developed in 1969 to overcome the limitations of ionic contrast media that caused more intense sensations of heat and pain, and cardiac toxicity due to high osmolarity (1, 2), ongoing efforts have been made to develop media with fewer side effects.

Iopamidol is one of the most widely used nonionic contrast media with low osmolarity. To date, many clin-

<sup>1</sup>Department of Radiology, Seoul National University College of Medicine and the Institute of Radiation Medicine, SNUMRC

<sup>2</sup>Department of Radiology, Boramae Municipal Hospital  
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Address reprint requests to: Jin Wook Chung, M.D., Department of Radiology, Seoul National University College of Medicine and the Institute of Radiation Medicine, SNUMRC  
28, Yongon-dong, Chongno-gu, Seoul 110-744, Korea.  
Tel. 82-2-760-2584 Fax. 82-2-743-6385  
E-mail: chungjw@radcom.snu.ac.kr

ical studies involving its use in aortography (3, 4), peripheral angiography (5 - 7), cardiac angiography (8 - 10), cerebral angiography (11, 12), and visceral arteriography (13) have been performed, but to our knowledge, none have examined its use in hepatic arteriography. In conjunction with Dong Kook Pharmaceuticals, we therefore conducted the present investigation.

In this study, the clinical efficacy of two nonionic contrast media, iopamidol 370 (Pamiray ; Dong Kook, Seoul, Korea) and iopromide 370 (Ultravist(r); Shering, Seoul, Korea) was compared in terms of safety, patient tolerance, and image quality (Fig. 1). Iopromide 370 is one of the nonionic contrast media most widely used in angiographic procedures such as abdominal aortography and visceral arteriography, and its osmolarity and viscosity are similar to those of iopamidol 370 (Table 1). In our study, the two media were used serially during transcatheter arterial chemoembolizations (TAE) undergone by each of the patients involved.

## Materials and Methods

### Patients

Between February and April 2001, 30 patients [M:F = 27:3; age, 40 - 74 (mean, 57) years] in whom hepatocellular carcinoma had been diagnosed prior to February 2001 underwent TAE once using iopamidol 370 after written consent to its use had been obtained. Prior to February 2001, TAE was performed at least once, using iopromide 370.

All patients except one (Patient 28) were in relatively good general condition. Any one who were medically

unstable or pregnant; had moderate to severe cardiac, hepatic, or renal failure; suffered from paraproteinemia, multiple myeloma, thrombocytopenia, or sickle cell anaemia; had an allergic or hypersensitive condition for which a drug had been prescribed; or had received any other contrast medium within the previous 48 hours, were excluded from the study.

### Procedures

Before chemoembolization, patients underwent angiography to determine the location and extent of the tumor. Local anesthesia with 1% lidocaine was performed prior to femoral arterial puncture for insertion of an arterial sheath. A 5-Fr RH catheter (Cook, Bloomington, U.S.) was inserted into the aorta and its branches under fluoroscopic guidance, and angiography of the celiac trunk was performed. The amount of contrast medium used ranged from 42 to 48 mL and the injection rate was 7 to 8 mL/second. If it was suspected that an aberrant hepatic artery originated from the superior mesenteric artery, this was examined angiographically after the injection of contrast media at a rate of 6 - 8 mL/second.

Using a 3-Fr microcatheter, if necessary, selective angiography of the right or left hepatic, or inferior phrenic artery was performed to determine the exact location of

Table 1.

