

Drugs & Aging

Trazodone and risk of orthostatic hypotension, syncope and falls in geriatric outpatients with hypertension

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Supplementary Table 1. Medical therapy in the overall sample and stratified by trazodone use.

	Overall sample (n=123)	Trazodone users (n=12)	Others (n=111)	p
ACEi, n (%)	61 (49.6)	6 (50)	55 (49.5)	0.976
ARBs, n (%)	49 (39.8)	3 (25)	46 (41.4)	0.269
CCBs, n (%)	61 (49.6)	8 (66.7)	53 (47.7)	0.213
Beta-blockers, n (%)	48 (39)	1 (8.3)	47 (42.3)	0.022
Diuretics, n (%)	53 (43.1)	3 (25)	50 (45)	0.183
Alfa-blockers, n (%)	21 (17.1)	2 (16.7)	19 (17.1)	0.969
Benzodiazepines, n (%)	15 (12.2)	0	15 (13.5)	0.174
SSRI/SNRI antidepressants, n (%)	37 (30.1)	5 (41.7)	32 (28.8)	0.357
L-Dopa, n (%)	5 (4.1)	0	5 (4.5)	0.453
Antipsychotics, n (%)	9 (7.3)	4 (33.3)	5 (4.5)	< 0.001
AChEIs, n (%)	12 (9.8)	2 (16.7)	10 (9)	0.396
Memantine, n (%)	15 (12.2)	3 (25)	12 (10.8)	0.154

ACEi, Angiotensin-Converting Enzyme (ACE) Inhibitors; ARBs, Angiotensin II Receptor Blockers; CCBs, Calcium Channel Blockers; SSRIs, Selective Serotonin Reuptake Inhibitors; SNRIs, Serotonin-Norepinephrine Reuptake Inhibitors; AChEIs, Acetylcholinesterase Inhibitors

Supplementary Table 2. Univariate and multivariate Cox regression analysis for the composite outcome of syncope and falls: medical therapy, blood pressure values and orthostatic response

	Unadjusted HR (95% CI)		Unadjusted HR (95% CI)
Charlson Comorbidity Index*	1.178 (0.930-1.493)	Memantine	1.808 (0.680-4.806)
Depression	1.300 (0.585-2.885)	AChEIs	3.115 (1.048-9.261)
Parkinson's disease	0.589 (0.080-4.358)		
Heart failure	1.968 (0.459-8.448)	Office systolic BP	0.989 (0.971-1.008)
Stroke/TIA	0.956 (0.387-2.363)	Office diastolic BP	1.012 (0.984-1.040)
Diabetes	0.719 (0.273-1.892)	Orthostatic hypotension	1.216 (0.578-2.559)
Parkinson's disease	0.589 (0.080-4.358)	Systolic BP _{T0}	0.993 (0.979-1.008)
Frailty	1.246 (0.592-2.624)	Δ systolic _{T0}	1.004 (0.981-1.028)
BADL Disability	2.143 (0.928-4.947)	Systolic BP _{T1}	0.995 (0.981-1.009)
Nr. daily medications	1.052 (0.916-1.207)	Δ systolic _{T1}	0.998 (0.978-1.018)
Nr. daily antihypertensives	0.927 (0.657-1.308)	Systolic BP _{T3}	0.994 (0.978-1.010)
ACEi	1.352 (0.642-2.849)	Δ systolic _{T3}	0.997 (0.971-1.023)
ARBs	0.826 (0.385-1.769)	24h systolic BP	0.989 (0.966-1.012)
CCBs	0.718 (0.338-1.524)	24h diastolic BP	1.011 (0.972-1.052)
Beta-blockers	1.198 (0.569-2.521)	Daytime systolic BP	0.990 (0.966-1.014)
Diuretics	0.835 (0.384-1.814)	Daytime diastolic BP	1.010 (0.972-1.050)
Alfa-blockers	0.199 (0.027-1.465)	Home systolic BP	0.967 (0.921-1.015)
Antidepressants	1.317 (0.607-2.859)	Home diastolic BP	0.979 (0.922-1.039)

HR, hazard ratio; CI, confidence interval; ACEi, Angiotensin-Converting Enzyme (ACE) Inhibitors; ARBs, Angiotensin II Receptor Blockers; CCBs, Calcium Channel Blockers; AChEIs, Acetylcholinesterase Inhibitors; BP, blood pressure.

