# THE SAFETY OF I.V. IODINATED LOW OSMOLAR CONTRAST MEDIUM IN PATIENTS WITH PENICILLIN ALLERGY IN CT SCAN EXAMINATIONS.

Abdulameer Abudi Mohammed. F.I.B.M.S. and D.M. Radiology*.

## ABSTRACT:

**Background:** Intravenous (I.V.) low osmolar contrast media (LOCM) is commonly used during computerized tomography CT scan examinations, especially in diagnosis and staging of tumours, trauma and abdominal examinations. Many radiologists are relactant to do enhanced examination if patients had history of penicillin allergy. This study aims to evaluate the incidence of LOCM-related side-effects in patients with penicillin allergy compared to patients without penicillin allergy.

**Methods and patients**: Prospective study of 357 patients examined in CT scan unit in Al-Yarmouk teaching hospital, 44 of them had history of penicillin allergy, all given i.v. contrast medium (LOCM), and the prevalence of LOCM related side effects calculated for both groups.

**Results:** The prevalence of contrast medium related side effect was 0.64% in patients without history of penicillin allergy, while of the 44 patients with penicillin allergy, no side effects has been encountered.

**Conclusion:** No significant increase in LOCM related side effect was seen in patients with penicillin allergy.

**Keywords:** *Iodinated LOCM, penicillin allergy, CT scan.*

## INTRODUCTION

Iodine (atomic weight 127) is the only element that has proved satisfactory for general use as an intravascular radiological contrast medium (RCM). The iodine provide the radio-opacity: the other elements of the RCM molecule provide no radio-opacity but ac as a carriers of the iodine, greatly increasing the solubility and markedly reducing the toxicity of the total molecule.[1] The first report of opacification of the urinary tract by renal excretion rather than by retrograde introduction of contrast agent appeared in 1923 when Osborne et al.[2] although the iodized oil lipiodol was successfully introduced into myelography by Sicard as the first useable X-ray CM other than air in 1921.[3] The problem has always been how to package the iodine so that it may be delivered safely into very sensitive arterial systems (e.g. brain, heart, kidney) in the very large amounts required to produce adequate film-screen radio-opacity.[1] Intra-vascular organic iodinated RCM were introduced in clinical practice in 1928-9 by Moses Swick.[4] Introduced in the 1920s, iodinated contrast agents have evolved into one of the most frequently

* Lecturer in Faculty of Medicine, Kufa University, Radiologist in Al-Yarmouk Teaching Hospital, Baghdad, Iraq.

administered IV medications in hospitals and outpatient facilities. Revolutionizing radiologists' ability to differentiate soft-tissue densities, this advance has come with the added risk of adverse contrast effects. Although physiologic responses such as nausea and vomiting used to be ubiquitous with high-osmolar contrast agents, serious adverse effects were rare enough to allow widespread use. Immediate adverse effects of high-osmolar contrast media have been reported among 12.7% of patients. With the advent of low-osmolar contrast material, this number has decreased to 3.1% of patients. Overall, mortality was estimated at one death per 100,000 examinations on the basis of findings from 1991. With the widespread use of low-osmolar agents, the incidence of adverse effects likely has changed, as have the features of these events.[5] Since the introduction of multidetector computed tomography (MDCT) technology, the number of patients undergoing contrast enhanced CT scan studies has steadily increased. In addition, the patients population subjected to CT is becoming progressively older with more comorbid condition. The benefits of contrast enhanced CT are well recognized in the diagnosis of diseases, the evaluation of trauma patients and guidance of interventional and therapeutic procedures. However, adverse reactions to contrast administration may occur and remain a source of concern, particularly the development of contrast induced nephropathy.[6] Informed consent is essential for any invasive procedure (angiography, angioplasty, vascular embolization, biopsy, etc), but probably is not essential in many countries for uncomplicated procedures (e.g. intravenous urography IVU) in a reasonable fit patient, as it may alarm the patient to learn that there is a risk (however small) of a severe or fatal adverse drug reaction. Like every other drug, contrast agent should be administered only when there are clear and defensible clinical indications and when the prospects of benefit to the patient outweigh the risks and discomfort that may occur. With modern contrast agents (either LOCM or HOCM), it is more likely that a complication occurring during a radiological arterial procedure will be due to the consequences of the instrumentation (e.g. vessel damage, thromboembolism) rather than to the contrast agent, if the latter is used in an appropriate dose and manner.[1]

