CASE REPORT

Alternative routes to intravenous procedural sedation to cardiovert unstable wide complex tachycardia: case report and review of literature

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ABSTRACT

Background: Cardioversion is the treatment of choice in an unstable patient with arrhythmia. It requires analgesia and sedation, which is usually given via intravenous (IV) route. However, when IV access is not obtainable, alternative routes to IV sedation and analgesia are needed.

Case Presentation: A 59-year-old male patient was presented to the emergency department (ED) complaining of chest pain and palpitation. His electrocardiogram showed new onset rapid narrow complex atrial fibrillation, which then converted to wide complex tachycardia. Initially, the patient remained hemodynamically stable, but his blood pressure dropped when cardioversion was indicated. In this case, intranasal (IN) and intraosseous (IO) routes were used, both of which are uncommon to be used for sedation in an unstable patient. The sedatives’ bioavailability and dosage via non-IV (non-IV) routes are not commonly used, and hence, literature was reviewed to find out the appropriate sedative dosage via non-IV routes specifically in IN and IO routes for moderate sedation in ED, to facilitate procedures such as cardioversion.

Conclusion: IN and IO routes are good alternatives to IV routes when timely vascular access cannot be secured and when emergency medication administration is required.

Keywords: Non-IV route in resuscitation, intraosseous access, sedative bioavailability, procedural sedation, analgesia.

Introduction

Electrical cardioversion is a painful procedure that requires sedation and analgesia [1]. Selection of anesthetic and analgesic agent and its appropriate dose in a patient, who is unstable hemodynamically due to arrhythmia, can be challenging. In addition, delivering sedation and analgesia through nonintravenous routes (non-IV) is not commonly practiced which can lead to delayed management.

In the emergency department (ED), establishing adequate vascular access for patients needing resuscitation can be challenging. Most commonly an IV access is used for resuscitation purposes and occasionally central venous access, whenever time allows for its insertion. The Intraosseous (IO) route has been widely used over the past few years when the establishment of the peripheral line is not possible [2]. However, the commonly used route for resuscitation or during cardiac arrest to administer code medications is via the IO route, which is not commonly practiced specifically in unstable patients.

Hence, knowledge about the bioavailability and half-life of common sedatives and analgesia administered via the non-IV route is not readily available to emergency physicians. The uncertainty, in this case, motivated me...
to perform a narrative literature review to outline the common sedative and analgesia bioavailability and their dosage, when administered via the non-IV route, and provide a one-stop reference to the emergency physicians to refer, when needed.

**Case Presentation**

A 59-year-old male patient, known to have diabetes mellitus type 2, hypertension, and end-stage renal disease on hemodialysis (HD) was presented to ED with chest pain and shortness of breath. The presented symptoms were started while the patient was undergoing his routine HD session at the dialysis center. Initial electrocardiogram (ECG) showed regular supraventricular tachycardia (SVT) with a premature ventricular complex (PVC), left ventricular hypertrophy (LVH), and anterolateral and inferior ST depression along with avR ST elevation (Figure 1).

The patient was given intranasal (IN) fentanyl 37.5 mcg for chest pain because IV access was difficult to obtain. While trying to secure an IV line, a repeat ECG showed wide complex tachycardia with morphology criteria strongly favoring ventricular tachycardia (VT) and BP was 175/89 mmHg (Figure 2).

The patient was treated with two doses of amiodarone 150 mg each; however, no change in rhythm was noted. The patient blood pressure then dropped to 63/38 mmHg and he became diaphoretic, hence, synchronized cardioversion was indicated. Regarding low BP, sedation doses were kept to a minimum, and were started with 5 mg IN midazolam which was 25% of the recommended dosage (0.3 mg/Kg), which did not sedate the patient. Hence, IO ketamine (30 mg) was given, however, the patient was still aware. Then, another 30 mg of ketamine IO was followed, though the patient was still aware, and BP changed neither the rhythm. After that, a dose of IN ketamine (20 mg) was given, however patient maintained full awareness.

