

ORIGINAL ARTICLE

Healthcare Associated Inadvertent Intra-Arterial Injection as a Cause of Acute Limb IschemiaFAHAD MEMON¹, MOHAMMAD FAHAD TARIQ BARLAS², AREEBA SALEEM¹, WARYAM PANHWAR³, NAJAM UDDIN RAJPER³, KHALIL U REHMAN³, AYESHA KHAN⁴¹Fellow Vascular Surgeon, Department of Vascular and Endovascular Surgery, SMBBIT, Karachi, Pakistan²Assistant Professor, Department of Vascular and Endovascular Surgery, SMBBIT, Karachi, Pakistan³Consultant Vascular Surgeon, Department of Vascular and Endovascular Surgery, SMBBIT, Karachi, Pakistan⁴Consultant Urologist, Department of Urology, JPMC, Karachi, PakistanCorrespondence to: Fahad Memon, Email: fahadhameedmemon@gmail.com**ABSTRACT****Background:** The present study aimed to determine the outcome of healthcare related inadvertent intra-arterial injection as a cause of acute upper limb ischemia in terms of limb function and salvageability.**Methods:** A retrospective observational study was undertaken at the Department of Vascular and Endovascular Surgery, Shaheed Mohtarma Benazir Bhutto Institute Of Trauma, Karachi between 1st January 2020 to 31st December 2021. All patients who presented with ischemia secondary to inadvertent intra-arterial injection between the ages 18-70 years were included in the study. Files of the patients were reviewed and data was gathered to fill proformas. Follow up of the patients was reviewed for up to four months. Acute limb ischemia, limb salvageability, and limb function was assessed post-treatment.**Results:** In 14 (46.67%) no amputation occurred, 5 (16.67%) had minor amputation while 11 (36.67%) had major amputation. Seriousness of presenting symptoms was significantly associated with major amputation ($p = 0.022$). The majority of the patients who presented with pain, discoloration, sensory loss, motor loss, and gangrene had major amputations i.e. 4 (36.4%). memory loss was significantly associated with major amputation [8 (72.7%); $p < 0.0001$]. Gangrene was also significantly associated with major amputation [8 (72.7%); $p = 0.002$].**Conclusion:** A number of mechanisms, including direct artery damage, arterial spasm, toxicity from the drug, embolism can result in ischemia following intra-arterial drug injection. In order to avoid such incidents and to make prompt diagnosis, healthcare providers should broaden their awareness of typical local injection practices, phases of injection drug use and the hazards connected with it.**Keywords:** Acute limb ischemia, gangrene, Injections, Intra-Arterial, Ischemia**INTRODUCTION**

The worldwide incidence of unintentional intra-arterial injection is estimated to be 1:3500 – 1:56000 patients visiting emergency department.^{1,2} Most venous access in hospitals and all healthcare facilities is achieved through peripheral venous cannulation.³ Given that 90% of the patients attending the emergency department and 60% of all hospital inpatients will undergo peripheral venous cannulation,⁴ it is likely that the modern-day vascular surgeon will encounter this complication several times during his/her career. Injection into a preexisting arterial cannula or the erroneous and misunderstood cannulation of an artery rather than a vein are the leading causes of these mishaps and injuries.⁵ Although few drugs have been administered into arteries without undue consequence, a number of medicines have been observed to be associated with severe morbidity, leading to acute limb ischemia and amputation, raising the importance of early incidence recognition and treatment.

