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The relationship between enhanced plaques with Gadovist and Magnevist contrast brain magnetic resonance imaging and the neurological deficit in the acute phase of relapsing remitting multiple sclerosis

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Keywords
Multiple Sclerosis, Magnetic Resonance Imaging, Contrast, Neurological Deficit

Abstract

Background: Magnetic resonance imaging (MRI) is the standard method for observing brain plaques and contrast material injection is necessary for demonstrating the active plaque.This study compared the rate of enhancement of plaques with Gadovist and Magnevist in relapse phase of MS.

Methods: In this double blind study, after neurological examination of 62 patients in the attack phase of MS, two consecutive MRIs were performed with Gadovist and Magnevist with 48 hours interval. The two contrast materials were injected in first and second imaging randomly and the reporting radiologist was blind about the contrast material.

Results: With both contrast materials, the probability of enhancement of supratentorial plaques was higher than the infratentorial ones. The probability of observing a symptomatic infratentorial enhanced plaque was higher than the supratentorial region and when the symptoms were due to supratentorial lesions, the corresponding enhanced plaque was more probable. It was detected that the number of enhanced plaques was the highest if the imaging was performed in the second week after the relapse, although there was no statistically significant difference when the imaging was done within the first month after the beginning of the symptoms.

Conclusion: It seems that both Magnevist and Gadovist could be used as the contrast material to detect enhancing plaques in relapse phase of multiple sclerosis.

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Introduction

Multiple sclerosis (MS) is caused by demyelination of the neuron sheaths of the central nervous system. MS often appears as relapsing attacks of neurological deficit relieved by immunosuppressive therapy. It may be presented also as a progressive disease disabling the patient after a fewyears.[1] According to McDonald's criteria, the diagnosis is based on detection of demyelination in different locations and different times in the central nervous system (CNS).[2]

Magnetic resonance imaging (MRI) is the standard method for demonstration of brain plaquesand in order to observe active plaques, contrast material injection must be done.[3-9] In the active phase, as the result of inflammation, detection of the plaque is based on contrast material absorption and evaluation of the plaques in specific brain MRI sequences.

The main point is that plaques are sometimes difficult to be detected in the active phase. Accordingly, any tool and technique that improve the sensitivity of MRI enhancement could be appreciated.[8-10] Various types of contrast materials such as Magnevist, Dotarem and Omniscan have been used. Recently, Gadovist contrast agent with cyclic structural properties has been introduced for brain imaging. This study compared the rate of enhancement of plaques with Gadovist and Magnevist in relapse phase of MS.

Materials and Methods

Relapsing remitting MS patients who were referred to our university hospital in their relapse phase were entered in our study. First, neurological examination was carried out to determine the neurological deficit occurring in the recent attack. Then, for each patient two MRIs were performed on two separate occasions 48 hours apart based on MRI protocol consensus guidelines in MS. Half of the samples randomly received Magnevist first and then Gadovist 48 hours later and the other half vice versa.

One tenth mmol/kg Gadovist and 0.2 mmol/kg Magnevist were injected in 30 seconds. Multiple images were acquired after contrast administration with the lag periods of 30 seconds and 5, 10, 15 and 30 minutes. Data were analyzed by SPSS 18 for Windows (SPSS Inc., Chicago, IL, USA) and $P < 0.005$ was determined as statistically significant.

Results

Sixty-two patients, 55 (88.7%) females and 7 (11.3%) males were enrolled into the study within 2009-2011. The patients' mean age and the duration of the disease were 31.3 ± 7.2 and 4.39 ± 4.2 years, respectively. It was seen that 54.8% of the patients had not received any immunomodulators, while 28 (45.2%) subjects had received beta interferons. A mean of 1.12 ± 1.5 years was the interval from the last corticosteroid pulse for treatment of attacks. There was a mean of 15.8 ± 8.3 days interval between the beginning of symptoms and MRI.

The neurological presentation of the relapse was a new one in 42 patients, whereas 20 patients had experienced the same deficit in the same anatomical site in their prior relapses. These neurological syndromes were monoparesis, ataxia, optic neuritis, ophthalmoparesis, hemiparesis, paraparesis, hemiparesthesia, internuclear ophthalmoplegia, monoparesthesis and cranial neuropathy with different frequencies. In 8 patients the relapse was polysymptomatic.

The mean number of enhanced plaques in consequent time sequences in images with Gadovist and Magnevist showed an increment. The highest number of plaques was seen in the images which were performed 15 minutes after injection of contrast. In the image after 30 minutes, there was a considerable decrement in the number of enhanced plaques. Therefore, the patients' 15-minute images were used to compare the contrast materials.