Observing the stability of the patient with all micro sedative doses, the decision was made to use ketofol (ketamine-30 mg and propofol-30 mg) via the IO route, and the patient was sedated. Furthermore, a synchronized 100 J shock was delivered which reverted his rhythm to narrow complex irregularly irregular tachycardia (atrial fibrillation, AF), with LVH and anterolateral and inferior ST depression associated with ST elevation in aVR, with BP of 110/65 mmHg (Figure 3).

The cardiac catheterization laboratory was activated, and the patient was found to have an occlusion in the left anterior descending (LAD), hence, a stent was placed.

**Discussion**

Tachydysrhythmias are common in the setting of acute myocardial infarction (AMI) and might be of atrial origin (e.g., sinus tachycardia and AF) or ventricular (e.g., VT and ventricular fibrillation) [3]. AF is associated with coronary heart disease, specifically, if it is complicated by AMI or heart failure [4]. AMI due

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*Figure 1.* Regular SVT with a PVC, LVH, and anterolateral and inferior ST depression along with avR ST elevation.

*Figure 2.* Wide complex tachycardia with morphology criteria strongly favoring VT.
to left main coronary artery and LAD artery occlusion manifests in ECG as ST-segment elevation in lead aVR, with widespread ST-segment depression in leads V4–V6 with inverted T waves, as presented in the current study patient.

AF is a narrow complex rhythm with QRS < 120 ms; however, the QRS can be wide (>120 ms) if it is combined with a bundle branch block [5]. When QRS is wide, it should be decided whether the underlying rhythm is of ventricular origin or supraventricular origin. There are several criteria to try and make the distinction; however, they are specific yet not sensitive, and most of the time the distinction with certainty cannot be made. Hence, it is safer to presume wide complex tachycardia is of ventricular origin [6].

As per American Heart Association guidelines, amiodarone, procainamide, or sotalol can be used to treat stable VT and there were no strong studies to favor one over another [7]. The recommended amiodarone dose is 150 mg over 10 minutes through intravascular access which can be repeated if the patient did not revert [8].

At any time during medical management, if the patient becomes unstable then a synchronized cardioversion should be done with 100 J [8]. To deliver synchronized cardioversion, a patient should be properly sedated, as it is a painful procedure [9].

IN access is another alternative route, if an IV access is not obtained. It is commonly used in children for seizure control, sedation, and analgesia, and there is some literature about its use in adults [10]. The effect of medication given through the IN route depends on three main factors including the drug permeability and solubility, drug vehicle (solid; powder, semisolid; gel, emulsion, or liquid; solution), and delivery device [11]. In addition, there are other factors related to the nasal cavity itself which include the surface area, nasal temperature, and extensive vascularization of the nasal mucosa [12]. It is preferred to use an IN mucosal atomization device to deliver medication via the IN route, as it provides a greater bioavailability due to the expanded surface area reached, which allows a greater distribution of the medication and decreases the loss of medication because of runoff if used as drops [13].

IO route is another alternative to IV and is widely used when IV access is difficult to obtain specifically in unstable patients. The bone marrow of long bones contains a rich network of vessels that drains into a central venous canal and, hence, provide alternative access via IO needle for IV medication administration when peripheral or central venous access is not obtainable [14]. There are different types of IO needles, the most commonly used is inserted via a special needle insertion driver [14]. Improved tools for IO access have made this route of administration safe and easy to learn and apply in day-to-day practice, with no significant serious complications rate such as osteomyelitis and fat embolism of less than 1% [15].

The most commonly reported complications of IO are pain at insertion, difficulty injecting medications, difficulty of aspiration, infection at the injection site, which might rarely result in severe osteomyelitis, damage to the growth plate in children, and needle dislocation or malposition and extravasation of medication to subcutaneous tissue which can be detrimental, if not detected early [16].

IO cannulation is a temporary measure until an IV line is obtained, which should be done within 24 hours of IO insertion, as IO needles are not kept for longer than 24 hours to avoid some of the complications related to long-term use [16].

