

Risk of suicide among users of calcium channel blockers: population based, nested case-control study

Christiane Gasse, Laura E Derby, Catherine Vasilakis, Hershel Jick

Lindberg et al reported the results of two studies, which they interpreted as showing that calcium channel blockers may increase the risk of suicide.¹ They found a significant correlation between rates of suicide and use of calcium channel blockers ($r=0.29$, $P<0.001$) in a cross sectional ecological study and an increased risk of suicide (relative risk 5.4, 95% confidence interval 1.4 to 20.5) in users of calcium channel blockers compared with non-users. But they did not control for important independent risk factors such as depression and did not validate diagnoses of suicide.

We aimed at investigating further the possible association between use of calcium channel blockers and risk of suicide among people with hypertension, given the limitations of Lindberg et al's study.²

Subjects, methods, and results

The study was based on information derived from the General Practice Research Database.^{3,4} The database has been shown to record suicides reliably.⁴ We identified 153 458 patients with hypertension who had received a prescription for an antihypertensive drug between January 1991 and August 1998. This base population formed the cohort for a nested case-control study.

We identified 46 subjects among the base population who committed suicide (Oxford Medical Information System code 3009D) between January 1991 and August 1998. The date of death was considered to be the index date. Cases had to have been currently exposed to one of the exposures of interest: a calcium channel blocker (with or without a diuretic or a β blocker) or any other antihypertensive drug alone or in combination (β blockers, angiotensin converting enzyme inhibitors, diuretics, other (methyldopa, vasodilators, α blockers)). Current exposure was defined as a prescription for antihypertensive drug(s) within the six months before the index date. Seven patients had not received such a prescription within this period and were therefore excluded. One patient was excluded because of illicit drug use.

We then identified 140 controls who were currently being treated with an antihypertensive drug; they were matched to the 38 cases for age, sex, practice, and index date. Altogether, 161 (90%) cases and controls received a prescription for an antihypertensive drug within the three months before the index date, and 157 had received antihypertensive treatment of any kind for at least one year. The age and sex distributions were similar in cases and controls because of matching. Thirty two (84%) cases were over 60 and 32 (84%) were male.

We conducted conditional logistic regression analysis, adjusting for body mass index (weight (kg)/(height (m)²)), smoking, and history of mental illness. The adjusted relative risk estimate for suicide was 0.98 (0.30 to 3.18) for users of calcium channel

blockers compared with users of other antihypertensive drugs (table). We found an independent increased risk of 15.7 (5.4 to 45.8) for suicide associated with a history of mental illness and a protective effect for body mass index ≥ 25 (relative risk 0.33, 0.11 to 0.98). The restriction in the analysis to subjects who were exposed within the three months before the index date did not change the results.

Comment

We did not find an increased risk of suicide associated with use of calcium channel blockers compared with use of other antihypertensive drugs. Because of the relatively small number of cases and wide confidence intervals, however, we cannot rule out some effect of the drugs on the risk of suicide.

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Boston Collaborative Drug Surveillance Program, Boston University School of Medicine, Lexington, MA 02421, USA

Christiane Gasse
pharmacoepidemiologist
Laura E Derby
assistant professor of public health
Catherine Vasilakis
pharmacoepidemiologist
Hershel Jick
associate professor of medicine

Correspondence to:
C Gasse
cgasse@bu.edu

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Crude and adjusted* estimates of relative risk of suicide

	No (%) of cases (n=38)	No (%) of controls (n=140)	Estimate of relative risk (95% CI)	
			Crude	Adjusted
Taking other antihypertensive drugs†	29 (76)	107 (76)	1.0	1.0
Taking calcium channel blockers	9 (24)	33 (24)	1.01 (0.41 to 2.49)	0.98 (0.30 to 3.18)
Body mass index:				
<25†	11 (29)	25 (18)	1.0	1.0
≥ 25	13 (34)	64 (46)	0.50 (0.20 to 1.22)	0.33 (0.11 to 0.98)
Unknown	14 (37)	51 (36)	0.60 (0.21 to 1.71)	0.67 (0.17 to 2.63)
Smoking status:				
Non-smoker or former smoker†	23 (61)	99 (71)	1.0	1.0
Cigarette smoker	7 (18)	14 (10)	2.10 (0.75 to 5.85)	1.30 (0.31 to 5.36)
Unknown	8 (21)	27 (19)	1.40 (0.40 to 4.97)	1.30 (0.23 to 7.33)
History of mental illness:				
No†	13 (34)	121 (86)	1.0	1.0
Yes	25 (66)	19 (14)	13.04 (4.89 to 34.80)	15.70 (5.37 to 45.80)

*Adjusted for all other covariates simultaneously. †Reference group.