ORIGINAL ARTICLE

The Effect of Intravenous Contrast Agents on Renal Functions in Children and Adolescents at King Abdulaziz University Hospital, Jeddah

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Submission: 03 Jan 2020
Accepted: 09 Apr 2020

Citation
Ahmad RG, Albugmi FM, Aleiidi SA, Almoallim RM, Basalem DA, Helabi NW. The Effect of intravenous contrast agents on renal functions in children and adolescents at King Abdulaziz University Hospital, Jeddah. JKAU Med Sci 2020; 27(1): 55-61. DOI: 10.4197/Med.27-1.8

Abstract

Computerized tomography scanning is a diagnostic imaging tool that can be enhanced through the use of contrast agents. However, this process has been found to promote adverse effects, particularly those on the renal function. This study assessed the effects of intravenous iodine-based contrast agents on the kidney function in children and adolescents in the King Abdulaziz University Hospital in Jeddah, Saudi Arabia. It included 112 participants with hospital records, aged 15 years old and younger, who underwent chest or abdomen tomography scans between January 2018 and January 2019. The participants were made up of 46.4% females and 53.6% males, with a median age of 5.5 years. Majority (87.5%) of them possessed various comorbidities. This study found out that the glomerular filtration rate before and after the administration of intravenous contrast was not affected by a specific disease category, or even with no known comorbidities. However, future studies in this area should be conducted to cover more centers and regions of Saudi Arabia, but with the use of the recently identified biomarkers of AKI, such as the acute kidney injury, such as the neutrophil gelatinase-associated lipocalin and the kidney injury molecule-1, in order to match specific independent factors, such as age groups, gender, and variable comorbidities.

Keywords

Intravenous contrast media; Estimated glomerular filtration rate; Renal function

Introduction

Computed tomography (CT) scanning is a diagnostic imaging tool that uses radiation to build cross-sectional images of the body[1]. While the CT processes are typically associated with a high dose of exposure to radiation, the risk is generally minimal. One of the best ways to minimize the exposure to radiation is to consider the avoidance of CT scans that are not clearly required for diagnostic assessment, or to consider alternatives, such as magnetic resonance imaging or ultrasound, which also provide significant information for assessments. These alternatives may be especially important to pediatric groups, which are broadly more sensitive to radiation[2].

Computed tomography scanning is, nevertheless, a primary diagnostic procedure in many medical purposes, but it incorporates contrast agents in order to enhance the images produced, which were found to have adverse effects[10]. A contrast agent or a contrast material or medium is a substance that is introduced into the bloodstream, before an exam is carried out through a number of routes, such as through injection. The agent causes a specific organ or tissue to be more clearly visible during the scanning[3]. The contrast differentiates the targeted areas of the body and their surrounding anatomy, thereby enhancing the visibility of the specific blood vessel or tissue[4] that is targeted. In 2014, approximately 81.2 million CT scans were performed in the United States, and almost 52% of these had used contrast agents[5]. Despite their useful roles in imaging, their adverse effects can range from mild physiologic disturbances to life-threatening complications. The kidneys can be adversely affected by the contrast agents[6], which may lead to an acute kidney injury that is sudden, rapid, and can progressively worsen the renal function that results in the accumulation of wastes products[7]. This can be explained by the complications caused in the kidney through the excretion of contrast agents[8]. These adverse effects, however, differ according to the types and doses of the contrast agent used and whether the patient has any allergies or comorbidities.

The effects of contrast agents on the renal function have been examined in a number of studies. In 2017, a study on the effect of an intravenous (IV) contrast agent on the level of serum creatinine in neonates did not appear in neonates, and renal failure was not detected in them[6]. Furthermore, a retrospective study published in 2010, reported that the administration of IV contrast agent in cancer ICU patients with normal creatinine was to have no significant differences in their creatinine levels, compared to patients, who either did not undergo CT or had received contrast agents for their CT procedures[9]. But in another study that was conducted in 2016 on children and adolescents, the incidence of acute kidney injury that was associated with contrast agent was found in 10.3%[10] of those who were studied.

The importance of contrast agents in imaging studies and their associated adverse effects are well known in various medical disciplines, especially in radiology. Despite this awareness, we have found a paucity of relevant literature that explores this issue on contrast agents in children and adolescents, especially in Saudi Arabia. For this reason, we set out to assess the effects of IV iodine-based contrast materials on the kidney function in pediatric settings in the King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia.

Materials and Methodology

Study Design and Participants

This is a retrospective study that included 112 participants from the KAUH, using hospital records that date from January 2018 to January 2019.

Inclusion Criteria

All patients, who were 15 years old and younger and who underwent enhanced CT scans of the chest and the abdomen, were included in this study.