The bioavailability of the drug is defined as its ability to be absorbed and utilized by the body. Hence, the literature to assess whether sedative agents commonly used in the ED would perform similarly, if given via IO, IN, intra muscular, or subcutaneous route. In general, the IO drug infusion specifically during resuscitation has been reported to have similar pharmacokinetics to IV infusion [17].

In the ED, there are many procedural sedation medication options that can be used to produce sedative, anxiolytic, and/or analgesic effects. Ketamine produces a state of dissociation, or detachment from immediate surroundings, characterized by profound analgesia,
sedation, and amnesia. Unlike other agents used for procedural sedation, ketamine possesses both analgesic and anxiolytic properties [18]. IN ketamine alone is not efficacious for sedation due to the high dose required for effect (1-9 mg/kg), however most studies showed that 3 mg/kg is the efficacious dose except a pilot study that tried three different dosages of IN ketamine for laceration repair and concluded that the minimal sedative effect was reached at a dose of 9 mg/kg [19]. IN ketamine has the advantages of early and rapid sedation and it has no reported serious adverse events [10]. The most common adverse effect of IN ketamine was vomiting, reported in 10 studies at doses of at least 1 mg/kg. Only one patient had transient desaturation at a dose of 3 mg/kg [10,19]. To date, there have been no studies about IN ketamine sedation dosage in adults. Likely, it would be similar to a pediatric dosage of 3-9 mg/kg which, in an adult would be a big volume to administer IN, as the recommended volume of administration for IN medications is 0.3 ml per dose per nostril. When the volume to be administered is more than 0.3 ml, then the total volume needs to be administered in small doses alternating between both nostrils [20]. The IV and IO bioavailability of ketamine is equivalent too, however, when given IM its bioavailability is 93%, with peak plasma concentrations achieved within 5-30 minutes of administration. And when given via IN route the bioavailability drops by 45%-50%. However, with rapid absorption and less invasiveness, it is considered as an appropriate alternative to IV route [21]. The subcutaneous route is only studied for analgesia and depression and seems to be effective, but not for sedation [22].

Midazolam is a benzodiazepine with sedative, amnestic and anxiolytic effect. It is twice as potent as diazepam and has been used in the ED for procedural sedation due to its safe profile. It can be given IV/IO at (0.02-0.1 mg/kg) and can be repeated every 3-5 minutes. The most significant side effects are respiratory depression and hypotension when given via the IV/IO route and specifically when combined with opioids [23]. The IN route for midazolam has been very popular in the pediatric population for seizures as well as minimal sedation to facilitate procedures. The IN dose is 0.1 mg/kg (10 mg maximum even for adults) and can be divided in both nostrils; however, it is noted that it causes a burning sensation and can be minimized by pretreatment with 4% IN lidocaine [24]. There is increasing literature about its use for adult procedural sedation. The bioavailability of midazolam when given IO is 100% compared to IV, 85% if given IN or IM, and 96%, if given subcutaneously [25].

Propofol is 2, 6-diisopropylphenol sedative agent that works via the GABAA receptors in the brain and is commonly used in ED for rapid sequence induction (RSI) as well as procedural sedation due to its safety and efficacy. The IV/IO dose for procedural sedation is IV/IO 0.5-1.5 mg/kg. Propofol’s main side effects are hypotension, pain on injection, respiratory depression, and apnea [26]. The current propofol IV formulation cannot be given intranasally but there is ongoing research about a new formulation that can be used through IN or buccal routes for other indications such as migraine and nausea [27].

Fentanyl is a synthetic opioid that is 100 times more potent than morphine [28]. It is a selective Mu opioid receptor and has a lipophilic structure. Hence, it is absorbed rapidly when given intranasally, and like all other opioids, it is metabolized in the liver [29]. For adults, it is commonly used via the IV route at a dose of 0.5-1.5 mcg/kg/hour; however, the IN route is becoming popular for its easy use and effectiveness. Side effects of fentanyl when given IV are like all other opioids ranging from mild dizziness to respiratory depression leading to cardiac arrest, if untreated timely. Side effects are not common with the IN route especially if the lowest dose for the desired effect is used and varies from mild dizziness to local effects such as nasal discomfort and irritation [30]. The bioavailability of the fentanyl transmucosal (buccal) route is 52% with a peak effect in 20 minutes with a time to onset analgesia of 5 minutes, IN route is 90% with a peak effect of 12 minutes with a time to onset of analgesia of 2 minutes, for IM route the onset of analgesia is about 8 minutes [31].

