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The use of gadolinium-based contrast agents in Ghana with a focus on residual intracranial gadolinium deposition

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ABSTRACT

Introduction: The aim of the survey was to identify current practice of the use of gadolinium-based contrast agents (GBCAs) in the wake of recent reports on gadolinium deposition in the brain following repeated administration of GBCAs.
Method: A total of 13 facilities in Ghana with magnetic resonance imaging (MRI) departments were contacted via email with a two-page questionnaire.
Results: A response rate of 69.2% (n = 9) was achieved. Gadodiamide (Omniscan) was the most commonly used GBCA. Slightly more than half of respondents were aware of residual deposition of GBCAs in the brain. Majority of the respondents were aware of GBCA deposition in individuals with abnormal renal function, but not aware of its deposition in those with normal renal function. A great majority of the respondents do not record the type and dose of GBCA after each intravenous administration, and such information is not provided in MRI reports. More than half of the respondents do not check eGFR prior to the administration of GBCA even when a high-risk agent is used.
Conclusion: Gadodiamide (Omniscan) a high-risk agent remains the most commonly used GBCA in Ghana. Awareness of current findings of GBCA deposition in the brain following repeated doses are not encouraging as revealed in this study. The need to adopt international standard guidelines into practice cannot be overemphasized in order to reduce the potential long-term effect of this deposition.

Introduction

Since its first approval in 1988 by the U.S. Food and Drug Administration (FDA) and now 9 in total, gadolinium-based contrast agents (GBCAs) have been used internationally over a quarter century in more than 300 million patients providing crucial, life-saving medical information.[1,2] In fact they have become indispensable adjuncts to MRI.[1] However, since the year 2000 when Cowper et al.[3] issued the first report of 14 cases of nephrogenic systemic fibrosis (NSF), a rare but potentially fatal acquired systemic disease thought to occur predominantly in patients with severe renal insufficiency, there have been much concern about the safety profile of GBCA. From then till 2006, all GBCAs were still considered to be extremely safe. Then in 2006, Grobner[4] and Marckmann et al.[5] established an association between NSF and GBCAs. This was in contrast to previously held notion established by Prince et al.[6] that unlike iodine-based contrast media, GBCAs were not nephrotoxic. Nevertheless, since the middle of 2009, specifically in the developed countries, NSF has been almost completely eliminated following the establishment and implementation of restrictive guidelines such as screening patients for potential presence of renal disease, judicious use of GBCAs among patients with compromised renal function, by performing unenhanced studies or half-dose GBCA studies in patients at high risk, and by reducing or avoiding high-risk GBCAs in patients with substantial renal disease.[2,7]

Again, we were awakened with a report of gadolinium deposition in specific areas of brain tissues after repeated doses of GBCAs over their lifetimes, even in the absence of clinically evident disease (i.e. Renal or liver disease) and in the setting of an intact blood brain barrier.[2] This eye-opening report, first revealed by Kanda et al.[8] noted residual gadolinium deposition in patients with normal

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renal function, which was characterized by dose-related T1 shortening in the globus pallidus (GP) and the dentate nuclei (DN) in patients who had been intravenously administered repeated previous doses of gadodiamide (Omniscan) and/or gadopentetate dimeglumine (Magnevist). Following this report, other authors[9–14] confirmed this novel observation. Indeed, in two recent studies[12,15] of autopsy specimens, it was proven that T1 shortening results from gadolinium retention in neuronal tissues of the GP, DN, thalamus, and pons. Overall, gadodiamide (Omniscan) is the agent most associated with this finding[7–9,12,14]; however, reports have also been shown with gadopentetate dimeglumine (Magnevist).[8,10]

In a recent survey on the use of GBCAs in Ghana,[16] it was revealed that gadodiamide (Omniscan), a high risk GBCA accounted for 67% of first-line agents, i.e. being the preferred standard, or first choice. Gadodiamide has been widely reported in the literature to be the agent most associated with NSF; yet it was found to be the most commonly used agent in many MRI facilities nationwide.[16] The aim of the present nationwide survey was to identify current practice of the use of GBCAs in the wake of recent reports on gadolinium deposition in the brain following repeated administration of GBCAs.

