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Hypertension associated with clonidine, guanfacine and tizanidine overdose

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Objective: Over dose of clonidine and other imidazoline derivatives with central alpha-2 and imidizalone receptor agonist activity have a well-known potential to result in bradycardia, hypotension and CNS depression in overdose. While early, transient periods of hypertension have been reported after clonidine and guanfacine overdose, significant, prolonged hypertension has rarely been described. We investigated the incidence of hypertension in single substance ingestions of clonidine, tizanidine and guanfacine.

Method: case selection based on ingestion of clonidine, guanfacine or tizanidine as a single substance reported to one poison center from 2004 to 2017. Demographics, clinical effects, therapies and outcome were recorded. All cases with either hypertension or hypotension had the individual case notes reviewed for severity and duration of effects, response to therapy and accuracy of coding.

Results: From 2004 to 2017 there were: 1) 1755 clonidine ingestions of which 852 (54%) were male and 1438 were <19yrs (82%); 2) 571 tizanidine ingestions of which 371 (65%) were female and 177 were <19yrs (31%) and 3) 400 ingestions of guanfacine of which 274 (68%) were male and 382 were <19yrs (95.5%). Hypertension occurred in 2.5 to 4% of patients (see table) and 1.1 to 2.5% of children <19. Hypertension tended to occur in ingestions of larger doses: (>3 mg clonidine, >60 mg tizanidine and >40 mg guanfacine) and was not transient, lasting 12 to >24 hours. Bradycardia occurred in 72-80 % of patients with hypertension.

Discussion: Due in part to the fact that clonidine, tizanidine and guanfacine metabolism is poorly understood and in part due to the rarity of these events, the underlying pathophysiology for the prolonged and sometimes severe hypertension in these patients is unknown.

Conclusion: Hypertension following overdose, while infrequent, is not transient, can be severe and can be associated with other expected clinical effects such a CNS depression and bradycardia.

	Clonidine	Tizanidine	Guanfacine
Total number of patients	1755	571	400

With hypertension	72 (4.1%)	25 (4.3%)	10 (2.5%)
With hypotension	251 (14.9%)	58 (10.2%)	31 (7.6%)
With bradycardia	340 (19.4%)	87 (15.2%)	59 (14.8%)

