



# The Use of Insulin-Euglycemic Therapy by Medical Toxicologists

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## Introduction

In 1999 it was first reported that insulin-euglycemia therapy might provide benefit for calcium channel blocker overdose. Since 2010, the Toxicology Investigators Consortium (ToxIC) Registry has collected detailed information on all clinical consults seen by a nationwide multi-center network of medical toxicologists. This Registry can readily provide information about medical toxicology practices.

## Research Question

In cases of presumed single drug poisoning what are the most common indications for medical toxicologists to use insulin-euglycemia therapy?

## Methods

The ToxIC registry was queried for the period January 1, 2010 and December 31, 2014 regarding the use of insulin-euglycemia therapy. Single agent exposure cases treated with insulin-euglycemia therapy were identified and further analyzed by agent name and class, and by outcome.

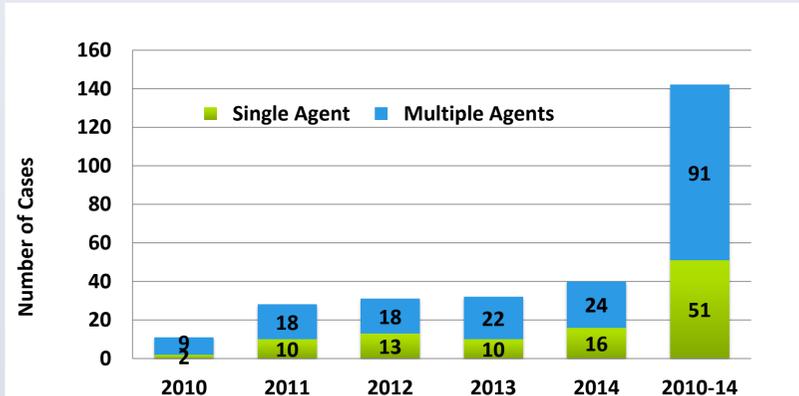


Figure 1. Number of Cases Reporting Use of Insulin-Euglycemic Therapy

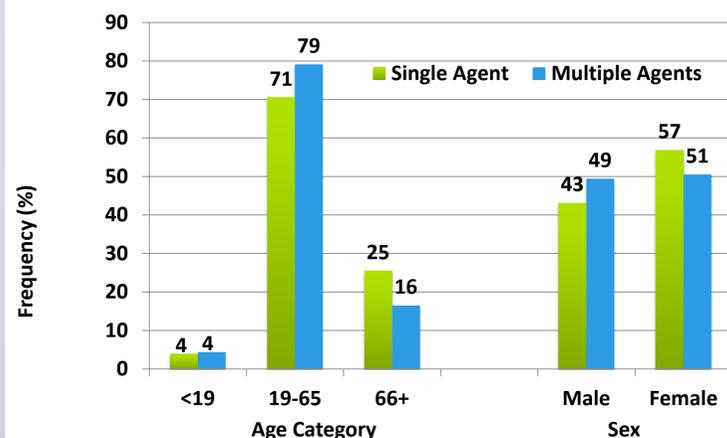


Figure 3. Insulin-Euglycemic Therapy Cases: Age & Sex Distribution

## Results

Of 35,903 cases in the Registry between January 2010 and December 2014 entered by 50 sites, 144 patients (0.4%) received insulin-euglycemia therapy - 51 single agent cases and 91 multi-agent cases (Figure 1). Two cases with insufficient/conflicting agent data were excluded from this descriptive analysis. The 51 single agent cases were reported by 32 ToxIC participating sites. Of these cases 70% involved calcium channel blockers (n=25) or beta blockers (n=11) (Figure 2). Insulin-euglycemia therapy was used most commonly for diltiazem (n=10), verapamil (n=7) and amlodipine (n=7) poisoning - all calcium channel blocker (Table 1). Among poisonings associated with beta blockers, metoprolol and propranolol (n=4 cases each). A variety of other pharmaceuticals were associated with the remainder of cases.

