

Treatment of calcium channel blocker poisoning: a systematic review

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Introduction:

- Cardiovascular drugs are the substance category with the 3rd increased rate of exposure (Bronstein et al., 2010).
- No systematic review has been published for the treatment CCB poisoning.
- CCB poisoning carries a high mortality (6%) and, morbidity (50%) (St-Onge et al., 2012).

Objective:

Evaluate the efficacy of interventions considered for the treatment of CCB poisoning in adults.

Research question:

- P:** In adults poisoned with a CCB
I: which intervention(s)
C: when compared to no-intervention or to other intervention(s)
O: improve primary outcomes (mortality, hemodynamics, functional outcomes) or secondary outcomes (hospital LOS, ICU, LOS, duration of vasopressors, CCB serum level)
S: as shown by any type of study?

Eligibility criteria:

- All types of studies including case reports published/unpublished in any language.
- In-hospital adults or animals treated for a CCB poisoning.
- Defined intervention(s) meant to improve the targeted outcomes.

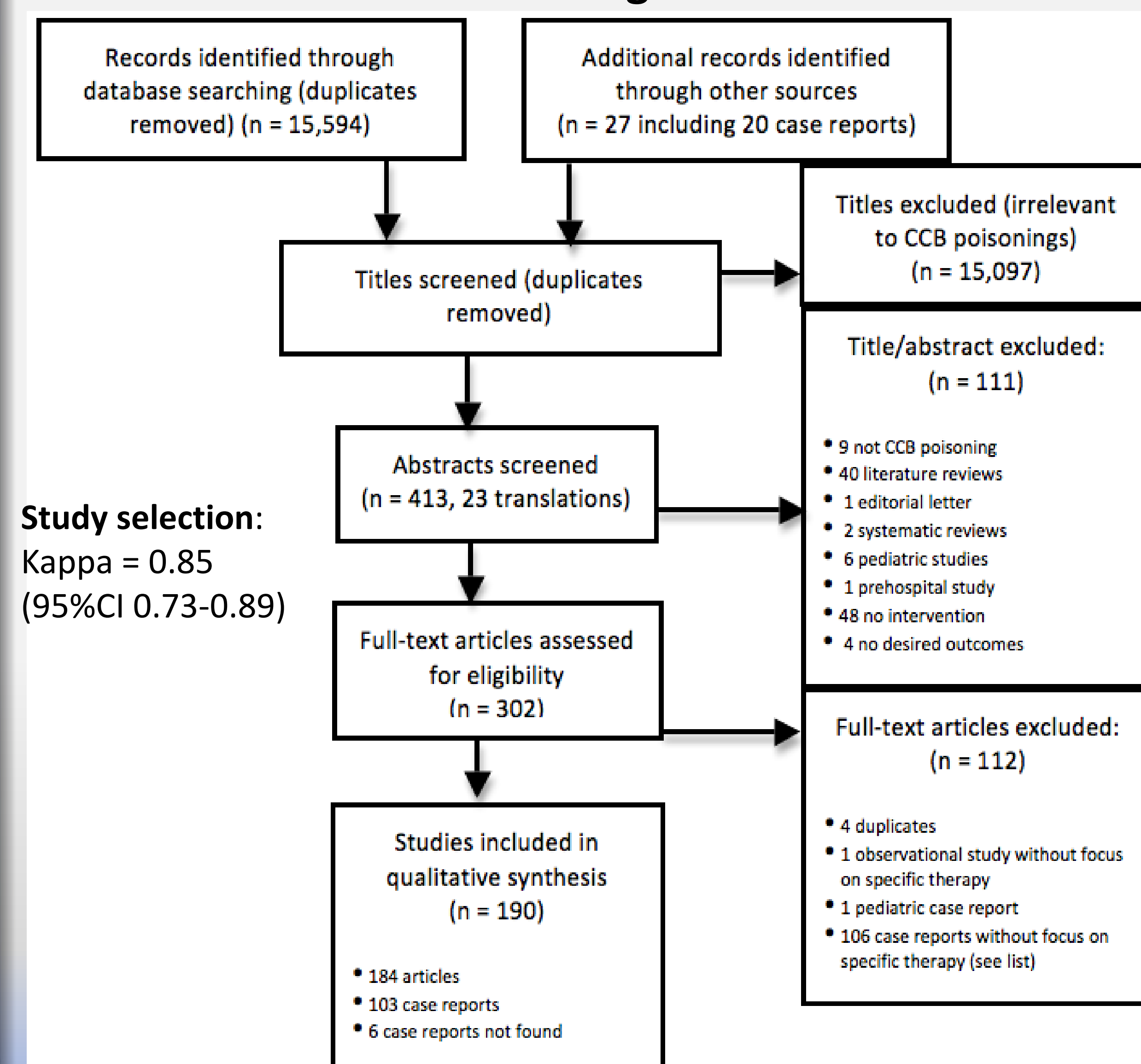
Information sources (up to August 2012):

- Cochrane, Medline/OVID, Pubmed, EMBASE, Toxline, International pharmaceutical abstracts, conference abstracts, trials registries, Google scholar searched, and selected authors contacted.