# PATIENTS & METHODS

Total examinations of 1154 patients were included from August 2009 to December 2010 done in CT scan unit in Al-Yarmouk teaching hospital, 367 (31.8%) of them required the administration of i.v. contrast medium, 10 (2.7%) patients of them spared the contrast administration due to variable contra-indications (7 uraemic, 2 toxic thyroid nodules and one apprehensive and afraid of contrast administration). A total of 357 patients (97.3%) had been given contrast medium (LOCM) in a total dose 50-100 ml intravenously. Of those 357, 44 (12.3%) patient gave a history of penicillin allergy, while the remaining 313 (87.7%) had no such history. The contrast medium used was Iohexol 350 mg./ml concentration used in Iraqi hospital licensed by Ministry of health. We included only the acute adverse effects in this study. Adverse effect was defined as a reaction occurring in the radiology unit during contrast administration or within 30-60 minutes of administration. In our study, delayed adverse effects (> 60 minutes after injection) were not included

because of incomplete capture of these events if they would have occurred, making estimation of their frequency unreliable.

Adverse reactions to RCM may be divided into:

A- idiosyncratic anaphylactoid reactions: these the most dreaded and most serious and fatal complications of RCM injections as they occur without warning, cannot be reliably predicted and are not preventable in the present state of our knowledge. Unlike the chemotoxic and hyperosmolar reactions, the earlier mentioned anaphylactoid reactions are not dose dependent and death has been known to occur following a 1 ml IV test dose, or after the full dose of RCM has been given after a negative test dose.

B- non-idiosyncratic reactions: unlike the idiosyncratic reactions, these non-idiosyncratic reactions are dose dependent and therefore related to the chemical composition, osmolality and concentration of CM and the volume, speed and multiplicity of the injection.

C- combined A and B reactions.[1]

anxiety, apprehension and fear of the radiological procedure probably play a significant part in adverse reactions by activating a hypothalamic reaction resulting in cardiovascular and respiratory collapse and even death.[7] An excellent (1999) review of adverse reactions, their mechanism, prophylaxis and treatment is presented by Sidhu [8] and Dawoson.[9] We used the guidelines of the American College of Radiology Manual on Contrast Media version 7 [10] to classify the severity of adverse effects as mild, moderate, and severe. Although this system is a uniform way of comparing our results with those of other studies, it should be noted that nausea and vomiting are considered a mild effect in this classification. Although nausea and vomiting are recorded as an adverse effect for the purposes of our database, in the absence of other symptoms, nausea and vomiting would not be considered an anaphylactoid reaction to contrast reaction and would not preclude future administration of contrast media. Infiltration of the injection site and isolated effects on the extremity (e.g., coolness, local pain) at the injection site were not included, as they are attributed to instrumentation effects.

# RESULTS

Among 357 patients who received i.v. CM, adverse effects were identified in only 2 patients (0.6 % of all doses). From the 313 patients without penicillin's allergy, only 2 patients (0.64%) developed mild side effects. While from the 44 patients with penicillin allergy, no patient (0%) developed side effects. No moderate or severe side effects were seen, no death encountered. The majority of adverse effects were mild, represented by mild rash, urticaria, nausea and vomiting. Most of these adverse effects were managed with reassurance of the patients, observation and/or i.v. hydrocortisone. There was no need for more aggressive treatment, such as transfer to the emergency department or administration of epinephrine or adrenalin.

# DISCUSSION

The actual prevalence of adverse effects after the administration of intravascular (IV) contrast media is difficult to determine since similar signs and symptoms may be due to concomitant medications, local anesthetics, needles, catheters, and anxiety, among other things. Underreporting or variation in the

categorization or classification of reactions affects statistics regarding incidence.[11]. Most adverse effects are mild and do not require treatment. Historically, adverse effects have occurred in 5% to 15% of all patients who receive ionic high-osmolality contrast media (HOCM). Many patients experience physiologic disturbances (e.g., warmth or heat), and this is often not recorded. [11] The non-ionic X-ray CM have a very low incidence of adverse effects, particularly of mild and moderate reactions. Accordingly, in order to establish a safety profile based on more medically important reactions, patients populations larger than those surveyed in preregistration trials are needed. The drug monitoring performed by Schrott et al in Germany on 50,000 patients [12] and the cohort surveys performed by Katayama et al. in Japan on 338,000 patients [13] and Palmer in Australia on 110,000 patients [14] have not only documented the superiority of non ionic over ionic CM in the incidence of of the usual mild and moderate adverse effects found in preregistration trials, but have also convincingly demonstrated that there are fewer medically relevant reactions. The use of HOCM for IV use is now uncommon. Use of low-osmolality ionic and nonionic contrast media (LOCM) is associated with a lower overall incidence of adverse effects, particularly of non-life threatening ones. Cochran et al [15] reported an overall incidence of adverse effects of 0.2% for nonionic contrast administered at a single institution. A second study report a prevalence of 0.2-0.4% for non-life threatening reactions and 0.04% for life threatening reactions [16] .A slightly higher overall incidence of 0.7% was reported from a second institution upon review of 29,508 patients given iopromide over a 2-year period. More recently Wang reported an overall incidence of 0.6% upon review of 84,928 patients who received Iohexol, iopromide, or iodixanol [17]. In our study, the adverse effects rate was 0.6% among 357 doses. All of these adverse effects were mild in severity and were managed with reassurance of patients.