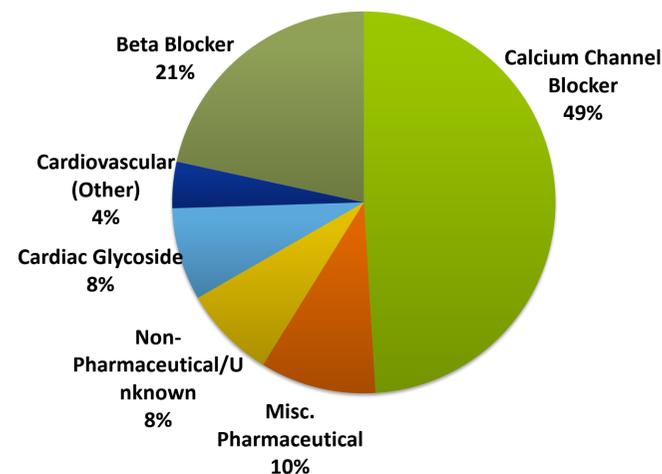


Figure 2. Single Agent Poisoning Cases with Insulin-Euglycemic Therapy: Frequency of Primary Agent by Class

Figure 3 provides a summary frequency of the basic demographics for the single and multi-agent poisoning cases. A slightly larger proportion of the single agent poisoning cases occurred among females and older (>65 years) relative to the multi-agent reports.

Table 1. Single Agent Poisoning Cases with Insulin-Euglycemic Therapy: Frequency of Reported Responsible Agent

Class / Agent	#	%	Class / Agent	#	%
Calcium Channel Blocker	25	49.0	Cardiovascular (Other)	2	3.9
Amlodipine	7		Propafenone	1	
Diltiazem	10		Antihypertensive (NOS)	1	
Nifedipine	1		Misc. Pharmaceutical	5	9.8
Verapamil	7		Acetaminophen	1	
Beta Blocker	11	21.6	Opioid (NOS)	1	
Atenolol	1		Quetiapine	1	
Carvedilol	1		Trazodone	1	
Labetalol	1		Amitriptyline	1	
Metoprolol	4		Non-Pharmaceutical/Unknown	4	7.8
Propranolol	4		Caustic (NOS)	1	
Cardiac Glycoside (Digoxin)	4	7.8	Unknown agent	3	

Table 2. Number & Frequency of Signs & Symptoms among Single Agent Poisoning Insulin-Euglycemic Therapy Cases

Major Vital Sign Abnormalities	#	% Total Cases
Hypotension (SBP<80)	31	60.8
Bradycardia (P<50)	32	62.7
<b>Pulmonary</b>		
Aspiration Pneumonitis	6	11.8
Acute Lung Injury/ARDS	10	19.6
Respiratory Depression	16	31.4
<b>Nervous System</b>		
Coma/CNS Depression	26	51.0
<b>Metabolic</b>		
Metabolic Acidosis (pH<7.2)	16	31.4
Elevated Anion Gap (AG>20)	4	7.8
<b>Renal/Muscular</b>		
Acute Kidney Injury (Creatinine>2.0)	12	23.5

\*Each individual case may have more than 1 sign/symptom within a given category.

The most common signs and symptoms reported by general category include:

- Major Vital Signs (n=44, 86.3% cases)
- Nervous System (n=31, 60.8%)
- Pulmonary (n=23, 45.1%)
- Metabolic (n=18, 35.3%).

Table 2 lists the major individual signs and symptoms reported.

In the case of toxicologic treatment, 80.4% (n=41) of these insulin-euglycemic therapy cases received at least one other antidote, the most common being calcium (n=25, 49%), glucagon (n=20, 39%), and lipid resuscitation (n=14, 28%). Common pharmacologic support included use of vasopressors (n=38, 75%), while common non-pharmacologic support included IV fluid resuscitation (n=32, 63%), intubation (n=25, 49%), CPR and pacemaker (both at n=9, 18%).

A total of six recorded deaths, or 11.8% of the cases, occurred among this group due to amlodipine (n=2), diltiazem, metoprolol, propranolol, and an unknown opioid.

## Discussion

Data on the use of unusual antidotes such as insulin and glucose in the treatment of severe cardiovascular agent poisonings is often limited to isolated case reports and small case series. Such data sources do not provide information regarding the frequency of use of insulin-euglycemia therapy. Data from the ToxIC Registry can readily be used to describe antidotal use by medical toxicologists. The development of a more detailed sub-registry on insulin-euglycemia therapy could offer the opportunity to increase our understanding of this novel therapy and its efficacy and pitfalls.

## Conclusions

Insulin-euglycemia therapy is most commonly used for calcium channel blocker and beta blocker poisoning, and is used in approximately 1 in 250 cases cared for by medical toxicologists.

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