Multiple elements are directly to blame for limb ischemia caused by intra-arterial (IA) injection, depending on the injection site, medication type, and drug dose.⁶ Risk factors for intra-arterial injury include difficult venous access, morbid obesity, dark skin pigmentation, patients unable to communicate and abnormal vascular anatomy.³ The radial and brachial arteries are commonly affected in the upper extremities because of their proximity to and accessibility to target veins like the cephalic and basilic veins.^{7,8} Inadvertent injection of intra-arterial medication may manifest immediately, or several days following the event. At the time of infusion, patients may complain of discomfort at, or distal to, the site of injection³ in the form of altered sensation, motor deficits, and cutaneous manifestations such as flushing or mottling. In severe cases, patients may develop upper limb ischemia, gangrene and amputation. If the consequence of the eventual results isn't noticed for a while, or if the accountable healthcare personnel opt not to disclose the error, underreporting may occur.⁹

Due to the disastrous consequences associated with inadvertent accidental intra-arterial injections, prompt recognition and a thorough clinical assessment is the key to successfully manage these patients. In seven (23.1%) cases, amputation of a

digit or limb was observed.⁶ It is comprehensible that no precise treatment strategies have been developed and that the majority of our efforts focus on thrombosis prevention and vascular patency maintenance.¹⁰ A protocol that includes anticoagulation and intra-arterial injection of thrombolytics and prostaglandins might enhance prognosis. However, the optimal treatment methods are still undetermined. Embolectomy, steroids, vasodilators, and sympathetic blockers do not seem to have any overall impact on amputation rates.⁵ Therefore the aim of this study is to raise awareness in healthcare workers regarding incidence of inadvertent intra-arterial injection and its outcomes along with management strategies to minimize the grave consequences.

The present study aimed to determine the outcome of healthcare related inadvertent intra-arterial injection as a cause of acute upper limb ischemia in terms of limb function and salvageability.

MATERIAL AND METHODS

A retrospective observational study was undertaken at the Department of Vascular and Endovascular Surgery, Shaheed Mohtarma Benazir Bhutto Institute of Trauma, Karachi between 1st January 2020 to 31st December 2021. Subjects were selected for the study using a non-probability consecutive sampling method. All patients who presented with ischemia secondary to inadvertent intra-arterial injection between the ages 18-70 years were included in the study.

Patients with past history of peripheral vascular disease (PVD), valvular disorders, cardiomyopathy, previous history of upper limb ischemia, and intravenous drug abusers were excluded from the study.

Patients presented to the Emergency room or Out Patient Department with history of acute limb ischemia secondary to inadvertent intra-arterial injection from 1st January 2020 to 31st December 2021, were included in the study. Files of the patients were reviewed and data was gathered to fill proformas. Follow up of the patients was reviewed for up to four months.

Depending on the injection site, acute limb ischemia was characterized as sudden, severe pain in the affected limb

accompanied by bluish discoloration or gangrenous alterations in the affected limb and the presence or absence of a brachial, radial, or ulnar pulse, presenting within 2 weeks of incidence.

Limb Salvageability was measured in terms of minor (fingers amputation except thumb) and major amputation(thumb or below elbow amputation). Limb function was assessed in terms of viable functional hand with maintained routine activities at the end of 4 months post incidence with treatment.

Functional hand was compared with the opposite normal hand. Mild impairment was defined as the ability to perform daily activities but not the same as the normal hand. Moderate Impairment was the development of contractures but still some movements reserved. Severe impairment was a complete non-functional hand. Gangrene was defined as the necrosis of tissue associated with ischemia (dry gangrene) or infection (wet gangrene).¹¹

A P-value less than 0.05 was deemed statistically significant when data were inputted and analyzed using SPSS version 20. Frequency and percentage calculations were performed for categorical variables such as gender, whereas Means ± SD calculations will be conducted for numerical variables such as age. To compare Categorical variables, the Chi-square test was utilized.

RESULTS

The study included 30 patients with a mean age, weight, and height of 45.43 ± 16.08 years, 61.37 ± 9.98 kg, and 160.37 ± 5.61 cm respectively. In the majority, the symptoms appeared in less than an hour.

Most common presenting complaint was pain, followed by Discoloration, Sensory loss, and Memory loss with a frequency of 22 (73.3%), 19 (63.3%), 14 (46.7%), and 9 (30%) patients.

In 14 (46.67%) no amputation occurred, 5 (16.67%) had minor amputation while 11 (36.67%) had major amputation.