Data Collection

The data in this study were collected from the KAUH records. The collected data included the ages of the participants at the time of the study, their gender, anthropometric measurements, comorbidities, such as *diabetes mellitus*, renal, liver, and heart diseases, and their history of creatinine pre-contrast and post-contrast administration of the iodinated non-ionic low-osmolality contrast medium, iobitridol (Xenetix). We calculated the estimated glomerular filtration rate (eGFR), using the Bedside Schwartz equation *i.e.*, (height in cm x k)/serum creatinine in mg/dL, where the constant k = 0.413 is used for children above one year-old and k = 0.45 for children younger than one year. This formula was updated in 2009 and is currently considered as the standard method for the measurement of eGFR measurement in children.

Data Analysis

The data was collected using Google Sheets (Google, LLC., Mountain View, CA, USA), and entered in the data sheet using IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armonk, NY USA). Data analysis was carried out using descriptive statistics and inferential tests, such as frequency tables, the Pearson correlation, the Shapiro-Wilks test, and the Wilcoxon signed rank test. These tests were used to assess the effects of the IV contrast agent on the kidney function in children and adolescents. A *P*-value of <0.05 was set as statistically significant.

Results

A total of 112 participants were included in this study, *i.e.*, 46.4% females and 53.6% males. Their ages ranged from one-week to 15 years, and majority were between 6 and 12 years old (Table 1). Their median age was 5.5 years. Their descriptive data are tabulated in Table 2. Majority of the participants were known to have comorbidities, accounting to 87.5% of them, and are distributed among the various categories shown in Table 3.

The correlation between the participants' plasma creatinine before and after the administration of IV contrast agents was strongly positive, with $r = 0.961$ and a P-value of < 0.0001 (Fig. 1). The correlation between their eGFR before and after the administration of IV contrast agents was moderately positive, with $r = 0.686$ and a P-value of < 0.0001 (Fig. 2).

We used the Wilcoxon Signed Rank Test to compare the differences between the medians of the plasma creatinine and the eGFR before and after the IV contrast administration. We found no significant difference between the two (Table 4-6). We also found out that the eGFR before and after IV contrast administration was not affected by a specific disease category in comparison with the other disease categories, or even in those with no known comorbidities.

Table 1. Ages of the participants

Age Group		Frequency	Percent
Valid	Neonate (1 week to 1 month)	3	2.7%
	Infant (1 month to 1 year)	20	17.9%
	Toddler and preschool (2 to 5 years)	33	29.5%
	School age child (6 to 12 year)	34	30.4%
	Adolescent and young adult (13 to <18 y)	22	19.6%
	Total	112	100.0%

Discussion

This study used a number of different methods to assess renal function, with the serum creatinine and the eGFR being the most traditional. More sensitive and specific biomarkers for the diagnosis of acute kidney injury (AKI) had been discovered in recent years, including the neutrophil gelatinase-associated lipocalin (NGAL) , kidney injury molecule-1 (KIM-1), cystatin-C, Interleukin-18, and liver fatty acid-binding protein[11]. We used the eGFR to assess the renal function, because the new biomarkers were not then used, and thus, were not reflected in the medical records of our sample population.

The results show no significant effects on renal function, when the iodine-based contrast material was

Table 3. Disease categories

Diseases		Frequency	Percent
Valid	None	14	12.5%
	Gastrointestinal disease	13	11.6%
	Respiratory disease	13	11.6%
	Oncological disease	23	20.5%
	Central nervous system disease	7	6.3%
	Cardiovascular disease	17	15.2%
	Renal disease	11	9.8%
	Others	14	12.5%
	Total	112	100.0%

Table 2. Descriptive statistic forof the data on the ages, height, plasma creatinine before and after IV contrast administration, and eGFR before and after IV contrast administration

		Age at the Time of the Study (Years)	Height in cm	Plasma Creatinine before IV Contrast Administration	eGFR before IV Contrast Administration (UMOL)	Plasma Creatinine after IV Contrast Administration	eGFR after IV Contrast Administration (UMOL)
Mean		6.61	108.56	52.40	172.98	49.19	174.32
Median		**5.50**	**107.00**	**27.35**	**130.95**	**27.15**	**131.60**
Std. Deviation		4.91	33.53	109.06	120.46	96.61	122.58
Range		15.64	120.00	679.80	695.43	662.00	701.10
Minimum		0.05	50.00	4.20	6.67	5.00	1.00
Maximum		15.69	170.00	684.00	702.10	667.00	702.10
Percentiles	**25**	**2.00**	**80.50**	**17.05**	**100.60**	**16.68**	**103.20**
	50	**5.50**	**107.00**	**27.35**	**130.95**	**27.15**	**131.60**
	75	**11.56**	**137.50**	**39.60**	**213.75**	**39.08**	**213.75**