# CONCLUSION AND RECOMMENDATIONS

No significant increases of side effects were seen in patients with penicillin's allergy. The presence of penicillin allergy is not a contra-indication for administration of i.v. iodinated LOCM. Our study have faced some limitations, being a prospective study and although it continue for about one and a half year, the total number of patients was 357, of them, 44 patients gave history of penicillin allergy, we can not include all the patients during this period, because radiologists omit those patients from contrast studies as they afraid from the development of serious side effects. We recommend further larger group study so that its results can be compared with similar studies. Although we did not faced adverse effects in penicillin's-allergy patients, we recommend oral methylprednisolone tablet, 32 mg, 12 and 2 hourly before examination as a medico-legal precaution and reassurance for staff. We also recommend an annual training programs and work shops for the managements of the iodinated LOCM side effects for the radiologists and the radiographers, so radiology staff will be familiar with these side effects and their emergency management.

# TABLES

**Table**-1: Distribution of the age groups of patients non- allergic to penicillin.

| Age groups (years) | total |
|---|---|
| 12-20 | 35 (11.2%) |
| 21-30 | 42 (13.4%) |
| 31-40 | 65 (20.8%) |
| 41-50 | 58 (18.54%) |
| 51-60 | 51 (16.3%) |
| 61-70 | 40 (12.8%) |
| 71-80 | 22 (7%) |
| | 313 (100%) |

**Table**-2: Distribution of the age groups and gender of patients allergic to penicillin.

| Age groups (years) | male | female | total |
|---|---|---|---|
| 18-20 | 1 | 4 | 5 (11.4%) |
| 21-30 | 2 | 3 | 5 (11.4%) |
| 31-40 | 4 | 5 | 9 (20.5%) |
| 41-50 | 2 | 6 | 8 (18.2%) |
| 51-60 | 3 | 4 | 7 (15.9%) |
| 61-70 | 2 | 4 | 6 (13.5%) |
| 71-80 | 1 | 3 | 4 (9.1%) |
| | 15 (34.1%) | 29 (65.9%) | 44 (100%) |

# REFERENCES:


1- A. Adam, A. K. Dixon, R. G. Gainger, D. J. Allison. Diagnostic radiology text book of medical imaging, Churchill Livingstone 2008, Vol. 1, 2:27, 34.

2- Osborne, E. D. Sutherland, C.G., Scholl, A.J., et al. Reontegnography of the urinary tract during excretion of sodium iodide. 1923, JAMA 80, 368-373.

3- P. Dawson, W. Clauss. Contrast media in practice questions and answers. Springer-Verlag Berlin Heidelberg 1999.chap 1 P 1,43.

4- Swick M Darstellung Der Niere und Harnwege in Roentgenbild durch intravenose Einberingung eines neuen Kontraststoffes: des Uroselectans. 1929, Klin Wochenscher 8: 2087-2089.

5- Christopher H. Hunt; Robert P. Hartman; Gina K. Hesley, Frequency and Severity of Adverse Effects of Iodinated and Gadolinium Contrast Materials: Retrospective Review of 456,930 Doses, Am J Roentgenol. 2009;193(4):1124-1127.

6- John R. Haaga et al, CT and MRI of the whole body, Mosby 2009. Vol. 2, 39:1807.

7- Lalli A F 1980 contrast media reactions:data analysis and hypothesis.Radiology 134: 1-12

8- Sidhu P S, Dawson P 1999 adverse reaction to contrast media. Isis medical media, oxford, ch. 9: pp 99-119.

9- Dawson P, Cosgrove D O, Grainger R G 1999 textbook of contrast media, ch. 11, ch. 15 Isis medical media, oxford.

10- American College of radiology manual on iodinated contrast media version 7, 2010, ACR, Chicago. P 17.

