The Comparison of X-ray Attenuations of Contrast Media in Different Dilutions: An experimental Study

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ABSTRACT

Aims: Iodinated contrast materials are used as contrast material in radiologic examinations. There is an intense competition between the contrast media companies in the contrast market in areas such as price, effectivities, and lack of side effects. This experimental study was carried out for comparing the effectiveness of contrast agents. We measured X-ray attenuations of contrast agents because image quality depends on these attenuation amounts. **Materials and Methods:** Contrast agents are divided into two main groups in iodinated contrast materials; ionic-iodinated contrast agents and nonionic-iodinated contrast agents. Nonionic contrast materials are iopamidol, iohexol, iopromide, iobitridol, and iomeprol. In this study, by using contrast agents in different dilutions, X-ray attenuations were examined in Hounsfield units by using computed tomography. **Results:** There was no statistically significant difference between the slopes of five commercial forms according to dilutions. **Conclusion:** From our study, we concluded that iopamidol, iohexol, iopromide, iobitridol, or iomeprol are same in clinical usage.

Key words: Computed tomography; contrast agents; X-ray attenuations

Introduction

Radiographic contrast agents are the compounds which are used to improve the visibility of tissue and organs in a radiologic image. Radiographic contrast media are divided into positive and negative contrast agents. The positive contrast agents attenuate X-rays more than body's tissue and space.[1,2]

Iodinated contrast materials are most commonly used as contrast agents in radiologic examinations. Water-soluble iodinated contrast agents are used for angiography, computed tomography (CT), and radiography. There are two main groups in iodinated contrast materials; ionic-iodinated contrast agents and nonionic-iodinated contrast agents. In clinical usage, nonionic contrast agents are preferred for intravenous applications due to effectivities and fewer side effects.[1-4] Commercially available nonionic contrast media are iopamidol, iohexol, iopromide, iobitridol, and iomeprol. There are competitions between the pharmacological companies in the contrast market, in areas such as price, effectivities, and lack of side effects.

In clinical use, the success of contrast agents is known to be dependent on many factors. These factors are hemodynamic, renal functions, hydration, etc., Some basic parameters affect the success of contrast agents, remaining are unchanged, and the effectivity of contrast media has been observed to be more different.[2,4] X-ray attenuation values directly affect contrast agents' efficiency. In this experimental study, by

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using contrast medium in different dilutions, phantoms were created, and then X-ray attenuations were examined in Hounsfield units (HU) by using CT.

Materials and Methods

Primarily, commercial forms of iopamidol, iohexol, iopromide, iobitridol, and iomeprol containing 300 mg iodine were provided. The total volume was 10,500 μL for each item. The dilutions were done by a 10-year experienced biochemistry specialist by using bi-distilled water.

Each dilution set contained nine tubes, the dilution proportions are as follows [Table 1]:

X-ray attenuation values were calculated. Results were compared statistically for each compound. Each set was placed on Styrofoam™ tube pads so that phantoms were created. To avoid beam hardening and to obtain real density values as much as possible, we placed phantoms center of field of view. Each phantom was scanned in 80–120 Kvp, in 5 mm and 10 mm slice thickness, by using 64 MDCT TK LIGHT SPEED GE Medical System. After scanning, we obtained digital imaging and communications in medicine images, and we measured density as HUs by using GE work station and MVIS work station. In 0.5 cm^2 circular area, HUs were measured. All values were transferred into graphic images, and statistical evaluation was carried out by SPSS for Windows version 17.0 statistics software program (Microsoft, Seattle, USA).

Results

At the determined rates in the dilution of contrast media, results of the measurements were shown in Tables 1-6.

To compare the dilution values in the five commercial forms (iopamidol, iohexol, iopromide, iobitridol, and iomeprol), we used a one-phase exponential decay model. More explicitly, the exponential decay model was established using the following equation:

Measure = Initial level × exp(−t × k),

where, t and k signify dilution and exponential rate constant, respectively.

We estimated the relevant rate constants by nonlinear regression of the one-phase exponential model on the

Table 1: Contrast material diluton ratios

Dilutions	Contrast material (μL)	Total volume (μL)
1/100	105	10,500
1/125	84	10,500
1/150	70	10,500
1/175	60	10,500
1/200	53	10,500
1/225	47	10,500
1/250	42	10,500
1/275	38	10,500
1/300	35	10,500

Table 2: Iohexol

Dilution	Mean (HU)	SD	Sum	Minimum	Maximum
1/100	101,511	6014	18,475	88	122
1/125	80,599	4780	15,072	65	92
1/150	70,156	4909	13,049	54	86
1/175	60,587	4777	11,451	46	72
1/200	54,172	5480	10,076	42	69
1/225	46,326	5250	8663	33	60
1/250	42,532	5034	7996	32	55
1/275	34,573	5236	6396	22	45
1/300	29,417	4249	5501	17	39

SD – Standard deviation; HU – Hounsfield unit

Table 3: Iomeprol

Dilution	Mean (HU)	SD	Sum	Minimum	Maximum
1/100	72,503	4055	13,413	64	86
1/125	67,935	6023	12,500	56	85
1/150	59,522	5995	10,952	45	75
1/175	52,532	6271	9771	36	67
1/200	45,071	6163	8293	28	60
1/225	3350	5763	6211	21	53
1/250	26,086	6217	4852	9	40
1/275	22,947	4923	4337	12	35
1/300	14,620	4024	2690	5	24