eGFR: Estimated glomerular filtration rate; Std. Deviation: Standard deviation

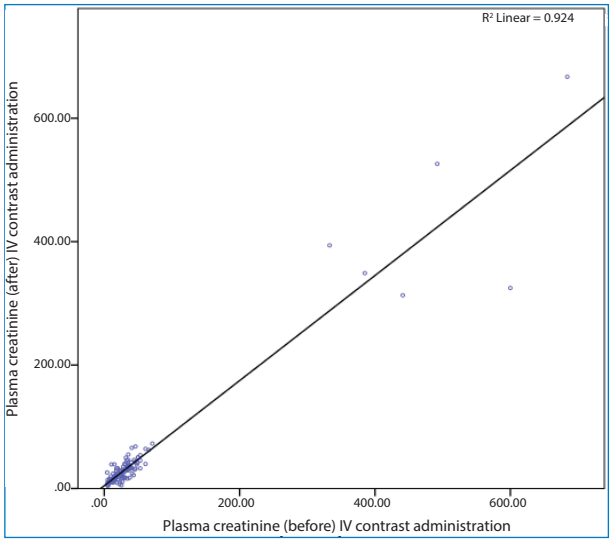

Figure 1. The correlation between the plasma creatinine before the administration of the IV contrast administration and after the administration.

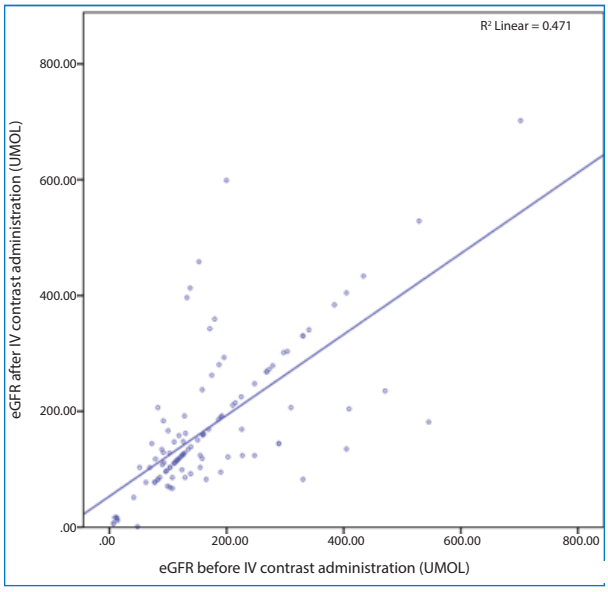

Figure 2. The correlation between the estimated glomerular filtration rate before the administration of the intravenous contrast media and after the administration.

Table 4. The difference of plasma creatinine and estimated glomerular filtration rate before and after IV contrast administration based on Wilcoxon Signed Ranks Test

Descriptive Statistics	N	Percentiles		
		25th	50th (Median)	75th
Plasma creatinine before IV contrast administration	112	17.0500	**27.3500**	39.6000
Plasma creatinine after IV contrast administration	112	16.6750	**27.1500**	39.0750
eGFR before IV contrast administration (UMOL)	112	100.6000	**130.9500**	213.7500
eGFR After IV contrast administration (UMOL)	112	103.2000	**131.6000**	213.7500

eGFR: Estimated glomerular filtration rate

Table 5. Ranks of the plasma creatinine and estimated glomerular filtration rate before and after IV contrast administration based on Wilcoxon Signed Ranks Test

Ranks		N	Mean Rank	Sum of Ranks
Plasma creatinine after IV contrast administration – Plasma creatinine before IV contrast administration	Negative Ranks	53[a]	58.31	3,090.50
	Positive Ranks	56[b]	51.87	2,904.50
	Ties	3[c]		
	Total	112		
eGFR after IV contrast administration (UMOL) – eGFR before IV contrast administration (UMOL)	Negative Ranks	28[d]	33.95	950.50
	Positive Ranks	34[e]	29.49	1,002.50
	Ties	50[f]		
	Total	112		

eGFR: Estimated glomerular filtration rate

[a]var13 plasma creatinine after IV contrast administration < var11 Plasma creatinine before IV contrast administration
[b]var13 plasma creatinine after IV contrast administration > var11 Plasma creatinine before IV contrast administration
[c]var13 plasma creatinine after IV contrast administration = var11 Plasma creatinine before IV contrast administration
[d]var14 eGFR after IV contrast administration (UMOL) < var12 eGFR before IV contrast administration (UMOL)
[e]var14 eGFR after IV contrast administration (UMOL) > var12 eGFR before IV contrast administration (UMOL)
[f]var14 eGFR after IV contrast administration (UMOL) = var12 eGFR before IV contrast administration (UMOL)

Table 6. The significant difference of plasma creatinine and estimated glomerular filtration rate before and after IV contrast administration