Materials and method

Initially, an online search was carried out to identify all healthcare facilities that owned MRI scanner for in vivo imaging. The main resources for this identification were tertiary hospitals, private hospital/clinics, and standalone diagnostic centres. In addition, assistance was provided by radiography professionals personally known to be performing MRI in identifying facilities that owned MRI scanners. This search resulted in a total of 13 functioning MRI facilities that were identified and approached nationwide. This number represented the total number of MRI scanners in Ghana. Email addresses and telephone numbers of the contact persons within each MRI department were sourced from radiography colleagues who were familiar with these persons. A two-page close-ended questionnaire was directly addressed to the contact persons via email for completion, as they were the Heads-of-department (Directors) of the MRI unit, and were actively responsible in the day to day management or work practice of the department.[17] Subsequently, the contact persons were prompted via the popular social media “WhatsApp” about the need to complete the questionnaire. Follow-ups were done via WhatsApp and phone calls to remind the contacts on the need to complete the questionnaire after a week. There was no need for approval from an ethical committee; however, a participant information leaflet and consent form was provided and participants were assured that the result of the study would only be used for the purpose of the study, and that their participation in the study was voluntary, anonymous, and confidential. The questionnaires were sent in May 2017 and responses received before the end of July 2017. Data were collated and descriptively analyzed using a 2013 Microsoft Excel Professional Plus.

Results

A total number of 13 MRI facilities were identified and approached to participate in the study. Completed questionnaires were returned by 9 MRI facilities resulting in an overall response of 69.2% (n = 9).

In Table 1, majority of the respondents 5 (56%) indicated they use Omniscan.

Table 2 demonstrates the knowledge and practice of administration of GBCAs in current practice. The questionnaire provided two response categories: Yes and No. The study demonstrated that all respondents administer the same GBCA in MR imaging of all body parts. Slightly more than half were aware of reports of gadolinium deposition in the brain after four or more contrast MRI scans. Majority (6[67%]) were not aware that GBCA(s) remain in individuals with normal renal function. Contrarily, the same majority were aware that GBCA(s) remain in individuals with abnormal renal function for great majority (7[78%]) lack departmental protocol on the administration of GBCA with regards to its residual deposition in the brain. All indicated that there was no information on how to reassess the necessity of repetitive administration of GBCA(s). Again, the majority (7[78%]) indicated that they do not record the type and dose of GBCA after each intravenous administration, and none of the respondents provide details of the type and dose of GBCA on MRI reports. Majority (6[67%]) ask patients if they have had previous intravenous administration of GBCA(s) and type. Also, all respondents indicated they often attend to patients who undergo multiple MRI examinations that involve repeating doses of GBCA. With regards to the awareness of statements issued by international organizations concerning GBCA deposition in the brain: 5(56%) were aware of that of the ACR-ASNR, only 2(22%) and 4(44%) were aware of that of the US FDA and the EMA respectively. Finally, 5(56%) do not check eGFR of patients prior to the administration of a GBCA.

Table 1
Summary of MR facility, type of facility, and type of GBCA in use.

MRF	Type of facility	Type of GBCA
1.	Tertiary Healthcare	Gadovist
2.	Tertiary Healthcare	Gadovist
3.	Tertiary Healthcare	Omniscan
4.	Tertiary Healthcare	Gadovist
5.	Private Hospital	Gadovist
6.	Private Hospital	Omniscan
7.	Private Hospital	Omniscan
8.	Tertiary Healthcare	Omniscan
9.	Tertiary Healthcare	Omniscan

MRF – MR facility.

Table 3 illustrates responses of participants on what they considered as best practices with regards to the administration of GBCAs. A Likert scale was used. The study revealed that 6(67%) agreed the type of the GBCA and the diagnostic efficacy be considered. All respondents agreed that the following be considered: the rate of adverse reactions, dosing/concentration, and propensity to deposit in more sensitive organs be considered respectively. Interesting, 7(78%) agreed that linear agents be avoided. However, 7(78%) strongly disagreed that GBCAs should be avoided entirely. All respondents (9[100%]) agreed that: macrocyclic agents should be administered at low doses; the clinical benefit of the diagnostic information of GBCA-MRI should be weighed against the potential risk of deposition in the brain; and attention should be given to paediatrics who may require GBCA administration over the course of their lifetime.

Discussion

A response rate of 69.2% (n = 9) was achieved from both public and private healthcare centres (Table 1). The majority of responses were from public tertiary healthcare facilities. In the current study, we found that gadodiamide (Omniscan) was the most commonly used GBCA (Table 1) despite its widely reported association with NSF[18–20] and recently, intracranial deposition after repeated doses.[7–9,12,14] This finding is similar to a previous study conducted in Ghana.[16] Even though gadopentetate dimeglumine (Magnevist) has also been found to be associated with intracranial deposition of gadolinium,[8,10] this agent is currently not in use in Ghana. Both

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