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Iopamidol in comparison with meglumine sodium diatrizoate in different concentrations as contrast media in clinical endodontics – in vivo study

KEYWORDS: Endogram; Endodontic Anatomy; Radiopaque; Viscosity

Uday S. Mahale
Post Graduate Student, Department of Conservative Dentistry and Endodontics, A. B. Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, India

Mithra N. Hegde
Senior Professor and Head of the Department, Department of Conservative Dentistry and Endodontics, A. B. Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, India

Aditya Shetty
Reader, Department of Conservative Dentistry and Endodontics, A. B. Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, India

Amit B. Patil
Senior Lecturer, Department of Conservative Dentistry and Endodontics, A. B. Shetty Memorial Institute of Dental Sciences, Mangalore, Karnataka, India

ABSTRACT *The purpose of this study was to evaluate the clinical efficiency of the newly adopted contrast mediums Iopamidol (IP) in comparison with Meglumine sodium diatrizoate (DZ) at different concentrations in endodontics.*

Methods : 48 patients with mandibular premolars indicated for root canal therapy were selected. IP and DZ were studied in 30%, 50% and 75% concentrations to form six groups (n=8). The different radiographic contrast mediums were introduced into the pulp space after gaining access. The radiographic images before and after introduction of the contrast mediums were evaluated by three endodontists based on a standardized questionnaire. Inter observer agreement (Kappa) was calculated.

Results: The number of root canals observed after introduction of IP75% and DZ50% were increased. DZ50% showed significantly more lateral canals (p = 0.026). IP50% and DZ50% revealed more canals throughout the length as compared to rest of the groups. 50% and 75% concentrations of both the contrast media showed desirable radiopacity. The Odds ratios for intergroup comparison were 20.83 for DZ50% and 14.92 for IP50%, keeping DZ75% as base for the comparison.

Conclusion: The newer contrast medium IP showed results comparable with DZ. 50% concentration of both the contrast media showed desirable flow and radiopacity. Hence Iopamidol can be used as contrast medium in endodontics.

Introduction

The human tooth has a complex pulp space anatomy. The presence of patent furcal, lateral and accessory canals are the portals of entry and exit between the root canal space and the periodontal ligament [1,2]. Radiographic identification of these portals may aid in the assessment of anatomy of the pulpal system.

The radiographic interpretation of the pulp space anatomy suffers from superimposition of the surrounding bone tissue [3].

Structures having similar average atomic number and densities are difficult to distinguish on a radiograph due to lack of natural contrast. The average atomic number of a hollow structure can be increased by the introduction a of liquid with greater average atomic number such as an iodinated contrast media[4]. The Contrast mediums are radiopaque dyes that could be introduced into the body parts to artificially alter subject contrast[5]. The radiographic appearance of the tooth pulp space after receiving a radiopaque contrast medium is known as "Endogram".

Iodinated contrast media are of two types, Ionic and non-ionic. Ruddle's solution, containing ionic medium, and Saigram, containing non-ionic medium, have been successfully used clinically in combination with chelating agent and organic tissue dissolving solvent, in the form of an irrigant [4,6,7]. Ionic contrast media have i) high osmolality which causes sensation of heat and discomfort, pain and potential irritation, if it extends beyond the apex, ii) high viscosity which requires more pressure to flow. Non-ionic contrast media are low in osmolality, less chemotoxic, better tolerated and less viscous[8]. Katayama et al observed four times reduction in the adverse reaction in non-ionic contrast media[9].

Studies have concluded the ineffective use of Ionic contrast media viz. Ultravist 370® and Hypaque-M 90% in root canals of extracted teeth[10,11]. Considering the concentration (more than 75%) of contrast mediums used in their study, we suspect the reason behind unsuccessful results could be high viscosity, which prevented contrast medium to flow into the narrow lateral canals.

Iopamidol has been adopted for endodontics in this present study. It is a non-ionic contrast medium, which has already been used in angiographic procedures in the medical field[12].