Wilcoxon Signed Rank Test		
	Plasma creatinine after IV contrast administration - Plasma creatinine before IV contrast administration	eGFR after IV contrast administration (UMOL) - eGFR before IV contrast administration (UMOL)
Z	-.281- [a]	-.182-[b]
Asymptomatic Sig. (2-tailed)	**0.779**	**0.855**

eGFR: Estimated glomerular filtration rate
[a]*Based on positive ranks*
[b]*Based on negative ranks*

administered to the participants in this study for the clinically indicated CT chest or abdomen examinations. Similar relationships were also concluded in previous studies. For example, Bedoya *et al.*[6] and McDonald *et al.*[12] reported no significant association between the administration of contrast material and the renal function.

One study, published in 2016, however, showed conflicting results with those found in our study. In this previous study, the incidence of acute kidney injuries were effected by the contrast agent, although this may be explained by the assessment method used. The 2016 study used the Kidney Disease Improving Global Outcomes definition, while our study used the eGFR assessment[9]. Our study was carried out carefully, but there are several limitations in the approach used. Firstly, there was a relatively low number of participants, owing to the limited use of the CT scans on pediatric patients. Secondly, the population data was collected from a single medical center, which arguably maybe not be sufficient to estimate the broad effects of *in vivo* confocal microscopy on the renal function. Thirdly, the population data were heterogeneous, which may have affected the accuracy of our results and our ability to identify variable risk factors.

Conclusions

This study revealed that there is no effect of *in vivo* confocal microscopy contrast agent on the renal function of the participants, particularly on the contrast effect on the eGFR regardless of the presence of comorbidities.

Future studies in this area should be considered to include more centers and regions of Saudi Arabia, and possibly, should use the recently established biomarkers of AKI, such as the NGAL and the KIM-1, to match specific independent factors, such as age groups, gender, and variable comorbidities.

Conflict of Interest

The authors declares that they have no conflict of interest that is related to this study and this article.

Disclosure

The authors did not receive any type of commercial support either in forms of compensation or financial for this study. The authors have no financial interest in any of the products or devices, or drugs mentioned in this article.

Ethical Approval

The approval for the conduct of this study was granted by the Head of the Radiology Department and the Research and Ethical Committee with reference number 479-18.

Availability of Data and Materials

The datasets used or analyzed in this study are available from the corresponding author upon request.

Author Contributions

All authors had coordinated and worked mutually in this research.

Acknowledgments

The authors are thankful to the personnel, who contributed to this research, in particular, the data collectors: Ms. Afnan Alzubaidi, Ms. Reem Alahmadi, Mr. Ammar Alharbi, Mr. Sultan Bajaifer, and Ms. Rahaf Slaghour.

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تأثير مواد التباين الوريدي على وظائف الكلى بين الأطفال في مستشفى جامعة الملك عبد العزيز، جدة، المملكة العربية السعودية

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المستخلص. الأشعة المقطعية هي نوع من أنواع الأشعة التشخيصية ويمكن استخدامها مع صبغه تسمى مواد التباين، والتي لها الآثار الجانبية خاصة على وظائف الكلى، و تهدف الدراسة إلى تقييم تأثيرمواد التباين الوريدي على وظائف الكلى بين الأطفال في مستشفى جامعة الملك عبد العزيز، جدة ، المملكة العربية السعودية ، حيث شملت هذه الدراسة الاستعادية ١١٢ طفل أعمارهم اقل من ١٥ عاما ممن أجريت لهم أشعة مقطعية للصدر أوالبطن من سجلات جامعة الملك عبد العزيز، بين يناير ٢٠١٨ إلى يناير ٢٠١٩ و تم تحليل البيانات باستخدام الحزمة الإحصائية للعلوم الاجتماعية الإصدار ٢١.

وقد كان ٤٦,٤٪ من العينة إناث و ٥٣,٦٪ ذكور (متوسط الأعمار ٥,٥ سنة) كما وجد أن غالبية المشاركين مصابون بأمراض مصاحبة والتي تمثل٨٧,٥٪ من العينة موزعة على عدد من الأمراض ، و لم يتأثر معدل ترشح الكبيبات المقدر قبل وبعد استخدام مواد التباين الوريدي بفئة مرضية محددة ، مقارنة بفئات أخرى أو حتى دون وجود أمراض مصاحبة معروفة وتوصي الدراسة بإجراء العديد من البحوث المستقبلية في هذا المجال في عدد من المراكزالطبية في مناطق المملكة العربية السعودية، والتي سوف تتناول عوامل مستقلة محددة مثل العلامات الحيوية لفشل الكلية الحاد مثل (NGAL, KIM-1) وايضا الفئات العمرية والجنس والأمراض المصاحبة المتغيرة.