

Original research-Orijinal araştırma

Assessment of physicians' awareness levels on nephrogenic systemic fibrosis

Klinisyenlerin nefrojenik sistemik fibrozis hakkındaki farkındalık düzeyinin araştırılması

Sema Yıldız*, Hasan Cece, Sibel Sezer, Zeynep Aktı, Süleyman H. Konar, Tülay Doğantürk, İhsan Kaya, Kadir Yetişgin

Department of Radiology (S. Yıldız, MD, H. Cece, MD, S. Sezer, MD, Z. Aktı, MD, S. H. Konar, MD, T. Doğantürk, MD, İ. Kaya, MD, K. Yetişgin, MD), Harran University School of Medicine, TR-63100 Şanlıurfa

Abstract

Aim. Nephrogenic systemic fibrosis (NSF) has recently defined as a systemic disorder that is identified after performing contrast-enhanced magnetic resonance imaging in patients with renal failure. We aimed to assess the levels of awareness of physicians on the NSF with a questionnaire. **Methods.** It is a cross-sectional survey study among 124 physicians working in university, state, and private hospitals. Information on awareness of physicians on the association of NSF and renal dysfunction and the presumption and prevention of NSF in the presence of renal dysfunction were obtained using a self-administered structured questionnaire. **Results.** The awareness of physicians working in university, state and private hospitals on the novelties and prevention of NSF with performing hemodialysis, were significantly different with best and worst awareness in physicians from university and state hospitals, respectively ($p<0.05$). **Conclusion.** Findings of the present study revealed fairly low level of physicians' awareness on the NSF and revealed the necessity of physician education to improve the level of awareness on the NSF to avoid NSF and associated damages.

Keywords: Questionnaire, awareness, physician, nephrogenic systemic fibrosis, renal failure

Özet:

Amaç. Nefrojenik Sistemik Fibrozis (NSF), böbrek yetmezliği olan hastalarda kontrastlı manyetik rezonans görüntüleme sonrasında tanımlanan sistemik bir hastalıktır. Bu çalışma ile klinisyenlerin NSF hakkındaki bilgi düzeylerinin değerlendirilmesi amaçlanmıştır. **Yöntem.** Üniversite, devlet ve özel hastanelerde çalışan 124 klinisyen üzerinde kesitsel bir anket çalışması olarak planlandı. NSF'nin böbrek yetmezliği ile olan ilişkisi, böbrek yetmezliği hastalarında NSF'nin önceden tahmin edilip önlenmesine yönelik bilgi düzeyi sorgulandı. **Bulgular.** NSF hakkındaki yenilikleri takip etme ve hemodiyaliz yaparak NSF'yi önlemeye çalışma konusunda gruplar arasında anlamlı farklılık vardı ve farkındalık açısından üniversiteden katılan klinisyenler en iyi, devlet hastanesinden katılanlar ise en kötü olduğu tespit edildi ($p<0,05$). **Sonuç.** Bu çalışmanın sonuçlarına göre NSF konusundaki bilgi düzeyini arttırmak için klinisyenlerin eğitilmesi gerektiği ortaya çıkmıştır.

Anahtar sözcükler: Anket; farkındalık; klinisyen; nefrojenik sistemik fibrozis, renal yetmezlik

Geliş tarihi/Received: September 27, 2011; **Kabul tarihi/Accepted:** October 31, 2011

*Corresponding author:

Sema Yıldız, MD, Radyoloji Anabilim Dalı, Harran Üniversitesi Tıp Fakültesi, TR-63100 Şanlıurfa. E-mail: drsemayildiz@yahoo.com

Introduction

Nephrogenic systemic fibrosis (NSF) has recently been defined as a systemic disorder that is identified after performing contrast-enhanced magnetic resonance imaging in patients with impaired renal function [1-3]. Despite gradually increasing number of reports enlightening the nature and pathophysiology of NSF, many aspects of disease is still controversial and/or unknown. With respect to renewed information, European Society of Urogenital Radiology's (ESUR) Contrast Media Safety Committee [4], and the American College of Radiologists (ACR) have released modified guidelines so as to clarify the clinicians [5]. NSF presents with cutaneous hyperpigmentation and induration and joint contractures, but fibrosis may also develop in other organs. Since there is no definite curative treatment of NSF [6], the awareness of clinicians on the NSF is crucial for estimating the subjects under risk and appropriate follow-up and avoiding the disease. Accordingly, we aimed to assess the level of awareness of physicians on the NSF with a questionnaire in hospitals of our province.