In the present study, we have compared a newer non-ionic contrast medium, Iopamidol with an ionic contrast medium, meglumine sodium datrizoate at various dilutions as an aid in improving the radiographic visualization of the root canal anatomy. The purpose of dilution was to reduce the viscosity of the contrast media. However, dilution also caused reduced radio opacity of the contrast media. Therefore, this study was conducted to determine the optimum concentration at which the contrast medium had desirable flow and radio opacity.

Materials and Methods

This was an open labeled, multi-arm parallel-group study. The study protocol was approved by the Institutional Ethical Committee of Nitte University (ref. ABSM/EC/123/2010). This study included 48 patients totally, who had visited the Department of Conservative Dentistry and Endodontics, A B Shetty Memorial Institute of Dental Sciences, Mangalore, India between January 2011 to February 2012. 'Convenience Sampling' method was used[13]. Patients within age group of 20 to 40 years with mandibular premolar indicated for root canal therapy were included in this study. Detailed case history was recorded. Pulp vitality testing and radiographic evaluation was done. Only vital teeth were included as the

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vitality affects dye penetration[14]. The reason behind selecting this age group was that, by the age of 20 years, pulp space is completely developed and beyond the age of 40 years, chances of pulp calcifications are more. Following patients were excluded from the study: teeth with open apices, calcification in the pulp space, resorbed apex, non- vital teeth and patients with history of allergy to any allergen [14,8].

Only those patients, who had read, understood and signed the consent form allowing their inclusion in the study were enrolled. The consent form included information regarding the pros and cons of the procedure and radiation exposure.

Contrast Media Used
Sterile samples of Iopamidol (IP) (Iopamiro370, Bracco, Patheon Italia S.p.A. Ferentino, Italy) and Maglumine sodium diatrizoate (DZ) (Urografin76%, Bayer ZydusPharma Pvt. Ltd., Thane, India) were prepared in concentrations of 75%, 50% and 30%.These contrast media are safe with respect to adverse reactions and nephrotoxicity[15,16].

Both contrast media were diluted by water for injection to eliminate the chances of forming any chemical byproducts or changing the properties of the solution. Density and viscosity of the prepared contrast media samples were measured.

TABLE 1:- Groups of contrast media with their viscosities and densities

Chief Ingredient	Concentrations used	Density (ρ) gm/cc	Viscosity (mPa.s) at 25°C
Iopamidol (Nonionic) (Group IP)	30%	1.163	2.20
	50%	1.269	4.43*
	75%	1.367	14.67
Maglumine sodium Diatrizoate (Ionic) (Group DZ)	30%	1.166	2.13
	50%	1.274	3.98*
	75%	1.418	14.23

Table 1:- Viscosities of different Groups of contrast media based on their concentrations
* àMarked reduction in viscosity by reducing concentration of contrast medium from 75% to 50%

Clinical Procedure to Introduce Contrast Media into Pulp Space

Each subject was imaged using digital radiography before commencement of access cavity preparation. Access cavities were made after rubber dam (Hygenic, Coltene/Whaledent Inc., Ohio) application under local anesthesia with adrenalin 1:80,000 (Lignox, Indoco Remedies Ltd., Mumbai, India) Pulp tissue was extirpated. The canals were irrigated using 3% sodium hypochlorite (Vension India, Bangalore, India) and distilled water. Care was taken to prevent enlargement of the apical foramen to avoid periradicular flow of the contrast medium. Liquid EDTA (Comet, Comodent Corp., Mumbai, India) was flooded into the canal to remove the smear layer[17]. Canals were dried with the help of paper points (Dentsply Maillefer, Ballaigues, Switzerland).

Contrast media were introduced into the pulp space using Incremental Passive Injection Technique [18]. This technique was modified by using counterclockwise rotation of 4% tapered 25 number rotary file (Race, FKG Dentire, La Chaux-de-Fonds) [19,20]. This helped in the apical flow of contrast media by Archimedes Screw Effect (fig. 1E).

Digital radiographic images were obtained after introduction of the radiopaque contrast media. Contrast media was retrieved using copious irrigation by saline followed by instrumentation with 15# k file. Retrieval of the contrast media was confirmed by a digital radiograph.

