Do calcium channel blockers increase the risk of breast cancer? A systematic review

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Reports of an association between calcium channel blockers (CCBs) and an increased risk of breast cancer could have important public health implications if confirmed. Through a comprehensive and systematic literature review, we conclude that it is unlikely that there is an association for use less than 10 years. Further well-designed observational studies would be useful to resolve remaining uncertainty, especially for long-term use.

Our research in brief

By what mechanism could calcium channel blockers cause breast cancer?

The hypothesised mechanism for CCBs increasing the risk of developing cancer is through decreased influx of calcium inhibiting apoptosis (Figure 1). The plausibility of this hypothesis was reviewed by Mason, who considered studies showing CCB-related inhibited apoptosis of non-cancerous cells, and others showing the opposite effect. Despite inconclusive evidence supporting a biological mechanism for breast cancer potentiation by CCBs, observational data supporting an association has continued to emerge.

Methods

We searched MEDLINE, EMBASE and the Cochrane Library to 28 June 2016, checked references and citing articles, and contacted authors when necessary. Two co-authors selected articles and extracted data on research assessing the association between CCB use and risk of breast cancer. The variation in study design and outcome measures meant that no meta-analysis was performed.

Results

Twenty-nine studies fulfilled eligibility criteria (Figure 2). Of these, eight studies showed an association between CCBs and breast cancer beyond that likely explained by chance, as part of the authors’ analysis. The findings of an association were generally with immediate-release/short acting preparations, whereas longer-acting preparations such as controlled-release nifedipine/felodipine or amlodipine are predominantly used in contemporary practice. However, one recent study showed an association (adjusted odds ratio ~ 2.5) for use beyond 10 years and this could not be easily explained.

Discussion

It is reassuring that the majority of the 29 reviewed studies found no important association between taking CCBs and developing breast cancer. For the most part, studies finding an association did so for shorter-acting calcium channel blockers no longer in popular use and/or used study designs that were prone to bias. However, this review is unable to definitively refute an association between taking CCBs and developing breast cancer, especially for use beyond 10 years, as there are credible data showing an association.

References


The references of included studies are available upon request. Email Cameron.wright@curtin.edu.au

Figure 1. “Calcium regulation in mammary gland epithelial cells” (from Figure 11).