Table 1: Sociodemographic and clinical parameters of study participants

Characteristic	Mean / N(%)
Age	45.43 ± 16.08
Weight	61.37 ± 9.98
Height	160.37 ± 5.61
Symptoms appeared after how long (minutes)	
<1 hour	18 (60%)
<1 day	6 (20%)
<1 week	1 (3.3%)
<1 month	1 (3.3%)
>1 month	4 (13.3%)
Gender	
Female	15 (50%)
Male	15 (50%)
Hypertension	9 (30%)
Diabetes mellitus	8 (26.7%)
Asthma	2 (6.7%)
Others	8 (26.6%)
Status at time of presentation	
Pain	22 (73.3%)
Discoloration	19 (63.3%)
Sensory loss	14 (46.7%)
Memory loss	9 (30%)
Gangrene	12 (40%)
None	5 (16.7%)
Type of therapy given	
Heparin	17 (56.7%)
Dexamethasone	8 (26.7%)
Antibiotics	30 (100%)
Ascard	29 (96.7%)
Outcomes in terms of salvageability	
No amputation	14 (46.67%)
Minor amputation	5 (16.67%)
Major amputation	11 (36.67%)

Seriousness of presenting symptoms was significantly associated with major amputation (p = 0.022). The majority of the patients who presented with pain, discoloration, sensory loss, motor loss, and gangrene had major amputations i.e. 4 (36.4%). memory loss was significantly associated with major amputation [8 (72.7%); p<0.0001]. Gangrene was also significantly associated with major amputation [8 (72.7%); p=0.002].

Table 2: Association of salvageability with sociodemographic and clinical characteristics

Parameters	Outcomes in terms of salvageability			p-value
	No amputation	Minor amputation	Major amputation	
Gender				0.27
Female	7 (50%)	1 (20%)	7 (63.6%)	
Male	7 (50%)	4 (80%)	4 (36.4%)	
Hypertension	3 (21.4%)	2 (40%)	4 (36.4%)	0.625
Diabetes Mellitus Type 2	2 (14.3%)	1 (20%)	5 (45.5%)	0.202
Symptoms appeared after how long (minutes)				0.099
<1 hour	8 (57.1%)	3 (60%)	7 (63.6%)	
<1 day	1 (7.1%)	1 (20%)	4 (36.4%)	
<1 week	0 (0%)	1 (20%)	0 (0%)	
<1 month	1 (7.1%)	0 (0%)	0 (0%)	
>1 month	4 (28.6%)	0 (0%)	0 (0%)	
Status at time of presentation				0.022
discoloration, sensory loss, motor loss, gangrene	0 (0%)	0 (0%)	1 (9.1%)	
gangrene	0 (0%)	1 (20%)	1 (9.1%)	
pain, discoloration	4 (28.6%)	0 (0%)	0 (0%)	
pain, discoloration, gangrene	0 (0%)	1 (20%)	0 (0%)	
pain, discoloration, sensory loss	4 (28.6%)	1 (20%)	0 (0%)	
pain, discoloration, sensory loss, motor loss	0 (0%)	1 (20%)	3 (27.3%)	
pain, discoloration, sensory loss, motor loss, gangrene	0 (0%)	0 (0%)	4 (36.4%)	
pain, gangrene	1 (7.1%)	1 (20%)	2 (18.2%)	
Symptoms				
pain	9 (64.3%)	4 (80%)	9 (81.8%)	0.576
discoloration	8 (57.1%)	3 (60%)	8 (72.7%)	0.714
sensory loss	4 (28.6%)	2 (40%)	8 (72.7%)	0.085
memory loss	0 (0%)	1 (20%)	8 (72.7%)	<0.0001
gangrene	1 (7.1%)	3 (60%)	8 (72.7%)	0.002
Type of therapy given				
Heparin	9 (64.29%)	3 (60%)	5 (45.45%)	0.632
Dexamethasone	5 (35.71%)	1 (20%)	2 (18.18%)	0.576
Antibiotics	14 (100%)	5 (100%)	11 (100%)	-
Ascard	13 (92.86%)	5 (100%)	11 (100%)	0.554

DISCUSSION

The present study aimed to evaluate the outcomes associated with inadvertent intra arterial injection at a tertiary care center. 30 such cases were reported, the majority of these cases presented to the hospital within one hour of symptoms.