All digital radiographic images were taken using the charged couple device based on a direct digital sensor (Skanray, Mysore, India). The digital sensor was positioned with the help of a sensor holder. Position of the sensor was fixed to the holder with the help of rubber based impression material. This was done to facilitate constant angulation for obtaining radiographic images before and after introducing contrast media in each case. The intraoral X-ray unit used in this study had an X-ray tube model OX/70-P (CEI, Bologna, Italy) with a nominal focal spot size of0.8IEC60336 and total filtration of 3mm aluminium equivalent. The generator was operated at 60kVp and 8mA with computer controlled timer. Short cone collimation (22cm) resulted in a >6cm aperture diameter. Optimal exposure time was determined by a series of images at different exposure time. 0.08 s was used for all radiographic images. The digital images were stored using IntraSkanDigi software program (Skanray Technologies, Mysore, India).

Evaluation of Radiographic Images
The digital radiographic images before and after the introduction of radioopaque contrast media were presented to three practicing endodontists. All images were examined and assessed as per the following questionnaire.

Q1. Number of root canals

Q2. Presence of lateral/accessory canals (yes/no)

Q3. Whether contrast medium is visible along the entire length of the root (yes/no)

Q4. Is Contrast of radiopaque medium satisfactory? (yes/no)

by Bedford, D. M. Martin and C. C. Youngson [10] (Modified)

Statistical Methods
Inter observer reliability was calculated by Kappa statistics.

Statistical evaluation of Q1 and Q2 was done by Chi Square test to evaluate efficiency of each contrast medium by comparing data obtained before and after its introduction. Multinominal Logistic regression was used for intergroup comparison of all groups based on data obtained by Q3 and Q4 after introduction of the contrast media. SPSS (Statistical Package for Social Science) Software version 19 was used for statistical analysis.

Results
The degrees of inter observer reliability were assessed for three evaluators for each question in the questionnaire. Kappa scores were ranging from 0.4 to 0.9 which showed moderate to very good agreement.

After confirming reliability, 1st observer's readings were taken into consideration for the study.

To check whether there was any difference in the visualization of the number of root canals before and after introduction of the contrast media, Chi-Square test was used for each group of contrast media.

Table 2:- Findings of the radiographic assessment

Groups (n=8) à	IP30%		IP50%		IP75%		DZ30%		DZ50%		DZ75%	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Q1	8	5	8	8	8	9	8	5	8	10	8	7
Q2	0	0	1	2	0	0	0	0	0	4	1	0
Q3	1		6		2		1		7		2	
Q4	0		6		8		0		8		8	

Table 2:- Findings of the radiographic assessment
Q1 àTotal number of Canals Observed
Q2 à Number of cases in which lateral canals were observed
Q3 à Number of cases in which contrast media could be ob-

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served till entire length of canal
Q4 à Number of cases with Satisfactory Radiopacity
In cases of IP30% andDZ30%, the number of root canals seen, were more before the introduction of the dye as compared to, after introduction of contrast media. This suggests that the introduction of IP30% and DZ30% contrast media hampered the visualization of the total number of canals instead of enhancing it.

In case of IP50%, same number of root canals were seen before and after introduction of the contrast media. This suggests that IP50% contrast media did not make any difference in diagnosis of the number of canals.

The number of root canals seen were increased after the introduction of IP75% and DZ50%. But the result was not statistically significant (p=0.467).

Comparison of radiographic images before and after introduction of contrast media using Chi Square test showed significantly more lateral canals after the introduction of DZ50% (p=0.026).

IP50% also revealed lateral canals after the introduction. But the results were not statistically significant.

Visibility of lateral canals was reduced after the introduction of IP30% and DZ75%.

In most of the cases of IP50% and DZ50%, contrast medium could be observed throughout the length of the canal whereas in rest of the groups, contrast media could not be observed throughout the entire length.

IP30% and DZ30% showed unsatisfactory radiopacity. IP75% and DZ75% showed satisfactory radiopacity. IP50% and DZ50% contrast media were equally good.

Multinominal logistic regression was used for intergroup comparison of contrast media based on their ability to reach the apex and radiopacity.