	Iopamidol 370	Iopromide 370
Iodine concentration (mg/mL)	370	370
Osmolarity (mOsm/kg H <sub>2</sub> O)	796	780
Molecular weight	770	791
Viscosity at 37 °C (centipoises)	9.5	9.5

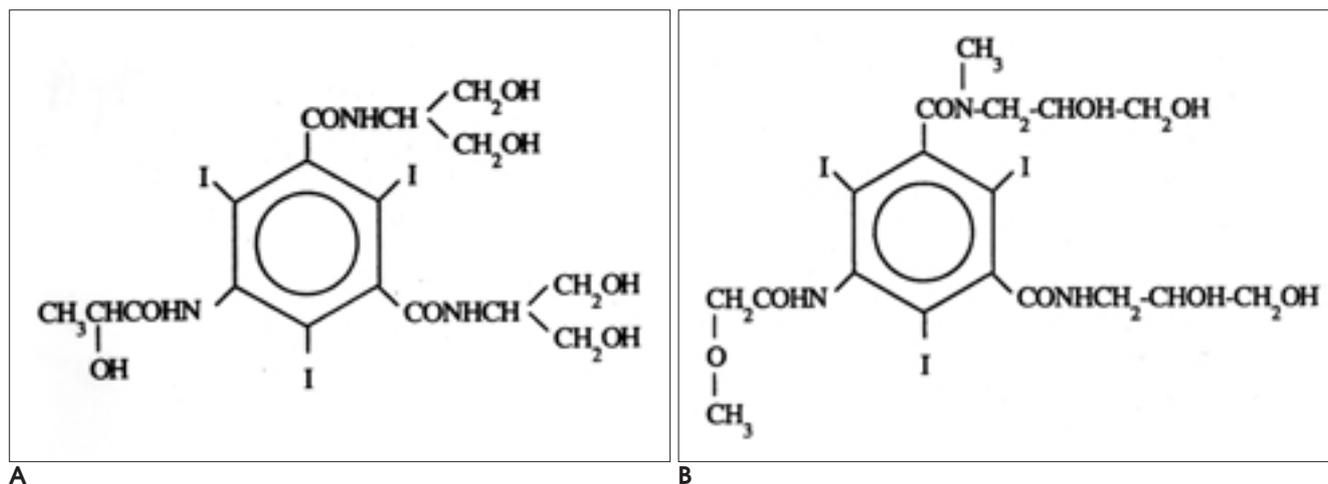


Fig. 1. Molecular structure of iopamidol and iopromide.

Iopamidol (A) and iopromide (B) have a tri-iodinated benzene ring and three highly hydrophilic side chains. They are stable in solution.

the tumor and to clarify the site of its feeding artery. The amount of contrast media used ranged from 3 to 14 mL, injected at 0.5 - 2 mL/second according to the size of the vessel.

The respective amounts of iopromide 370 and iopamidol 370 used were 42 - 105 (mean, 70.2) and 42 - 105 (mean, 68.6) mL, with no statistically significant difference between the mean volumes.

Angiographic images were obtained using a Siemens Polytron S-Plus DSA System in conjunction with a Siemens Angiostar Table equipped with a 13-inch intensifier.

### Safety and Efficacy Analysis

During hepatic angiography performed using iopamidol 370 between February and April 2001, patients were told that sensations of heat or pain might occur after contrast injection, and were asked to grade these sensations after the whole procedure as 'none', 'mild', 'moderate' or 'severe'. Investigators used a four-point scale, as follows, to assess the degree of a patient's distress or discomfort: 0, no evidence of distress; 1, slight movement and/or vocal complaint; 2, moderate movement and/or vocal complaint; 3, forcible movement and/or loud cries.

Side effects during the procedures were determined by direct questioning and observation. The severity of any side effect was graded as 'none', 'mild' (disappearing spontaneously, or no need for therapy), 'moderate' (necessitating therapy but responding immediately) or 'severe' (alarming or life-threatening, responding poorly or slowly to therapy). All patients were monitored for

side effects for at least 24 hours after the completion of procedures.

After the conclusion of angiography, patients were asked whether they were aware of any differences between iopamidol 370 and iopromide 370, which had been used in hepatic angiography before February 2001. The safety of iopromide 370 was analysed on the basis of the answers and the patients' medical records.