Gadovist imaging showed a mean of 3.2 supratentorial and 0.43 infratentorial enhanced locations. It was shown that 0.31 of the supratentorial and 0.29 of the infratentorial locations were symptomatic. The proportion of symptomatic locations to the total enhanced locations in these Gadovist images was 0.095 for the supratentorial and 0.68 for infratentorial groups. In contrast, Magnevist imaging showed a mean of 3.12 supratentorial and 0.47 infratentorial enhanced locations. In these images, 0.31 of the supratentorial and 0.31 of the infratentorial locations were symptomatic. The proportion of symptomatic locations to the total enhanced locations in Magnevist images was 0.11 and 0.6 for the supratentorial and infratentorial groups, respectively.

Another analysis was performed based on the clinical syndrome of relapse with the location of enhancing plaque including frontal periventricular, frontal subcortical, parietal subcortical, parietal periventricular, temporal subcortical, temporal periventricular, occipital subcortical, occipital periventricular, corpus callosum, basal ganglia, thalamus, internal capsule, midbrain, pons, medulla, cerebellum, and cerebellar peduncle. The neurological deficits were defined by each enhanced location and the relationship between clinical syndrome and location of enhanced plaque was evaluated. If an enhanced plaque, which accounts for the symptom was seen in the patient's MRI, it was considered as

the corresponding. Since the obtained MRI cuts were not appropriate for evaluation of the optical nerves, patients including optic neuritis were excluded. Patients with paraparesis were also excluded due to lack of accuracy in localization of paraparesis. Neurological deficits were categorized into supratentorial and infratentorial groups as below:

- Supratentorial: Monoparesis, hemiparesis, hemiparesthesia and monoparesthesia
- Infratentorial: Ataxia, diplopia, internuclear ophthalmoplegia, cranial nerve involvement

Existence of a corresponding Gadovist and Magnevist enhanced plaque in each group was compared (Tables 1-3). In the acute phase of MS, the relationship between the new neurological deficit and its corresponding enhanced plaque was evaluated (Tables 4 and 5).

Another analysis was performed regarding the period between the beginning of the attack and imaging, the minimum and maximum of which were 4 and 30 days. The patients were classified into three groups to evaluate the relationship between these periods of time and the number of enhanced plaques in MRI: within 4-7, 8-14 and 15-30 days.

Table 1. Corresponding and non-corresponding Gadovist and Magnevist enhanced plaque

Syndrome	Gadovist		Magnevist		Mismatch
	Corresponding plaque	Non-corresponding plaque	Corresponding plaque	Non-corresponding plaque	
	No. (%)	No. (%)	No. (%)	No. (%)	
Ataxia	4 (31)	9 (69)	5 (38.5)	8 (61.5)	3
Diplopia	2 (22)	7 (78)	3 (33)	6 (67)	1
Internuclear ophthalmoplegia	1 (50)	1 (50)	1 (50)	1 (50)	-
Cranial nerve involvement	1 (100)	0	1 (100)	0	-
Monoparesis	7 (53)	2 (47)	7 (53)	6 (47)	-
Hemiparesis	6 (75)	2 (25)	6 (75)	2 (25)	-
Hemiparesthesia	2 (50)	2 (50)	2 (50)	2 (50)	-
Monoparesthesia	1 (100)	0	1 (100)	0	-
Supratentorial	16 (61.5)	10 (38.5)	16 (61.5)	10 (38.5)	0
Infratentorial	8 (32)	17 (68)	10 (40)	15 (60)	4

Table 2. Corresponding and non-corresponding plaque in supra- and infratentorial symptoms in Gadovist contrast imaging

		Symptom		Total
		Supratentorial	infratentorial	
Non-corresponding plaques	Count	10	17	27
	% of supra or infratentorial plaques	37.0%	63.0%	100.0%
	% of enhanced plaques	38.5%	68.0%	52.9%
Corresponding plaques	Count	16	8	24
	% of supra or infratentorial plaques	66.6%	33.3%	100.0%
	% of enhanced plaques	61.5%	32.0%	47.1%
Total	Count	26	25	51
	% of supra or infratentorial plaques	51.0%	49.0%	100.0%
	% of enhanced plaques	100.0%	100.0%	100.0%

Table 3. Corresponding and non-corresponding plaque in supra- and infratentorial symptoms in Magnevist contrast imaging