DZ75% was considered as base of the comparison. IP50% in comparison to DZ75%was more likely to show the entire canal length with an odds ratio of 1/0.067 = 14.92. DZ50% in comparison to DZ75%was more likely to show the entire canal length with an odds ratio of 1/0.048 = 20.83

Multinominal logistic regression analysis showed that DZ50% is the best (roughly 21 times better than DZ75%) for visualization of the entire canal length with satisfactory radio opacity as compared to other groups in the study.

Discussion
IP has been proved to be a much safer contrast medium than DZ [12]. Nonetheless, considering the minimal quantity i.e. 0.2ml of contrast medium required in this Modified Incremental Passive Injection Technique and the confinement of DZ into the pulp space, it can be safely used.

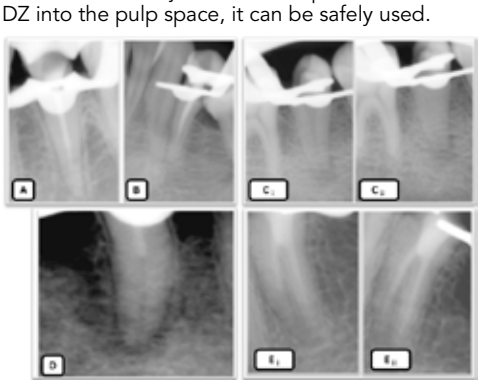

Figure 1:- Digital radiographic images are showing A) the inadequate penetration of contrast media short of apex.IP75% introduced into tooth number 35; B)the inadequate penetration of DZ75% introduced into tooth number 45; C i)Tooth number 35 before introducing contrast medium. Single root canal can be observed; C $_{ii)}$ Same tooth after introduction of IP30%. Root canal is not visible due to reduced subject contrast; D) Penetration of contrast medium restricted to coronal third of root canal. E $_{i}$) Inadequate penetration of contrast media with Incremental Passive Injection Technique. E $_{ii}$) Better penetration of contrast media in same tooth with Modified Incremental Passive Injection Technique

At 75% concentration (IP75% and DZ75%) media could not reach to the apex of the root canal although they demonstrated clinically desirable radioopacity (Fig. 1A, 1B). There was reduction in contrast at 30% concentration (Fig. 1C). When the room temperature was recorded below 20 degree Celsius, IP75% showed increased viscosity. This led to the lack of flow of the contrast media (Fig. 1D).

The advantage of conducting an in vivo study was that, we could assess the flow of contrast media with the limitation of minimal pressure for its introduction, unlike in vitro studies, where highly viscous 75-90% concentrated contrast media were forcefully introduced into the pulp space with help of high pressure or centrifuge [10,11,23,24,25,26].

Shortcoming of this study was that, we could not render patient's teeth for sectioning, clearing technique [10] or illumination [11] to check the actual anatomy of pulp space. The use of cone beam computed tomography (CBCT) to observe three dimensional pulp space anatomy was avoided as it would have exposed the patient to higher radiation with no extra benefits in endodontic outcome. Patient's exposure to radiation should be kept as low as reasonably achievable(ALARA) [27,28]. Therefore diagnostic specificity or sensitivity of contrast media could not be calculated.

The lateral canals were observed in few cases using DZ50%. However, the radiopacity of the contrast media which flowed into the lateral canals were not diagnostically satisfactory when compared to the one found in the main canal. This study is in accordance with the observations of previous studies, stating that the passive introduction of contrast media did not improve the demonstration of lateral canals [11,29].

The probable factors prohibiting the detection of accessory canals were narrow lumen of accessory canals [2,30], inadequate resolution of digital radiograph [30,31], two dimensional image leading to masking of buccally or lingually oriented accessory canals[11] and debris or smear layer clogging the opening of accessory canals[17].Therefore further research is needed to overcome aforementioned problems to demonstrate the lateral canals. Also research is required to increase the wettability of the contrast media, chemical interaction of surfactants and their effects on properties of the contrast media.

Conclusion
The results of this in vivo study demonstrated that DZ and newly adopted contrast agent IP worked best at 50% concentration by showing optimal flow and radiopacity. 50% concentrated IP can be used as an adjunct to available radiographic and clinical techniques as an aid in assessment of the complex root canal anatomy.

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