

# Correlation studies of barium on pulmonary infection under the assessment of VFSS

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**Abstract.** Stroke is a common clinical disease resulting in somatic dyskinesia as well as different degrees of dysphagia. The aim of the study was to assess the results obtained from the utilization of 60% barium sulfate suspension and iohexol as contrast agents in video fluoroscopic swallowing studies (VFSS), and compare the association between the clinical application of the two contrast agents and the incidence of pneumonia. A total of 60 cases of in-patients with dysphagia caused by stroke were selected and divided into two groups based on the diagnostic standard. No obvious differences were evident between the groups with regard to gender, age, position of stroke and the nature of stroke. The patients were divided into an iohexol group of 30 patients administered with 350 mgI/ml iohexol as a contrast agent, and a barium sulfate group of 30 patients administered with 60% barium sulfate suspension as a contrast agent. A VFSS evaluation was implemented before and after 3 weeks of treatment, respectively, and the pharynx transit time was compared between the two groups of contrast agents according to the position of stroke. By using case-control studies, the incidence of pneumonia between the two groups of patients within 2 weeks after hospitalization was analyzed and the association between the complication probability with different contrast agents was analyzed. After 2 weeks in hospital, the incidence of aspiration pneumonia of the two groups was statistically significant ( $P < 0.05$ ). The incidence of pneumonia of the iohexol group was markedly lower than that of the barium sulfate group, which may be important for barium aspiration. In conclusion, in the VFSS of dysphagia after stroke and barium sulfate increased the incidence of pneumonia, and that iohexol was widely used in video fluoroscopy.

## Introduction

Stroke is a common clinical disease that results in somatic dyskinesia such as hemiplegia, as well as different degrees of

dysphagia after stroke (DAS). Acute stroke patients (37-74%) have different degrees of dysphagia while patients (37%) with aspiration are likely to develop pneumonia (1). Oropharyngeal and swallowing functions are determined by swallowing study and the diagnostic basis for early dysphagia.

Video fluoroscopic swallowing studies (VFSS) are commonly regarded as the golden standard for the diagnosis of dysphagia (2). In clinic, the most common method involves producing 60% barium sulfate suspension via a mixture of barium powder with a specific amount of water (3). However, barium has a few shortcomings such as large in size, insoluble in water, non-absorbable by human body and easy precipitation. Additionally, the DAS patients may be at risk for aspiration. Barium aspiration under VFSS caused or aggravated pulmonary infection (4). Iohexol is a type of non-ionic contrast agent with low osmotic pressure, which is ~2-fold that of the plasma osmotic pressure (4). Iohexol was able to reduce its influence on red blood cells, vascular endothelial cells, and isohydria to the minimum. Iohexol has been widely used in enhanced computerized tomography (CT) scans (5). Since it can be metabolized and absorbed by the human body, even if aspiration occurs in the process of VFSS, it is not likely to produce any iatrogenic injuries. Thus, it constitutes as a viable substitute for VFSS on DAS patients.

The aim of the study was to assess the results obtained from the utilization of 60% barium sulfate suspension and iohexol as contrast agents in video fluoroscopic swallowing studies (VFSS), and compare the association between the clinical application of the two contrast agents and the incidence of pneumonia in 60 cases. The results showed that VFSS of dysphagia after stroke and barium sulfate increased the incidence of pneumonia and that iohexol may be used in video fluoroscopy

## Materials and methods

**Materials.** The Philips-TD digital multifunction gastrointestinal imaging camera used was purchased from the Royal Dutch Philips Electronics Ltd. (Amsterdam, The Netherlands). Barium sulfate powder was purchased from Qingdao Dongfeng Chemical Ltd. (Qingdao, China), and Iohexol was purchased from the Yangtze River Pharmaceutical Group (Taizhou, China). FA1004 konjac glucomannan was purchased from Zhejiang Hailisheng Pharmaceuticals Company (Zhejiang,

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China). FA1004 electronic balance was purchased from Shanghai Tianping Apparatus factory (Shanghai, China). The Sony HDR-XR150E digital camera was purchased from the Shanghai Suoguang Electronics Co., Ltd. (Shanghai, China).