Material and method

It is a cross-sectional survey study including 124 physicians from local hospitals and clinics: Five hospitals (one university, two state, and two private hospitals), and two private clinics were selected for the study. The doctors in the participating hospitals were selected by a simple random sampling to minimize bias; however, interns and basic sciences' physicians were excluded from this study. We used a self-administered structured questionnaire that was prepared using statements on guidelines of the ESUR, and ACR committee on contrast media. Demographic variables of physicians like age, gender, specialty and years of practice were obtained. In addition, each physician was asked to respond to six questions: First and second questions evaluated the frequency of whole subjects and patients with renal failure whom were sent to MRI. Third question evaluated physicians' knowledge level on the NSF. Fourth, fifth and the sixth questions assessed the awareness of physicians on the association of NSF and renal dysfunction, and the presumption and prevention of NSF in the presence of renal dysfunction. The study was approved by the Institutional Ethics Committee. Data were analyzed using SPSS statistical software version 11.5 (SPSS Inc., Chicago, IL, USA). Frequency and descriptive statistics were used to examine the general characteristics of the physicians. The participating physicians were stratified into three groups as university, state, and private physicians. Questionnaire variables were also evaluated with regard to years of practice and specialty. Difference(s) between three groups of physicians were evaluated with Chi-square test. $P < 0.05$ was considered as statistically significant.

Results

A total of 124 physicians from university (n=39), state (n=49) and private (n=36) hospitals-clinics were included in the study. Ninety-nine (79.8%) physicians were men, and 25 (20.2%) were women; their mean age was 35.5 ± 7.1 years. Other characteristics of the participating physicians were presented on Table 1. According to our study, 52 (41.9%), 34 (27.4%) and 38 (30.6%) physicians reported that the number of patients sent to MRI in a month was less than 3, 3-10 and more than 10 respectively. 43 (34.7%) physicians reported that they send patients with renal failure to MRI, and 81 (65.3%) physicians reported that they do not send patients with renal failure to MRI. The physicians whose specialties were neurology, physical treatment and rehabilitation, have the highest frequencies of patients sent to MRI (34.2% and 28.9% respectively), and also physicians from specialties of internal medicine, physical treatment and rehabilitation, neurology have the highest frequencies of renal failure patients sent to MRI (32.6%, 18.6% and 11.6% respectively).

Table 1. Characteristics of the participating physicians with regard to the affiliations.*

	University (n=39)	State (n=49)	Private (n=36)	Total (n=124)
Age (years; mean±SD)	33.3±5.1	34.5±5.4	39.4±9.1	35.5±7.0
Gender				
Male [n (%)]	33 (84.6%)	37 (75.5%)	29 (80.5%)	99 (79.8%)
Female [n (%)]	6 (15.4%)	12 (24.5%)	7 (19.5%)	25 (20.2%)
Years of practice				
<10 years [n (%)]	18 (46.2%)	21 (42.8%)	25 (69.5%)	64 (51.6%)
>10 years [n (%)]	21 (53.8%)	28 (57.2%)	11 (30.5%)	60 (48.4%)
Specialties				
GP [n (%)]	0	5 (10.2%)	3 (8.3%)	8 (6.5%)
Medical [n (%)]	25 (64.1%)	28 (57.1%)	18 (50.0%)	71 (57.3%)
Surgical [n (%)]	14 (35.9%)	16 (32.7%)	15 (41.7%)	45 (36.3%)

SD: standard deviation, GP: general practitioner

*None of the characteristics were different among groups.

Table 2. Distribution of physicians' responses to questions on NSF with regard to affiliations.

