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ORIGINAL ARTICLE

Metformin and intravenous contrast when time not help, a retrospective study at King Abdulaziz University Hospital, Jeddah, Saudi Arabia

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ABSTRACT

Background: Metformin is a common drug used for antihyperglycemic therapy in type 2 diabetes. Additionally, intravenous (IV) contrast may be administered when using various imaging techniques to enhance the visualization of body structures, and deterioration of renal function and lactic acidosis—contrast-induced nephropathy—may occasionally happen. The purpose of this research was to assess the current guideline of withholding metformin therapy in patients undergoing contrast-enhanced procedures in both emergency (ER) and inpatient settings.

Methodology: A retrospective study was conducted for all patients who were on metformin and underwent a contrast-enhanced imaging procedure (requiring IV contrast) between January and June 2016 at King Abdulaziz University Hospital in Jeddah, Saudi Arabia.

Results: This study involved 107 patients who were on metformin and who received a contrast-enhanced imaging procedure. Out of 107 patients, 26 were admitted through the ER. Independent *t*-tests were performed to compare the glomerular filtration rate and creatinine, before and after the procedure in both ER and ward patients; they all had non-significant associations.

Conclusion: In this study, none of the ER patients stopped their metformin before they were administered IV contrast.

Keywords: Metformin, creatinine, GFR, contrast, emergency.

Introduction

Metformin is a common drug used for antihyperglycemic therapy in type 2 diabetes [1]. It is also used in the treatment of polycystic ovary syndrome and non-alcoholic fatty liver disease [2]. Metformin increases the body's response to insulin and reduces liver gluconeogenesis and is excreted by the kidneys [3]. Additionally, intravenous (IV) contrast may be administered when using various imaging techniques to enhance the visualization of body structures [4], and deterioration of renal function and lactic acidosis, contrast-induced nephropathy (CIN), may occasionally happen [1]. Conditions with a higher risk of nephropathy include diabetes mellitus, dehydration, congestive cardiac failure, and concurrent use of nephrotoxic drugs [5]. There is a presumed association between metformin use and a higher risk of lactic acidosis when administering iodinated contrast media (ICM), that is, the potential for ICM to produce renal impairment [6]. The current US prescribing guidelines state that metformin should not be used if the patient's serum creatinine is ≥133 mmol/l in men and ≥124 mmol/l in women [7].

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In 2010, a study conducted at King Abdulaziz University Hospital (KAUH) showed that 25.0% of patients who were admitted in ICU and got computed tomography (CT) scans done or non-coronary angiography with intravenous ICM developed CIN [8].

A study in 2015 showed that discontinuation of metformin is not necessary after the administration of gadolinium-based contrast agents in the recommended dose range (0.1–0.3 mmol/kg body weight) [9].

According to the Canadian Medical Association Journal in 2012, for elective procedures, all nephrotoxic medications should be withheld 24–48 hours before administration of contrast in order to reduce the risk of CIN. In emergency (ER) cases, on the other hand, it is not always possible to stop the medication or delay the intervention long enough to avoid nephrotoxicity [1]. Therefore, metformin therapy should be stopped and the following precautions should be considered: the patient must be hydrated with ≥100 ml/hour of soft drinks or IV saline up to 24 hours after contrast medium administration (in hot areas, more fluid should be given); monitor renal function (serum creatinine), serum lactic acid, and blood pH; look for symptoms of lactic acidosis [10].

The association between the administration of IV contrast and metformin use by patients in the ER and outpatient settings has been observed in several studies, but no similar studies have been conducted in Saudi Arabia. The purpose of this research was to assess the current guideline of withholding metformin therapy in patients undergoing contrast-enhanced procedures in both the ER and inpatient settings at King Abdulaziz University Hospital.

Subjects and Methods

A retrospective study was conducted for all patients who were on metformin and underwent a contrast-enhanced imaging procedure (requiring IV contrast) between January and June 2016 at King Abdulaziz University Hospital in Jeddah, Saudi Arabia. This study was approved by the ethical approval committee of KAU. All patients on metformin who were administered IV contrast were included. The sample size was 107 patients, calculated by the special formula. Data were collected by the reviewers using Google online sheets. Also, the data were classified into ER and ward admitted patients, and the two categories were subclassified according to demographic variable (gender and age), chronic illness (diabetes and renal impairment), medications, current complaint, previous contrast exposure, creatinine level, and glomerular filtration rate (GFR) before and after the procedure. To analyze the data, the Statistical Package for the Social Science software was used. Correlation between ER and ward-admitted patients was conducted using logistic regression. Qualitative variables were submitted as percentage (frequency), and the correlation between patients using metformin and the risk of contrast-induced nephropathy was examined by the independent *t*-test and chi-square, p values < 0.05 were considered significant in both tests. Correlation between patients using metformin and the type and amount of contrast administered was conducted using the one-way analysis of variance test and correlation, respectively.