**Cases.** The study included 60 cases of stroke in-patients from the Department of Rehabilitation of the Central Hospital of Xuzhou (Xuzhou, China) between September 2010 and October 2011. Selection criteria were: i) Conform to the revised diagnostic criteria for acute cerebrovascular disease (6) as per the 4th National Academic Conference on the diagnosis of cerebrovascular disease in 1995. The cerebral infarction or cerebral hemorrhage was required to be confirmed by brain CT or magnetic resonance imaging. ii) degree II-IV for the Kubota drinking water test. iii) The first onset patients or patients with a past history of stroke, but without any sequelae including swallowing dysfunctions within 6-month course. iv) Between 20 and 70 years old with clear consciousness, 15 scoring points as per the Glasgow Coma Scale, stable vital signs, understanding and execution of simple instructions, and score >7 points under abbreviated mental test scale (7); showing stable vital signs, ability to undergo radiology tests.

**Contrast agent preparation.** The patients were divided into groups. The barium sulfate group was administered Liquid E-Z Paque barium sulfate suspension (60%) (Qingdao Chemical Engineering Ltd., Co., Shandong, China) comprising 150 g barium powder with 100 ml water. Semi-liquid barium sulfate comprised pasty barium food produced from a mixture of 60 ml of the 60% barium sulfate suspension with 1 g thickener (konjac glucomannan). Pasty barium sulfate comprised pasty barium food produced from a mixture of 60 ml of the barium sulfate suspension with 2 g thickener (konjac glucomannan). Solid barium sulfate was produced by spreading the semi-solid contrast agent, which was produced using 60% barium sulfate suspension, on whole wheat bread. For the iohexol group, liquid iohexol group was produced from 50 ml iohexol of 350 mgI/ml. Semi-liquid iohexol was produced from the mixture of 50 ml iohexol of 350 mgI/ml with 0.75-g thickener (konjac glucomannan). Pasty iohexol was produced from a mixture of 50 ml iohexol of 350 mgI/ml with 1.5-g thickener (konjac glucomannan). Solid iohexol was produced by spreading the semi-solid contrast agent, which was compounded by iohexol, on the whole wheat bread. Radiography was accomplished by the mutual efforts of the trained rehabilitation physicians and the senior radiologists and was subject to their consensus.

**Observation content.** Real-time video was implemented for the radiography, and the images captured by video camera (Sony HDR-XR150E; Shanghai Soguang Electronics Company, Shanghai, China) and radiographic machine (PHILIPS-TD digital, Philips, The Netherlands) were analyzed. The images were observed individually using slow video playback (24 frames per sec). Subsequently, the pharynx transit time (8) was observed and calculated. This transit time started from the moment when the bolus produced by the contrast agent reached the point where the tongue root conjoined with the lower jawbone and swallowing began when the head of the bolus reached the opening of the esophagus, which was the

upper border of cricopharyngeus muscle. Aspiration, which referred to the condition whereby barium entered the vestibulum laryngis and reached the vocal fold, was then observed. Latent inhalation referred to the condition where no cough or other clinical symptoms occurred 1 min after aspiration was identified using VFSS (9).

**Diagnostic criteria of aspiration of pneumonia.** The diagnostic criteria (10) for the aspiration of pneumonia included: i) Newly emerged cough and sputum or the aggravation of pre-existing respiratory diseases, and the appearance of purulent sputum, accompanied with or without chest pains; ii) fever; iii) lung solid variant syndrome and/or wet rate; iv) hemameba  $>10 \times 10^9/l$  or  $<4 \times 10^9/l$ , accompanied with or without nuclear left shift; v) chest X-ray shows flake-like, patch-like infiltrated shadow or interstitial changes accompanied with or without pleural effusion. The concurrence of any of the first four symptoms with the fifth symptom, excluding the possibilities of tuberculosis, lung tumor, non-infectious lung interstitial disease, pulmonary edema and pulmonary atelectasis, may be diagnosed as aspiration pneumonia. Patients with purulent sputum who did or did not develop aspiration pneumonia prior to VFSS or after undergoing VFSS twice, respectively, as per the above criteria were recorded.

**Statistical treatment.** SPSS 16.0 software (SPSS, Inc., Chicago, IL, USA) was used to perform statistical analysis for the data. Quantitative data were presented as mean  $\pm$  standard deviation. Normality and homogeneity tests were conducted on the obtained data. Tests were performed on the basis of the characteristics of the data. A comparative t-test was used in inter-group comparisons. The t-test was used in intra-group comparisons, and Fisher's exact test was used in qualitative data comparisons.  $\alpha=0.05$  was considered the standard of test, and  $p<0.05$  was considered to indicate a statistically significant difference.