Etomidate is an ultra-short acting sedative carboxylated imidazole that stimulates γ-aminobutyric acid receptors. Its effect on the CNS is similar to barbiturates though characterized by its hemodynamic stability, hence, becoming the preferred sedative agent for patients with cardiovascular disease. It is commonly used as RSI in the ED at a dose of 0.2 and 0.6 mg/kg with rapid onset of action (30-60 seconds) [32]. For procedural sedation, the dose is 0.2 mg/kg and can be used in pediatric patients from 6 years old and adults [33]. Etomidate is both hydrophilic and lipophilic, though it is hydrophilic in acidic media (PH < 7.35) and lipophilic in normal PH media (PH 7.35-7.45) [32]. Etomidate can be used via the IO route with the same dose as the IV; however, there is no literature about its use via the IN route.

Dexmedetomidine is a central alpha-2 agonist, that causes mild sedation effect without respiratory depression, hence, commonly used in intensive cases like

<table>
<thead>
<tr>
<th>Medication</th>
<th>IV dose</th>
<th>IN dose</th>
<th>IO dose</th>
<th>IM dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine</td>
<td>1-2 mg/kg</td>
<td>3-5 mg/kg</td>
<td>1-2 mg/kg</td>
<td>5 mg/kg</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.05-0.15 mg/kg</td>
<td>0.3 mg/kg</td>
<td>0.05-0.15 mg/kg</td>
<td>0.025-0.05 mg/kg</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1-2 mcg/kg</td>
<td>75 mcg</td>
<td>1-2 mcg/kg</td>
<td>-</td>
</tr>
<tr>
<td>Propofol</td>
<td>1-2 mcg/kg</td>
<td>-</td>
<td>1-2 mcg/kg</td>
<td>-</td>
</tr>
<tr>
<td>Etomidate</td>
<td>0.2-0.6 mg/kg</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>0.1-0.7 mcg/kg/hour</td>
<td>1-2 mcg/kg</td>
<td>-</td>
<td>2.5 mcg/kg</td>
</tr>
</tbody>
</table>
patients with acute respiratory failure who are managed with noninvasive ventilation [34]. It is commonly administered intravenously at a dose of 0.1-0.7 mcg/kg/hour; however, it can be given sublingual and IN at a dose of 1-2 mcg/kg with high bioavailability of about 84% making it an alternative for sedation, when vascular access is not available [35]. The main side effect is bradycardia and hypotension; therefore, dose reduction in renal and hepatic impairment patients as well as in the elderly is recommended [34,35]. Its use in ED settings is increasing in combination with analgesia for procedural sedation of painful procedures. However, more studies need to be conducted regarding IN, buccal, and IM use [35,36] (Table 1).

Conclusion
Securing immediate intravascular access in case of a cardiac emergency can be challenging. Learning about sedative and analgesic medication that can be administered via alternative routes such as IN or IO can facilitate emergency intervention until vascular access is obtained. The bioavailability of various sedative medications needs to be well understood and their dosage needs to be appropriate to achieve the desired effect. This paper provided a summary of common sedatives used in ED, their dosage, and bioavailability utilizing non-IV route.

List of Abbreviation
AF Atrial fibrillation
ECG Electrocardiogram
ED Emergency department
HD Hemodialysis
IN Intranasal
IO Intraosseous
IV Intravenous
LVH Left ventricular hypertrophy
PVC Premature ventricular complex
SVT Supraventricular tachycardia
VT Ventricular tachycardia

Conflict of interest
The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication
Informed consent was obtained from the patient.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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