The present study revealed that in 14 (46.67%) no amputation occurred, 5 (16.67%) had minor amputation while 11 (36.67%) had major amputation. Seriousness of presenting symptoms was significantly associated with major amputation (p = 0.022). The majority of the patients who presented with pain, discoloration, sensory loss, motor loss, and gangrene had major amputations i.e. 4 (36.4%). memory loss was significantly associated with major amputation [8 (72.7%); p<0.0001]. Gangrene was also significantly associated with major amputation [8 (72.7%); p=0.002].

Even though they are uncommon, intra-arterial injections (IA) can result in acute limb ischaemia with severe consequences. The limb gangrene may be prevented if the symptoms were recognised and treated early enough.¹² Previous published literature revealed that acute presentation with pain and discoloration succeeded by intravenous drug injection was an ominous sign of accidental intra arterial injection.¹³

For patients who had had an upper extremity intra-arterial medication injection, a thorough evaluation was conducted. Amputation was the main endpoint, and information on the intervention and outcome was retrieved and subjected to pooled analysis.¹⁴ According to the study's findings, the weighted mean incidence of amputations was 29% overall. The majority of treatments (77% of all treatments) employed anticoagulants. According to pooled analysis, usage of steroids was linked to a decreased frequency of amputation, but circumstances that required the use of antibiotics were substantially related with a greater incidence.¹⁴

A cross sectional study was performed in the cardiovascular department at Lady reading Hospital Peshawar to assess the burden of accidental Intra Arterial Injection and upper arm Ischemia. The study concluded that amputation of limb was observed in seven (23.1 %) cases.¹⁵

Inadvertent arterial cannulation and medicine delivery have a documented incidence of 1 in 3440 instances, according to Forsyth JM et al. Risk factors were found to include restricted venous access, communication problems, and abnormal vascular architecture. A multitude of processes, including arterial damage from a misplaced cannula and drug administration, can both result in ischemia episodes. We advise that individuals who accidentally injure their arteries have an urgent clinical evaluation and be treated based on the severity of upper limb ischemia.¹⁶

Accidental intra-arterial injection can lead to limb ischemia and even limb amputation so while injecting intravenous drugs, caution must be practiced. An amputation occurs about 30% of the time after intra-arterial medication injection of the upper extremity. Amputation rates were considerably greater in conditions needing supplementary antibiotic usage and in patients who received therapy later.¹⁴

These posited sources of tissue damage have been the focus of treatment approaches. Using a typical regimen of dexamethasone, heparin, and LMW dextran, Gaspar et al¹⁷ and Treiman et al¹⁸ have each authored series (19 and 45 cases, respectively) outlining their experiences treating intra arterial injection. Amputations occurred in 26% and 24% of these two case series, respectively. Reserpine, a single-agent vasodilator, was administered by Stueber et al¹⁹ to 14 patients, one of whom required an amputation.

It is preferable to rely on a thorough history and examination rather than getting reliant on the results of the duplex ultrasound. It took a diverse team approach to make a diagnosis and deliver the best care.

CONCLUSION

In order to avoid such incidents and to make prompt diagnosis, healthcare providers should broaden their awareness of typical local injection practices, phases of injection drug use and the hazards connected with it.