## Results

**Barium sulfate group.** A total of 30 cases of patients matching the criteria were selected. There were 17 men and 13 women aged 30-69 years, with an average age of  $51.83 \pm 9.94$  years. There were 22 cases of cerebral infarction, 8 cases of cerebral hemorrhage, 10 cases of unilateral cerebral hemisphere stroke, 10 cases of bilateral cerebral hemisphere strokes and 10 cases of brainstem strokes. The initial course of the disease was between 4 and 18 days, with an average of  $8.93 \pm 3.86$  days. In addition, there were 12 cases of degree II, 11 cases of degree III, and 7 cases of degree IV for the Kubota drinking water test.

**Iohexol group.** A total of 30 cases of patients matching the criteria were selected. Of these patients, there were 17 men and 13 women aged 24-70 years, with an average age of  $53.80 \pm 12.64$  years. There were 20 cases of cerebral infarction, 10 cases of cerebral hemorrhage, 10 cases of unilateral cerebral hemisphere stroke, 10 cases of bilateral cerebral hemisphere stroke, and 10 cases of brainstem stroke. The initial course of the disease was between 4 and 20 days, with an average of

Table I. General data comparison between the two groups.

Characteristics	Barium sulfate group	Iohexol group	t/ $\chi^2$ test	p-value
Age (mean $\pm$ SD, years old)	51.83 $\pm$ 9.94	53.80 $\pm$ 12.64	t=1.525	0.506
Gender (male/female)	17/13	17/13	$\chi^2=0.0$	1.0
Position of stroke (unilateral cerebral hemisphere/bilateral cerebral hemisphere/brain stem)	10/10/10	10/10/10	$\chi^2=0$	1.0
Type of stroke (cerebral infarction/cerebral hemorrhage)	22/8	20/10	$\chi^2=1.226$	0.581
Course (mean $\pm$ SD, days)	8.93 $\pm$ 3.86	9.30 $\pm$ 4.09	t=-0.196	0.722
Kubota drinking water test (II/III/IV)	11/12/7	12/11/7	$\chi^2=0.087$	0.957

Patient characteristics were not statistically significant (p>0.05). SD, standard deviation.

9.30 $\pm$ 4.09 days. In addition, there were 12 cases of degree II, 11 cases of degree III, and 7 cases of degree IV for the Kubota drinking water test.

The above two study groups were subsequently analyzed. Differences in patient characteristics such as gender, age, position and type of stroke, as well as the course of disease between the two groups was not statistically significant. The differences of the degrees in the Kubota drinking water test between the two groups were not statistically significant (Table I).

*Comparisons of the incidence rate of aspiration pneumonia between the two groups within 2 weeks after VFSS.* Incidences of aspiration pneumonia in the two groups of patients before VFSS were as follows: 5 of the 30 cases in the barium sulfate group were diagnosed with pneumonia while 3 of the 30 cases in the iohexol group were diagnosed with pneumonia. Total incidence of pneumonia was 13.3% as per the Fisher's exact test (p>0.05). Thus, no statistically significant differences with regard to the incidence of pneumonia were identified between the two groups.

The two groups of patients underwent VFSS in the first week in hospital, and subsequently swallowing training for 2 weeks, followed by another VFSS. Incidences of aspiration pneumonia in the two groups of patients after undergoing VFSS twice were: 13 cases in the barium sulfate group were diagnosed with pneumonia while 5 cases in the iohexol group were diagnosed with pneumonia. The total incidence of pneumonia was 30.0% as per the Fisher's exact test (p<0.05). Thus, no statistically significant differences with regard to the incidence of pneumonia were identified between the two groups. Additionally, the incidence of aspiration pneumonia in the iohexol group was lower than that in the barium sulfate group (Table II).

## Discussion

Dysphagia is a common and serious complication following stroke, and may be the only or most prominent symptom in certain patients (11). The mechanics of DAS have been closely associated with the following body parts: cortex, cortex-descending projection, cerebellum and extrapyramidal abnormalities, sensory loss, and swallowing-related cranial nerve loss. The central part of cortex swallowing is the antero-

Table II. Incidences of aspiration pneumonia between the two groups of patients.