Supplementary Table 3. Office, orthostatic, ambulatory and home blood pressure profile in the overall sample and by benzodiazepine use.

Blood pressure mean (SD)	Benzodiazepine users (n=15)	Others (n=108)	p
Office systolic BP	155.6 (19.7)	152.0 (21.4)	0.537
Office diastolic BP	81.8 (14.6)	78.9 (13.4)	0.444
24h systolic BP (ABPM)	141.7 (16.5)	147.9 (15.3)	0.147
24h diastolic BP (ABPM)	74.3 (7.2)	77.0 (9.0)	0.271
Daytime systolic BP (ABPM)	143.6 (17.2)	150.4 (14.9)	0.104
Daytime diastolic BP (ABPM)	76.5 (7.5)	79.3 (9.1)	0.258
Night-time systolic BP (ABPM)	133.6 (18.5)	138.7 (21.2)	0.382
Night-time diastolic BP (ABPM)	65.9 (8.7)	69.1 (10.4)	0.260
Hypotensive episodes (ABPM), n (%)	4 (26.7)	16 (14.8)	0.244
Home systolic BP	134.1 (9.7)	137.7 (12.2)	0.294
Home diastolic BP	72.7 (6.0)	73.9 (8.8)	0.630
Orthostatic blood pressure response			
Orthostatic hypotension, n (%)	5 (33.3)	48 (45.3)	0.383
Supine systolic BP	144.2 (18.6)	150.1 (21.4)	0.314
Systolic BP _{T0} (n=114)	127.9 (20.6)	135.1 (26.8)	0.336
Δ systolic _{T0} (n=114)	17.4 (12.5)	15.0 (15.3)	0.577
% Δ systolic _{T0} (n=114)	11.9 (8.5)	10.2 (10.4)	0.559
Systolic BP _{T1} (n=112)	132.2 (22.5)	140.1 (24.5)	0.259
Δ systolic _{T1} (n=112)	13.0 (16.7)	10.4 (18.9)	0.629
% Δ systolic _{T1} (n=112)	8.7 (11.2)	6.7 (11.7)	0.553
Systolic BP _{T3} (n=110)	135.9 (21.8)	143.2 (21.7)	0.242
Δ systolic _{T3} (n=110)	9.4 (14.5)	7.4 (14.5)	0.644
% Δ systolic _{T3} (n=110)	6.2 (10.3)	4.6 (9.3)	0.559
Supine diastolic BP	75.7 (9.8)	77.1 (12.2)	0.657
Diastolic BP _{T0} (n=114)	73.8 (7.7)	74.8 (13.6)	0.778
Δ diastolic _{T0} (n=114)	2.3 (8.9)	2.3 (8.6)	0.982
% Δ diastolic _{T0} (n=114)	2.1 (11.0)	2.8 (10.5)	0.819
Diastolic BP _{T1} (n=112)	75.0 (9.8)	76.6 (12.0)	0.626
Δ diastolic _{T1} (n=112)	1.1 (8.9)	0.8 (9.3)	0.920
% Δ diastolic _{T1} (n=112)	0.8 (11.2)	0.4 (10.7)	0.908
Diastolic BP _{T3} (n=110)	74.6 (9.4)	77.6 (11.2)	0.341
Δ diastolic _{T3} (n=110)	1.5 (8.1)	0.07 (7.7)	0.521
% Δ diastolic _{T3} (n=110)	1.4 (10.1)	-0.5 (8.6)	0.447

BP, blood pressure, ABPM, ambulatory blood pressure monitoring

Supplementary Table 4. Office, orthostatic, ambulatory and home blood pressure profile in the overall sample and by antipsychotic use.