Results

This study involved 107 patients on metformin who received a contrast-enhanced imaging procedure during the first half of the year 2016 at KAUH. Out of 107 patients, 26 were admitted through the ER (Table 1).

HTN, hypertension; DM, diabetes mellitus; CVD, cardiovascular disease.

The mean volume of contrast given was 87.238 ml. It was found that none of the ER patients stopped their metformin before they were administered IV contrast.

An independent-samples *t*-test was conducted to compare GFR before the procedure in ER patients and Wards patients. There was not a significant difference in the scores for ER patients [M = 91.92, standard deviation (SD) = 55.661] and wards patients (M = 91.09, SD = 40.046); $t_{(100)} = 0.081$, $p = 0.935$.

An independent-samples *t*-test was conducted to compare GFR after the procedure in ER patients and wards patients. There was not a significant difference in the scores for ER patients (M = 117.56, SD = 99.710) and wards patients (M = 92.62, SD = 44.798); $t_{(76)} = 1.509$, $p = 0.135$.

An independent-samples *t*-test was conducted to compare creatinine levels before the procedure in ER patients and wards patients. There was not a significant difference in the scores for ER patients (M = 117.68, SD = 185.332) and wards patients (M = 102.21, SD = 136.599); $t_{(99)} = 0.448$, $p = 0.655$.

An independent-samples *t*-test was conducted to compare creatinine levels after the procedure in ER patients and Wards patients. There was not a significant difference in the scores for ER patients (M = 124.00, SD = 219.016) and

Table 1. *Frequencies of patients in ER compared to patients in the ward.*

	ER	Ward
Frequency	26	81
Male	12	40
Female	14	41
Mean age	59.9231	57.716
Smokers	4	10
Previously admitted	15	49
HTN	15	36
DM	25	77
CVD	4	16

wards patients (M = 114.39, SD = 155.631); $t_{(75)}$ = 0.207, p = 0.836 (Figure 1).

Discussion

The aim of this study was to define the relationship between metformin use and the risk of contrast-induced nephropathy based on the current guidelines for a contrast agent used in patients taking metformin.

This study found that metformin was stopped in only 81 patients out of 107 who underwent an enhanced imaging procedure (CT scan, MRI, and DVI) during the first half of the year 2016 at KAUH, which were exclusively inpatients. The GFR levels were measured before (M = 91.29) and after (M = 98.37) the procedure in most cases. The GFR after the procedure was not measured in eight ER patients and 21 inpatients.

In adults, the normal GFR was above 90 ml/minute. The stages of chronic kidney disease according to GFR levels are shown in Table 1 [11].

The mean volume of administered contrast was 87.238 ml. There are no strict maximum permissible doses of contrast, but in general, volumes of over 250–300 ml in a 24-hour period should be avoided [12]. Despite that other studies, including Lautin et al. [13] and Barrett et al. [14]; Rudnick et al. [15]; and McCullough et al. [16] have demonstrated a dose-dependent risk of renal dysfunction [17].

There was no significant difference between the ward patients who had stopped metformin (M = 92.62, SD = 44.798) and the scores for ER patients who had not stopped metformin (M = 117.56, SD = 99.710); $t_{(76)}$ = 1.509, p = 0.135. Creatinine levels were measured after the procedure. There was no significant difference between the ward patients who had stopped metformin (M = 114.39, SD = 155.631) and the scores for ER patients who had not stopped metformin (M = 124.0, SD = 219.016); $t_{(75)}$ = 0.207, p = 0.836. These results suggested that metformin did not have an impact on the GFR or creatinine levels after the procedures. Furthermore, results from a study by Taheri et al. [18] stated that metformin protects against tubular injury by restoring the biochemical alterations and modulation of oxidative stress on the tubules.

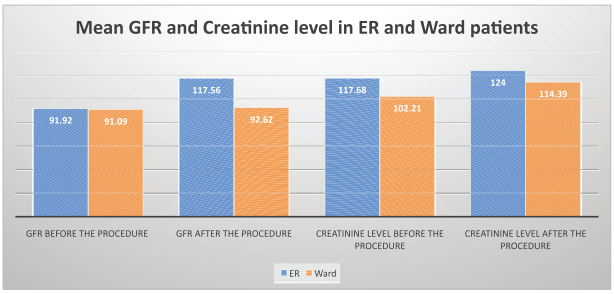

Figure 1. *The mean GFR and creatinine level in ER and ward patients.*

Conclusion

In conclusion, in ER cases which need enhanced emergent procedure, it is still hard to stop metformin at least 24 hours before administration of IV contrast, in this study none of the ER patients stopped their metformin before they were administered with IV contrast.

List of Abbreviations

CIN	Contrast-induced neuropathy
ER	Emergency
GFR	Glomerular filtration rate
IV	Intravenous

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Declaration of conflicting interests

None.

Consent for publication

Informed consent was obtained from all participants.

Ethical approval

This study was approved by the ethical approval committee of KAU.

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