SD – Standard deviation; HU – Hounsfield unit

Table 4: Iobitridol

Dilution	Mean (HU)	SD	Sum	Minimum	Maximum
1/100	78,930	5204	14,760	65	94
1/125	67,853	6519	12,485	54	83
1/150	58,306	4448	10,670	46	69
1/175	53,749	4942	10,051	45	73
1/200	44,222	4450	8181	33	57
1/225	35,204	5652	6548	21	47
1/250	34,032	5820	6415	24	53
1/275	24,935	4686	4588	13	35
1/300	15,930	4263	2947	6	25

SD – Standard deviation; HU – Hounsfield unit

Table 5: Iopromide

Dilution	Mean (HU)	SD	Sum	Minimum	Maximum
1/100	108,651	4848	20,209	97	119
1/125	78,064	4800	14,676	66	92
1/150	57,403	4980	10,677	44	68
1/175	56,092	5088	10,321	43	72
1/200	48,473	4579	9113	38	60
1/225	4803	5096	9047	31	62
1/250	35,149	5232	6608	23	47
1/275	22,476	5608	4203	9	35
1/300	20,357	3963	3766	11	30

SD – Standard deviation; HU – Hounsfield unit

Table 6: Ioversol

Dilution	Mean (HU)	SD	Sum	Minimum	Maximum
1/100	87,435	3822	16,283	79	96
1/125	58,622	5469	10,845	48	72
1/150	56,060	4284	10,203	44	67
1/175	5220	4774	9918	41	65
1/200	3709	4416	7010	26	47
1/225	2912	4267	5197	15	39
1/250	27,134	4061	5074	17	39
1/275	18,054	3799	3358	8	27
1/300	16,082	3291	2943	5	25

SD – Standard deviation; HU – Hounsfield unit

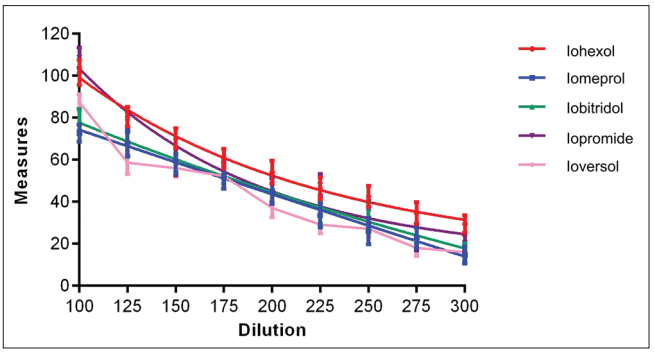

Figure 1: Slopes of dilution and X-ray attenuation values in the five commercial forms of contrast mediums

average measure in each commercial form. For the statistical comparison of the rate estimates, we used one-way ANOVA, in which the asymptotic standard errors of the estimates with their associated degree of freedom were used to calculate the F-statistics and the corresponding probabilities. Brown–Forsythe test was used for pair-wise comparison between the five commercial forms.

There is no statistically significant difference between the slopes of five commercial forms according to dilutions (F [4, 40] =0.7061, P = 0.5925) [Figure 1].

Discussion

Mainly, commercially available contrast agents contain iopamidol, iohexol, iopromide, iobitridol, or iomeprol. Manufacturers try to show the superior properties of their drugs as much as possible because this condition creates doubts among clinical users. Inevitably, they begin to compare their drugs.

Iomeprol, iopamidol, iohexol, iopromide, and iobitridol are monomeric nonionic, iodinated contrast agents. In the literature, it was reported that there was no difference between the diagnostic efficiencies of contrast agents significantly from that of others.[1,2] Our study results are the similar of the literatures. Despite the above-mentioned contrast agents show differences, enhancement effects are generally regarded as the same. Hemodynamic, cardiac, renal, and thyroid functions are tested *in vivo*.[3,4] Molecular structure of the iodinated contrast agents is based on single tri-iodinated benzene ring. The most recent class of agents is dimers that consist of a molecule with two benzene rings (again, each with three iodine atoms) that do not dissociate in water (nonionic) which are designated as iso-osmolar contrast agents.[3-5] The toxicity of contrast agents decreases as osmolality approaches that of serum. This has been accomplished by developing nonionizing compounds and then combining two monomers to form a dimer, the currently used iodinated agents are cleared almost completely by glomerular filtration. With reduced renal function, there is vicarious excretion primarily in bile and through the bowel. Circulatory half-life is 1–2 h, assuming normal renal function.[4,5]

Side chains of the contrast agents are slightly different. Although side chains have two hydroxyl and one amide group, the differences are on the conformation. The study demonstrated that the differences might not effect statistically on the absorption of X-ray.[1,3-5]

The results of these studies are subjective. Dimeric nonionic iodinated contrast has a lower osmolality than monomeric nonionic iodinated contrast, but it is available at lower iodine concentrations, less dilution of intravascular fluid by influx from the extravascular space is proposed to occur with decreasing osmolality, and there is less intravascular dilution of iso-osmolar contrast.[6] Injection of iodinated radiographic contrast media is generally safe; however, with increased use, adverse events are more likely to occur; the most important adverse effects include hypersensitivity reactions, contrast-induced nephropathy, and thyrotoxicosis.[7] In patients with moderate renal dysfunction, adequate hydration and use of as little contrast media as practical are recommended. Contrast-induced nephropathy is often transient.[7,8]

We aimed to compare the characteristics of attenuation of contrast agents objectively; this study reviews absorption data about X-ray contrast media *in vitro*. In some references, animal–human data are used in areas where no absorption data are available. These references report that the pharmacokinetic properties of all contrast media (iopamidol, iohexol, iopromide, iobitridol and iomeprol) are similar.

Conclusion

According to our study, there is no difference in the clinical usage of iopamidol, iohexol, iopromide, iobitridol, or iomeprol.

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Conflicts of interest

There are no conflicts of interest.

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