Blood pressure mean (SD)	Antipsychotic users (n=9)	Others (n=114)	p
Office systolic BP	153.0 (32.4)	152.4 (20.2)	0.933
Office diastolic BP	76.9 (11.9)	79.5 (13.7)	0.585
24h systolic BP (ABPM)	147.3 (7.8)	147.1 (16.0)	0.968
24h diastolic BP (ABPM)	80.0 (7.9)	76.4 (8.8)	0.241
Daytime systolic BP (ABPM)	150.1 (6.7)	149.6 (15.8)	0.919
Daytime diastolic BP (ABPM)	81.9 (8.9)	78.8 (8.9)	0.315
Night-time systolic BP (ABPM)	138.6 (18.0)	138.0 (21.2)	0.937
Night-time diastolic BP (ABPM)	73.7 (10.5)	68.3 (10.1)	0.130
Hypotensive episodes (ABPM), n (%)	1 (11.1)	19 (16.7)	0.664
Home systolic BP	135.0 (8.7)	137.2 (12.01)	0.751
Home diastolic BP	83.3 (5.8)	73.4 (8.3)	0.043
Orthostatic blood pressure response			
Orthostatic hypotension, n (%)	7 (77.8)	46 (41.1)	0.033
Supine systolic BP	142.2 (21.2)	149.9 (21.2)	0.294
Systolic BP _{T0} (n=114)	121.1 (21.9)	135.3 (26.3)	0.119
Δ systolic _{T0} (n=114)	21.1 (15.3)	14.8 (14.8)	0.222
% Δ systolic _{T0} (n=114)	14.7 (11.0)	10.0 (10.1)	0.188
Systolic BP _{T1} (n=112)	125.4 (15.7)	140.2 (24.6)	0.098
Δ systolic _{T1} (n=112)	14.4 (20.9)	10.5 (18.5)	0.569
% Δ systolic _{T1} (n=112)	9.1 (13.3)	6.8 (11.5)	0.591
Systolic BP _{T3} (n=110)	120.3 (9.9)	143.7 (21.6)	0.005
Δ systolic _{T3} (n=110)	17.0 (23.1)	7.0 (13.6)	0.078
% Δ systolic _{T3} (n=110)	10.7 (14.5)	4.5 (8.9)	0.089
Supine diastolic BP	78.2 (16.9)	76.9 (11.6)	0.743
Diastolic BP _{T0} (n=114)	74.2 (11.7)	74.8 (13.2)	0.907
Δ diastolic _{T0} (n=114)	4.0 (14.2)	2.2 (8.0)	0.546
% Δ diastolic _{T0} (n=114)	3.1 (16.3)	2.7 (9.9)	0.915
Diastolic BP _{T1} (n=112)	74.4 (10.2)	76.6 (11.9)	0.608
Δ diastolic _{T1} (n=112)	3.6 (16.9)	0.6 (8.4)	0.375
% Δ diastolic _{T1} (n=112)	1.7 (19.0)	0.4 (9.9)	0.749
Diastolic BP _{T3} (n=110)	74.0 (11.8)	77.4 (11.0)	0.429
Δ diastolic _{T3} (n=110)	5.9 (13.4)	-0.1 (7.1)	0.047
% Δ diastolic _{T3} (n=110)	5.4 (14.2)	-0.6 (8.3)	0.081

BP, blood pressure, ABPM, ambulatory blood pressure monitoring

Supplementary Table 5. Association of benzodiazepines and antipsychotics with the composite outcome of syncope and falls.

	Incidence, n (%)			Unadjusted HR (95% CI)	HR (95% CI) Model D	HR (95% CI) Model E
	Treated	Untreated	p			
Trazodone	7 (58.3)	22 (21.2)	0.005	3.803 (1.600-9.037)	2.901 (1.146-7.341)	3.437 (1.274-9.272)
Benzodiazepines	2 (15.4)	27 (26.2)	0.396	0.589 (0.140-2.476)	0.564 (0.123-2.589)	-
Antipsychotics	3 (33.3)	26 (24.3)	0.548	1.375 (0.416-4.551)	-	0.786 (0.203-3.046)

Variables included in model D: age, sex, fall history, trazodone use, benzodiazepine use. Variables included in model E: age, sex, fall history, trazodone use, antipsychotic use.