		Symptom		Total
		Supratentorial	infratentorial	
Non-corresponding plaques	Count	10	15	25
	% of supra or infratentorial plaques	40.0%	60.0%	100.0%
	% of enhanced plaques	38.5%	60.0%	49.0%
Corresponding plaques	Count	16	10	26
	% of supra or infratentorial plaques	60.0%	40.0%	100.0%
	% of enhanced plaques	61.5%	40.0%	51.0%
Total	Count	26	25	51
	% of supra or infratentorial plaques	51.0%	49.0%	100.0%
	% of enhanced plaques	100.0%	100.0%	100.0%

Table 4. The relationship between new neurological deficit and its corresponding Gadovist enhanced plaque

		New symptom		Total
		Yes	No	
Non-corresponding plaques	Count	16	12	28
	% of Gadovist enhanced	57.1%	42.9%	100.0%
	% of plaques	47.1%	70.6%	54.9%
Corresponding plaques	Count	18	5	23
	% of Gadovist enhanced	78.3%	21.7%	100.0%
	% of plaques	52.9%	29.4%	45.1%
Total	Count	34	17	51
	% of Gadovist enhanced	66.7%	33.3%	100.0%
	% of plaques	100.0%	100.0%	100.0%

Table 5. The relationship between new neurological deficit and its corresponding Magnevist enhanced plaque

		New symptom		Total
		Yes	No	
Non-corresponding plaques	Count	17	9	26
	% of Magnevist enhanced	65.4%	34.6%	100.0%
	% of plaques	50.0%	52.9%	51.0%
Corresponding plaques	Count	17	8	25
	% of Magnevist enhanced	68.0%	32.0%	100.0%
	% of plaques	50.0%	47.1%	49.0%
Total	Count	34	17	51
	% of Magnevist enhanced	66.7%	33.3%	100.0%
	% of plaques	100.0%	100.0%	100.0%

The number of enhanced plaques with Gadovist and Magnevist were evaluated and compared between the three groups. Although the number of enhanced plaques were more in the second group (second week), the difference was not statistically significant and it is seems that if the imaging was performed within the first month of attack, the time period between the beginning of symptoms and the imaging causes no difference in the number of enhanced plaques.

Discussion

Previous studies showed that Gadolinium is a sensitive tool for diagnosis, monitoring and treatment of MS.[7] A suitable chelator, an efficient dose and an efficient scan time will increase its sensitivity.[8,10] In the previous studies, the relationship between the enhanced plaques, the probability of another attack and the prognosis of MS were evaluated,[11-13] but the relationship between neurological deficit and the enhanced plaques have not been assessed. In this study, there was no significant difference between Gadovist and Magnevist enhanced locations in the whole brain, supratentorial and infratentorial or symptomatic enhanced location.

In the acute phase of MS, it is more probable to observe an enhanced plaque in the supratentorial region than the infratentorial region. Infratentorial enhanced plaques are more likely to become symptomatic in comparison to supratentorial enhanced plaques. When the symptom relates to the supratentorial region, the possibility of observing a corresponding enhanced plaque is higher. There was no difference between Magnevist and Gadovist regarding these mentioned findings. These findings are congruent with the fact that nervous paths are more compressed in the infratentorial region.

In the acute phase of MS, in the infratentorial region, there is a mismatch between Gadovist and Magnevist regarding corresponding plaques for the neurological deficits, but in the supratentorial region, these two contrast agents are congruent. In supratentorial motor syndromes, the possibility of observing plaques is higher compared to sensory syndromes of the supratentorial region. Due to the low number of samples in each group, evaluating their significance was not possible.

When the neurological deficit was new for the patient, Gadovist showed 52.9% of the corresponding plaques while this was 50% for Magnevist. When the symptom was not new, in the first group there were 70.6% non corresponding plaques while this area was 52.9% for the second group.

It seems that when there is no new neurological deficit in the acute phase of MS, Gadovist will show less corresponding plaques than Magnevist, but there is no difference between the old and new neurological deficits in Magnevist contrast imaging. In other words, if the enhanced plaques seen in Gadovist contrast imaging are congruent to neurological

deficits caused in the acute phase, there is a 78.3% probability that the patient experiences a new symptom in the recent attack.

Although the number of enhanced plaques was the highest in the second week of the attack, the difference was not significant and it seems that the time period between the beginning of symptoms and the imaging process shows no significant difference in the number of enhanced plaques and it is not possible to mention an appropriate time period from the beginning of the attack to achieve the best imaging result.

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