	University (n=39) n (%)	State (n=49) n (%)	Private (n=36) n (%)	Total (n=124) n (%)
1-How often do you send your patient to MRI?				
<3/month	17 (43.6%)	18 (36.7%)	17 (47.2%)	52 (41.9%)
3-10/month	12 (30.8%)	13 (26.5%)	9 (25.0%)	34 (27.4%)
>10/month	10 (25.6%)	18 (36.7%)	10 (27.8%)	38 (30.6%)
2-Do you send patients with renal failure to MRI?				
No, I do not	21 (53.8%)	32 (65.3%)	28 (77.8%)	81 (65.3%)
Yes, I do.	18 (46.2%)	17 (34.7%)	8 (22.2%)	43 (34.7%)
3-What do you know about NSF?*				
Never heard on NSF	16 (41.1%)	26 (53.0%)	17 (47.2%)	59 (47.6%)
Heard, but do not know anything about NSF	13 (33.3%)	20 (40.9%)	17 (47.2%)	50 (40.0%)
Heard and try to follow-up novelties on NSF	10 (25.6%)	3 (6.1%)	2 (5.6%)	15 (12.1%)
4-Do you calculate GFR before gad-MRI in patients with renal failure?				
No, urea and creatinine levels are enough	22 (56.4%)	16 (32.6%)	9 (25%)	47 (37.9%)
Yes, i do.	17 (45.6%)	33 (67.4%)	27 (75%)	77 (62.1%)
5-What is the threshold GFR level to alert the radiologist about the NSF risk associated with administration of gadolinium?				
I don't know	8 (20.5%)	15 (30.6%)	16 (44.4%)	39 (31.4%)
None of the GFR level	12 (30.7%)	18 (36.7%)	7 (16.5%)	37 (29.8%)
GFR<30 ml/min/1.73m ²	15 (38.5%)	13 (26.5%)	9 (25%)	37 (29.8%)
GFR<15 ml/min/1.73m ²	4 (10.3%)	3 (6.2%)	4 (11.1%)	11 (8.8%)
6-Do you advice performing hemodialysis after gad-MRI in patients with severe renal failure?^b				
I don't know, consultation is needed	0	12 (24.5%)	18 (50%)	30 (24.1%)
Yes, it is necessary	27 (69.2%)	20 (40.8%)	16 (44.5%)	63 (50.8%)
No, it is not necessary	12 (30.8%)	17 (34.7%)	2 (5.5%)	31 (25%)

* $\chi^2=10.196$, $p=0.037$, ^b $\chi^2=31.008$, $p<0.001$. gad-MRI: gadolinium enhanced magnetic resonance imaging, GFR: glomerular filtration rate, MRI: magnetic resonance imaging, NSF: nephrogenic systemic fibrosis.

Of 124 physicians, 59 (47.6%) reported that they have never heard about NSF, whereas 50 (40.3%) noticed that they have heard but did not know anything about NSF, 15 (12.1%) reported that they know NSF and they try to follow-up the novelties about NSF. Following the novelties on the NSF by physicians working at university, state and private hospitals were significantly different (Chi square: 10.196, $p=0.037$). Seventy-seven (62.1%) physicians reported that they calculate glomerular filtration rate (GFR) before

contrast-enhanced MRI in patients with renal failure, and 30 (29.8%) physicians chose the threshold GFR level of <30 ml/min/1.73m², and 11 (8.9%) physicians chose the threshold GFR level of <15 ml/min/1.73m² to alert the radiologist about gadolinium based contrast media associated NSF risk in patients with renal failure. There was no statistically significant difference among three groups with regard to estimating GFR, and choosing threshold GFR levels ($p>0.05$). Sixty-three (50.8%) physicians noted the necessity of performing hemodialysis after gadolinium enhanced MRI in patients with severe renal failure to avoid NSF. The level of awareness on the necessity of performing hemodialysis after gadolinium enhanced MRI in patients with severe renal failure was significantly different among physicians from university, state and private hospitals (Chi square: 31.000 $p<0.001$). Analysis of questionnaire variables with regard to specialty and years of practice revealed no statistically significant association. All responses to our questionnaire were presented on Table 2.