Study selection, data abstraction and quality analysis:

- Qualified independent reviewers using pilot tested forms.
- Cochrane risk of bias (CT), STROBE checklist (OS), Thomas' tool (OS), Institute of Health Economics' tool (CS), Arrive and, NRCNA checklist (AS).

Flow diagram



Studies characteristics and risk of bias across studies

Intervention s (n = number of articles including case reports (CR))	Observational studies			Case series n Institute of Health Economics (IHE) tool (/20)	Animal studies			
	n	STROBE checklist (/22)	THOMAS' tool		n	ARRIVE checklist (/20)	NRCNA checklist (/16)	
High-dose insulin (n = 33, 22 CR)	3	6 (4-9)	Weak	4	6 (4-13)	4	15 (11-18)	8 (6-9)
Extracorporeal life support (n = 11, 7 CR)	1	17	Weak to moderate	3	11 (9-15)	0		
Calcium (n = 38, 20 CR)	0			1	6 (2-10)	8	12 (5-16)	5 (3-7)
Vasopressors (n = 27, 10 CR)	0			8	6 (2-10)	9	14 (11-18)	6 (4-9)
Decontamination (n = 8, 2 CR)	0			6	6 (3-8)	0		
Pacemaker (n = 7, 2 CR)	0			5	7 (4-10)	0		
Glucagon (n = 16, 10 CR)	0			3	7 (3-9)	3	13 (11-15)	6 (6-6)
Atropine (n = 5, 0 CR)	0			3	7 (3-10)	2	11 (11-11)	6 (5-6)
4-aminopyridine (n = 10, 0 CR)	0			2	9 (8-9)	8	14 (10-17)	6 (5-8)
Lipid emulsion (n = 20, 16 CR)	0			1	8	3	14 (13-15)	7 (6-7)
Levosimendan (n = 8, 3 CR)	0			1	8	4	16 (14-16)	6 (5-8)
Plasma exchange (n = 3, 2 CR)	0			1	9	0		
BayK8644 and CGP 28932 (n = 3, 0 CR)	0			0		3	15 (14-17)	5 (5-6)
Digoxin (n = 3, 0 CR)	0			0		3	13 (12-14)	6 (5-7)
Phosphodiesterase inhibitors (n = 6, 4 CR)	0			0		2	16 (15-17)	5 (4-5)
Cyclodextrin (n = 2, 0 CR)	0			0		2	16 (15-16)	7 (6-7)
Liposomes (n = 2, 0 CR)	0			0		2	15 (14-16)	6 (6-7)
Albumin dialysis (n = 3, 2 CR)	0			0	8	1		
L-Carnitine (n = 1, 0 CR)	0			0		1	17	7
Bicarbonates (n = 1, 0 CR)	0			0		1	15	9
Fructose-1,6-diphosphate (n = 1, 0 CR)	0			0		1	14	7
PK 1195 (n = 1, 0 CR)	0			0		1	13	5
Triiodothyronine (n = 1, 0 CR)	0			0		1	15	6
CASE REPORTS ONLY								

• Methylene blue (n = 1)
 • Charcoal hemoperfusion (n = 4)
 • Dialysis (n = 3)
 • Intra-aortic balloon pump (n = 2)

Reported improvement in survival in the literature:

- OS: high-dose insulin (HDI) and extracorporeal life-support (ECLS)
- AS and CS: calcium, epinephrine, dopamine, norepinephrine
- AS: lipid emulsion for IV CCB intoxication

Reported improvement in hemodynamics in the literature:

- OS: HDI and ECLS
- AS and CS: epinephrine, dopamine, norepinephrine, 4-aminopyridine, levosimendan, plasma exchange
- AS: lipid emulsion, liposomes
- Inconsistent results: atropine, calcium, glucagon, pacemaker

Interrater agreement

- OS – STROBE checklist: Kappa of 0.90 (95%CI 0.82-0.99)
- CS – IHE tool: Kappa of 0.80 (95%CI 0.76-0.84)
- AS – ARRIVE checklist: Kappa of 0.90 (95%CI 0.88-0.92)
- AS – NRCNA checklist: Kappa of 0.98 (95%CI 0.96-0.99)

Summary and quality of evidence (QOE):

- This systematic review demonstrates a possible benefit of HDI on hemodynamics and on mortality while increasing the risks of hypoglycemia and hypokalemia. (low QOE)
- It underlines a possible role for the use of ECLS to improve survival in patients in cardiac arrest or severe shock. Complications included bleeding, thrombosis or limb ischemia (when a femoral cannulae is used). (low QOE)
- Calcium, dopamine, norepinephrine, epinephrine may improve hemodynamics. (very low QOE)
- Lipid emulsion may improve hemodynamics in models of IV verapamil overdose. Atropine, glucagon, the use of a pacemaker and plasma exchange demonstrated inconsistent results.

Conclusion:

- This study is the first systematic review to summarize the evidence concerning the effects of treatments for CCB poisoning.
- Head-to-head comparisons in human clinical trials should be done concerning the use of vasopressors, HDI and ECLS.

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