Group	Incidence rate of aspiration pneumonia	
	Before VFSS	After undergoing VFSS twice
Barium sulfate group, n=30	5/25	13/17
Iohexol group, n=30	3/27	5/25
P-value	>0.05	<0.05

VFSS, video fluoroscopic swallowing studies.

lateral cortex or the lateral motor cortex, or the anterior and caudal section in the face representation of the primary motor cortex, or the lower part of the precentral gyrus and the pars opercularis (12).

Dysphagia occurs in the brain stem and bilateral cerebral hemisphere, as well as in the unilateral cerebral hemisphere. The basal ganglia, hypothalamus, and amygdaloid nucleus are involved in the regulation of the swallowing reflex (8). Stroke causes muscle weakness in the tongue, lip, cheek and pharyngeal to the extent that food cannot be chewed, stirred fully and became food bolus to be delivered to the pharynx. The paralysis and patchy coverage of the soft palate causes severe choking cough when food or liquid enters the aditus laryngis, thus resulting in after stroke aspiration pneumonia. It has been previously reported (13) that 37-74% of the acute cerebral stroke patients have different degrees of dysphagia, and that the incidence of pneumonia on DAS patients increases by 3.17-fold, and the incidence of aspiration on DAS patients would increase by 11.5-fold. It has been estimated that 43-54% DAS patients experienced aspiration, 37% of whom developed pneumonia. Dysphagia was an independent dangerous factor that influenced mortality and poor prognosis of the stroke patients (11). VFSS was the most common method utilized to assess the oropharyngeal and swallowing functions. It was considered an ideal way for the evaluation of dysphagia, the 'gold standard' for the early diagnosis of dysphagia, and an important basis for the early detection of pharyngeal stage barrier and its severity (14). We used X-ray VFSS and video camera simultaneously to

record the swallowing movement and qualitatively analyzed its movement by means of slow playback using specific software, thereby identifying its abnormality.

In this study, DAS patients received 60% barium sulfate suspension and the non-ionic contrast agent, iohexol, respectively, and video fluoroscopic swallowing studies were conducted. Barium sulfate and iohexol were used in the oral cavity, pharyngeal cavity, and esophageal radiography. In this study, pharynx transit time was used as an evaluation index. It has been previously shown that approximately 45% of the healthy individuals developed aspiration in their deep sleep, but such aspiration did not incur aspiration pneumonia (14). It has been estimated that aspiration pneumonia of DAS patients may be associated with the sensory disturbance of unilateral or bilateral throat incurred by stroke and the weakened pharyngeal reflex. Thus the lower respiratory infections were closely associated with the sensory disturbance of throat and the weakened pharyngeal reflex (15). Pulmonary infection was the most common complication of acute strokes and the complication rate was 7-12% (16). It was one of the major factors that caused exacerbation and death. Aspiration pneumonia caused by DAS was one of the major causes of mortality of stroke patients. Chest radiography, showing a wide high-density shadow in the lung, supported an overinhalation of barium (17). Barium passed through the trachea to the lung and directly affected the respiratory function. Additionally, the majority of the DAS patients experienced coughing, general weakness, sputum, and incomplete coughing up of the aspirated barium. The remaining barium particles, which were not coughed up, were deposited in the lung over a long period of time and directly produced chemical stimulation and obstructions on the trachea and incurred airway hyper-responsiveness. In the early stages, foreign body giant cells, epithelioid cells, and mononuclear cell infiltration were incurred. Subsequently, fibrosis occurred around the sedimentary barium inflammation and formed barium nodule, resulting in an increasing incidence of complications such as the impairment of the lung and pneumonia, and a higher rate of pulmonary infection leading to iatrogenic damages. In the present study, the comparative differences between the two groups of patients prior to implementation of VFSS were not statistically significant. The two groups of patients underwent VFSS in the first week in hospital, and then took swallowing training for an additional 2 weeks, followed by VFSS again. After undergoing VFSS twice, the differences on the incidence of aspiration pneumonia between the two groups of patients were statistically significant. The incidence of aspiration pneumonia of the iohexol group was obviously lower than that of the barium sulfate group. The possible reason was that iohexol avoided aspiration of barium when it was applied in the VFSS of the stroke patients with dysphagia. Thus, it was not easy to cause pneumonia or reduce iatrogenic damages.

In summary, the results of the present study have shown that VFSS of dysphagia after stroke and barium sulfate increased the incidence of pneumonia, and that iohexol may be widely used in video fluoroscopy.

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