11- Dillman JR, Strouse PJ, Ellis JH, Cohan RH, Jan SC. Incidence and severity of acute allergic-like reactions to i.v. nonionic iodinated contrast material in children. AJR Am J Roentgenol 2007; 188:1643–1647.

12- Schmitt KM, Behrends B, Claus W, Kaufmann J, Lehnert J (1986) Iohexol in der Ausscheidungsurographie. Ergebnisse des Drug-monitoring. Fortscher Med 7:153-156

13- Katayama H, Yamaguchi K, Kozuka T et al. (1990) adverse reactions to ionic and non-ionic contrast media. A report from Japanese committee on the safety of contrast media. Radiol 11:52-66

14- Palmer FJ (1989) the royal Australian college of radiologists (RACR) survey of reactions to intravenous ionic and non-ionic media. In Enge I, Edgren J (eds) patients safety and adverse events in contrast medium examination. Elsevier, Amstrdam, pp 137-141

15- Cochran ST, Bomyea K, Sayre JW. Trends in adverse events after IV administration of contrast media. AJR Am J Roentgenol 2001; 176:1385–1388.

16- Wolfgang Dahnert. radiology review manual.Lippincott Williams and Wilkins, 2007. Vol. 2: 1132.

17- Wang CL, Cohan RH, Ellis JH, Caoili EM, Wang G, Francis IR. Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. AJR Am J Roentgenol 2008; 191:409–415.

# سلامة استعمال صبغة اليود الوريدية ذات الاوزمولارية الواطئة للمرضى الذين لديهم حساسية البنسلين في فحوصات المفراس الحلزوني

الباحث: د. عبدالامير عبودي محمد.*


## الخلاصة:

مقدمة: تستعمل صبغة اليود الوريدية ذات الاوزمولارية الواطئة بصورة شائعة خلال فحوصات المفراس الحلزوني، خصوصا في فحوصات تشخيص الاورام، تحديد مراحلها، حالات الشدة الخارجية وفحوصات البطن. ان عددا كبيرا من اطباء الاشعة يتجنبون اعطاء الصبغة الوريدية للمرضى الذين لديهم حساسية البنسلين مما يوثر على نتائج التشخيص النهائية.

## هدف الدراسة:

اثبات عدم وجود زيادة في نسبة ظهور الاعراض الجانبية لصبغة اليود الوريدية ذات الاوزمولارية الواطئة للمرضى الذين لديهم حساسية البنسلين مقارنة مع غيرهم من المرضى.

## الطريقة و المرضى:

فحص ثلاثمائة وسبعة و خمسون مريضا في وحدة المفراس الحلزوني، اربعة واربعون منهم لديهم حساسية البنسلين. اعطي جميع المرضى صبغة اليود الوريدية ذات الاوزمولارية الواطئة وتم تقييم نسبة ظهور الاعراض الجانبية لكلا المجموعتين ومقارنة النتائج.

## النتائج:

كانت نسبة ظهور الاعراض الجانبية لدى المرضى الذين لا يعانون من حساسية البنسلين ٠,٦٤%، بينما لم تظهر اي اعراض جانبية لدى المرضى الذين يعانون حساسية البنسلين.

## المناقشة والاستنتاج:

على الرغم من ان الدراسة اظهرت عدم وجود زيادة بنسبة الاعراض الجانبية لصبغة اليود الوريدية ذات الاوزمولارية الواطئة للمرضى الذين لديهم حساسية للبنسيلين بالمقارنة مع غيرهم من المرضى، فاننا نوصي بدراسات مستقبلية لعينات اوسع من المرضى لمقارنتها مع النتائج التي تم التوصل اليها في دراستنا.

ونوصي باستعمال دواء ميثيل بردنيزولون بشكل حبة ٣٢ ملغم، ١٢ ساعة و ٢ ساعة قبل اعطاء الصبغة الوريدية على الرغم من عدم حصول اي اعراض جانبية للمرضى الذين لديهم حساسية البنسلين. وكذلك فاننا نوصي باستحداث دورات تدريبية نظرية وعملية لاطباء الاشعة و المصورين الشعاعيين لتشخيص و علاج الاعراض الجانبية لصبغة اليود الوريدية ذات الاوزمولارية الواطئة والحالات الطارئة في حالة حدوثها بعد زرق الصبغة.


---

* مدرس في كلية الطب / جامعة الكوفة. زميل المجلس العراقي للأشعة التشخيصية (البورد العراقي) ، دبلوم عالي بالأشعة التشخيصية (بغداد). اختصاصي في الأشعة التشخيصية في مستشفى اليرموك التعليمي.