Image quality was assessed by three experienced independent radiologists blinded to a patient's identity and clinical profile and to the contrast media used. In addition, each was unaware of the other radiologists' assessment. Using original images, the diagnostic efficacy of contrast media in terms of overall image quality was assessed according to a five-point scale, as follows: 1, poor opacification; 2, insufficient opacification; 3, sufficient opacification; 4, good opacification; 5, excellent opacification. "Poor" indicated that image quality did not permit diagnosis, and "excellent" that vessel detail was visible. For statistical analysis of image quality, Wilcoxon's signed ranks test was used. Two-sided probability (p) values of <0.05 were considered statistically significant. The reproducibility of the three observers' assessment of image quality was assigned a (kappa) value.

### Results

No patient experienced sensations of heat or pain during angiography with either iopromide 370 or iopamidol 370, or showed any objective distress or discomfort. Two patients complained that the use of iopamidol 370 led to mild nausea, though none were aware of any dif-



Fig. 2. Image quality of hepatic angiography. Two hepatic angiograms were evaluated as "good opacification" (A) and "excellent opacification" (B) by all three radiologists.

ferences between the two media.

With regard to the reproducibility of observers' assessment of image quality, values of 0.58, 0.74, and 0.64 was assigned to observers 1 and 2, 1 and 3, and 2 and 3, respectively. Thus, interobserver agreement was good. The diagnostic efficacy of contrast media in terms of overall image quality was 'good' to 'excellent' in all patients, with no significant difference between iopromide 370 and iopamidol 370 ( $p=0.257, 0.763, \text{ and } 0.102$  in observer 1, 2, and 3, respectively) (Fig. 2).

## Discussion

Nonionic intravenously or intra-arterially administered contrast media have been proven to be better tolerated and safer than commonly used ionic media with high osmolarity (1, 2). Thus, larger amount of nonionic contrast media can be used with relative safety in high-risk patients. Since first becoming available, this type has thus become established as most suitable for most applications.

In high-concentration aqueous solution, iopamidol is chemically similar to other nonionic contrast media, iopromide and iohexol, in terms of its low osmolarity, low viscosity, and low capacity for protein binding. Iopromide has a slight advantage over iopamidol in terms of osmolarity and protein binding, though in this study, no differences in safety, patient tolerance or image quality were noted.

Extensive research in Europe and North America (3 - 13) has demonstrated the safety, diagnostic quality, and improved patient tolerance of the nonionic contrast media, iopamidol, relative to ionic contrast media, in peripheral arteriography, cardiac angiography, myelography, urography, cerebral angiography, abdominal aortography, and visceral arteriography. However, no equivalent study has provided a paired comparison of these contrast media for hepatic arteriography. In this study, we have determined whether there is any difference between the two nonionic contrast media, iopamidol and iopromide, as used in hepatic arteriography.

We found that iopamidol was equivalent to iopromide in terms of the sensations of heat or pain, or distress or discomfort induced; side effects; and diagnostic efficacy. Both media proved to be safe and well tolerated, providing good radiographic quality without untoward side effects. The one side effect reported by two patients was mild nausea during angiography with iopamidol.

Our study suffered certain limitations. First, our data

were collected from just 30 patients, which may have induced bias. To determine whether iopamidol and other contrast media, including iopromide, exert different effects because of differences in their formulation or physicochemical characteristics, studies involving more subjects are thus required.

Second, the safety of iopromide, including possible side effects, was evaluated prospectively on the basis of the patients' recollections and hospital records, and this may have induced bias. However, investigation of the safety of iopromide showed at least equal or better results than that of iopamidol, and conclusions may thus be reasonably drawn from our data.

In conclusion, the clinical efficacy of iopamidol 370, as used in hepatic arteriography, is comparable to that of iopromide 370 in terms of safety, patient tolerance, and diagnostic efficacy. In diagnostic angiography, including hepatic arteriography, iopamidol is thus a useful alternative to other nonionic contrast media.

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