Discussion

NSF was firstly described by Cowper et al. [7] as a scleromyxedema-like cutaneous disease in renal dialysis patients. Initially, it was named as ‘nephrogenic systemic dermatopathy’ [8, 9] after it became apparent that the disease affecting multiple organs such as nervous system, lungs, muscles, and heart [10-12]. Then the name was changed as ‘NSF’ to reflect the multiorgan involvement. NSF was described in patients with chronic renal disease, hepato-renal syndrome with renal insufficiency, and acute renal injury [13, 14]. The first publication about the role of gadolinium based contrast agents in NSF etiology was reported in 2006 [1, 2], and it was reported that the majority of cases were associated with administration of linear contrast agents such as gadodiamid [15] and gadopentetate dimeglumine [16]. The diagnosis of NSF should be confirmed using histological evaluation in conjunction with full assessment of the clinical picture of the patient, including careful inspection of the skin lesion [17, 18], and history of exposure to contrast agent including gadolinium [3, 19, 20]. Although the pathognomonic skin lesions are thickening, and hardening with contractures [2, 21] in patients with end-stage renal failure, other skin lesions may mimic NSF lesions. Consequently, the clinicians should consider in length the symptoms and history of the patients with severe renal failure about NSF. In our study 12.1% of physicians, mostly (66.6%) from university hospital, reported that they know NSF in depth and try to follow-up novelties on NSF. The National Kidney Foundation published the kidney disease outcomes quality initiative clinical practice guidelines of the stages of chronic kidney disease with GFR of the patients [22]. GFR shows the function of the kidneys, and it is recommended using the Modification of Diet in Renal Disease (MDRD) equation for adults which can be estimated as $175 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female})$ [5]. According to these guidelines; stage 1; kidney damage with normal or increased GFR >90 ml/min/1.73m², stage 2 mild reduction in GFR (60-89ml/min), stage 3 moderate reduction in GFR: 30-59 ml/min/1.73m², stage 4 severe reduction in GFR (15-29ml/min), stage 5 kidney failure (GFR <15 ml/min/1.73m²). In 2009 the ESUR’s Contrast Media Safety committee released a guideline for NSF [4]. They declared that patients with chronic kidney disease (CKD) stages 4 and 5 (GFR <30 ml/min/1.73m²) including those who require dialysis, and those who have reduced renal function who have had or are awaiting liver transplantation are at a higher risk. According to our results, 62.1 % of physicians reported that they calculate GFR before contrast-enhanced MRI in patients with renal failure to estimate the stage, and but only 29.8% of physicians regarded GFR <30 ml/min/1.73m² as a risk factor for NSF. The ACR committee on contrast media recommended that any contrast media administration should be avoided to patients whose GFR < 30 ml/min/1.73m². If MRI contrast media administration is deemed essential, judicious use of the lowest possible dose needed to obtain a diagnostic study [5]. In our study 29.8% of physicians chose the dangerous GFR level of <30 ml/min/1.73m², for renal failure patients to undergo contrast-enhanced MRI.

The ACR committee on contrast media also recommended performing hemodialysis immediately upon termination of the contrast enhanced MRI to patients with end stage renal disease on chronic dialysis, and it is considered that multiple dialysis sessions may be more protective than merely a single session [6]. The 50.8% of all physicians (and 69.2% of physicians from university) noted the necessity of performing hemodialysis after gadolinium enhanced MRI in patients with renal failure. Guidelines for avoidance of NSF also revealed that the use of linear gadolinium based contrast agents should be terminated in patients with severe renal failure. It was suggested that a well indicated MRI examination should not be denied, however the lowest possible dose of contrast agent should always be used [5]. Abdel-Kader et al. [23] surveyed the perceptions and practices of nephrologists regarding NSF and revealed that over 90% of nephrologists were aware of the morbidity and mortality associated with NSF, 69% were aware of an association with specific gadolinium agent brand and 50% believed stage 3 CKD patients were at risk to develop NSF. Facility policies concerning gadolinium use in CKD were widespread (>90%) and most nephrologists (56%) felt that enacted policies were appropriate, yet 58% were uncertain if the changes had benefited patients. Increased awareness of nephrologists on NSF compared to our study population might be due to the fact that the nephrologists encounter NSF more than other specialties included in our study. Heterogeneity in approaching gadolinium use in CKD with respect to NSF, similar to our findings, might suggest the need for a widely accepted NSF guideline based on prospective randomized trials [23]. There is no NSF report from Turkey although gadolinium enhanced MRI has long been performed even in the patients with renal diseases. It may be explained with low level of awareness of physicians on NSF, notwithstanding the growing literature. Best awareness in physicians from university can be explained with following up the novelties, worst awareness in physicians from state hospitals can be explained with huge amount of patients in routine clinical practice, and not following up the literature.

Although the number of participants and specialties (such as dermatology) was limited, the findings of the present study reveal the necessity of physician education to improve the level of awareness of physicians on the NSF and to avoid development of NSF and NSF associated harms. A more comprehensive future work including physicians and their patients who are under the risk of NSF require to verify our conclusion and to put it one step further for avoiding the development of the disease.

Acknowledgements

We would like to thank the clinicians whom participated in the study.

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