REFERENCES

- Cohen SM. Accidental intra-arterial injection of drugs. *Lancet* 1948; 2(6523):361.
- Samanta S, Samanta S. Accidental intra-arterial injection of diclofenac sodium and their consequences: report of two cases. *Anaesth Pain Intensive Care* 2013; 17(1):101–2.
- Forsyth JM, Webster PJ, Haldipur N. Iatrogenic intra-arterial injection in the upper limb: A pragmatic guide for the on-call vascular surgeon. *Indian J Vasc Endovasc Surg* 2020;7:260-4
- Rodríguez-Calero MA, Blanco-Mavillard I, Morales-Asencio JM, Fernández-Fernández I, Castro-Sánchez E, de Pedro-Gómez JE. Defining risk factors associated with difficult peripheral venous Cannulation: A systematic review and meta-analysis. *Heart Lung* 2020. pii: S0147-9563 (20) 30009-1.
- Lokoff A, Maynes JT. The incidence, significance, and management of accidental intra-arterial injection: a narrative review. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*. 2019 May;66(5):576-92.
- Seak CK, Kooi XJ, Seak CJ. Acute hand ischemia after intra-arterial injection of meprobamate powder. *The Journal of Emergency Medicine*. 2012 Sep 1;43(3):468-71.
- Sen S, Chini EN, Brown MJ. Complications after unintentional intra-arterial injection of drugs: risks, outcomes, and management strategies. *Mayo Clin Proc* 2005;80(6):783–95.
- Rautio R, Keski-Nisula L. Inadvertent intra-arterial drug injections: the role of angiographic and clinical findings. *Acta Radiol* 2006;47(6):554–8.
- Mariyaselvam, M., Hutton, A. & Young, P. Accidental intra-arterial injection: an under-reported preventable never event. *Crit Care* 19, P166 (2015).
- Bulic K, Antabak A, Lorencin M. Near-Complete Hand Loss Following an Unintentional, Intra-arterial Medicine Injection in an Infant. *Journal of pediatric intensive care*. 2018 Mar;7(01):043-5.
- Shin L, Armstrong D, Sanders LJ. Gangrene and Critical Limb Ischemia [Internet]. In: *Johns Hopkins Diabetes Guide*. ; 2020. [cited 2022 January 09].
- Salama T, El Mohtadi Aghoutane RE. Gangrène de la main après injection accidentelle intra artérielle de floxaciline: à propos d'un cas. *The Pan African Medical Journal*. 2016;25.
- Chekuri R, Pol MM, Manohar M, Yadav BP, Garg R. Intra-arterial injection of Diclofenac by informal health practitioner: A rare complication of a common drug. *Annals of Medicine and Surgery*. 2022 Nov 1;83:104736. <https://www.sciencedirect.com/science/article/pii/S2049080122014960>
- Devulapalli C, Han KD, Bello RJ, LaPorte DM, Hepper CT, Katz RD. Inadvertent Intra-Arterial Drug Injections in the Upper Extremity: Systematic Review. *J Hand Surg Am*. 2015 Nov;40(11):2262-2268.e5. doi: 10.1016/j.jhsa.2015.08.002. Epub 2015 Sep 26. PMID: 26409581.
- Malik A, Khan MG, SM AS, Ilyas M. Accidental Intra Arterial Injection And Limb Ischemia. *Journal of Ayub Medical College, Abbottabad: JAMC*. 2017 Apr 1;29(2):230-3.
- Forsyth JM, Webster PJ, Haldipur N. Iatrogenic intra-arterial injection in the upper limb: A pragmatic guide for the on-call vascular surgeon. *Indian Journal of Vascular and Endovascular Surgery*. 2020 Jul 1;7(3):260.
- Gaspar MR, Hare RR. Gangrene due to intra-arterial injection of drugs by drug addicts. *Surgery*. 1972;72(4):573e577.
- Treiman GS, Yellin AE, Weaver FA, Barlow WE, Treiman RL, Gaspae MR. An effective treatment protocol for intraarterial drug injection. *J Vasc Surg*. 1990;12(4):456e465.
- Stueber K. The treatment of intraarterial pentazocine injection injuries with intraarterial reserpine. *Ann Plast Surg*. 1987;18(1):41e46.