



ORIGINAL ARTICLE

The impact of dosing frequency on medication adherence in chronic cardiovascular disease: Systematic review and meta-analysis[☆]



Daniel Caldeira^{a,b,*}, António Vaz-Carneiro^{c,d}, João Costa^{a,b,c,d}

^a Laboratório de Farmacologia Clínica e Terapêutica, Faculdade Medicina da Universidade de Lisboa, Lisboa, Portugal

^b Unidade de Farmacologia Clínica, Instituto Medicina Molecular, Lisboa, Portugal

^c Centro de Estudos de Medicina Baseada na Evidência, Faculdade Medicina da Universidade de Lisboa, Lisboa, Portugal

^d Centro Colaborador Português da Rede Cochrane Iberoamericana, Portugal

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KEYWORDS

Medication adherence;
Patient compliance;
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Chronic disease;
Drug administration regimen

Abstract

Introduction and Objective: Non-adherence to drug treatment is a major health problem. In Europe, it has been estimated that 9% of cardiovascular events can be attributed to non-adherence. The complexity of dosing regimens is one of the factors identified as contributing to non-adherence. In this systematic review we aimed to assess the impact of dosing frequency on adherence to drug treatment in patients with chronic cardiovascular disease.

Methods: MEDLINE and the Cochrane Library (November 2013) were searched for randomized controlled trials (RCTs) comparing different dosing regimens (once-daily administration vs. two or more daily administrations) and assessing adherence to therapy in patients with chronic cardiovascular disease. Only trials with at least five months of follow-up were included. The results of the studies were pooled through a random effects meta-analysis. Relative risk (RR) and 95% confidence interval (CI) were derived. Statistical heterogeneity was calculated using the I^2 test.

Results: Four RCTs (a total of 2557 patients) were included. Dosing regimens with once-daily administration were associated with a significant 56% reduction in risk of non-adherence to drug therapy (RR: 0.44; 95% CI: 0.35–0.54, $I^2=25\%$).

Conclusions: Few clinical trials have assessed the long-term impact of dosing frequency on medication adherence in chronic cardiovascular disease. The best available evidence suggests that taking medication once daily decreases the risk of non-adherence to treatment by approximately 50%. The impact on clinical outcomes remains to be established.

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* Corresponding author.

E-mail address: dgaldeira@hotmail.com (D. Caldeira).

PALAVRAS-CHAVE

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Impacto da frequência posológica na adesão terapêutica em doenças cardiovasculares crônicas: revisão sistemática e meta-análise

Resumo

Introdução e objetivos: A não-adesão à terapêutica constitui um problema de saúde importante. Na Europa, foi estimado que 9% dos eventos cardiovasculares podem ser atribuídos à não-adesão terapêutica. A complexidade dos esquemas posológicos é um dos fatores apontados como contribuindo para a não-adesão terapêutica. Nesta revisão sistemática pretendemos avaliar o impacto, em doentes com patologia cardiovascular crônica, da frequência posológica na adesão terapêutica.

Métodos: Pesquisa na MEDLINE e Cochrane Library (novembro 2013) de ensaios clínicos controlados e aleatorizados (RCT) que comparassem, em doentes com patologia cardiovascular crônica, diferentes tipos de regimes posológicos (administração única diária *versus* duas ou mais administrações) e que avaliassem adesão terapêutica. Foram apenas incluídos ensaios com uma duração de pelo menos cinco meses. Os resultados dos estudos foram agregados através de uma meta-análise (efeitos aleatórios) e calculou-se o risco relativo (RR) e respetivo intervalo de confiança 95% (IC 95%). A heterogeneidade estatística foi calculada com o teste do I^2 .

Resultados: Foram incluídos quatro RCT (2.557 doentes). Os regimes posológicos com administração única diária estão associados a uma redução de 56% do risco de um doente ser não aderente à terapêutica (RR: 0,44; IC 95%: 0,35-0,54; $I^2=25\%$).

Conclusões: Poucos ensaios clínicos de longo termo avaliaram o impacto da frequência posológica na adesão terapêutica em doentes com patologia cardiovascular crônica. A melhor evidência disponível sugere que a toma de medicamentos em posologia diária única diminui o risco de não-adesão terapêutica em cerca de 50%. O impacto em termos de *outcomes* clínicos não está estudado.

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Abbreviations

HCTZ	hydrochlorothiazide
CVD	cardiovascular disease
CI	confidence interval
NNTB	number needed to treat to benefit
LDL	low-density lipoprotein
BP	blood pressure
MBP	mean blood pressure
RR	relative risk
UMPIRE	Use of a Multidrug Pill in Reducing Cardiovascular Events

Introduction

Cardiovascular disease (CVD) is the leading cause of death and loss of disability-adjusted life years worldwide.¹ Treatment, control and prevention of the consequences of CVD depend on adherence to interventions as much as on those interventions' efficacy and tolerability. Adherence to treatment includes patients' behavior in relation to physicians' recommendations, such as changes in lifestyle, adoption of a specific diet or taking medication.^{2,3}

The World Health Organization recognizes non-adherence to long-term therapies as a major problem that contributes

to morbidity and mortality and their associated direct and indirect costs.²⁻⁶ The magnitude of non-adherence is estimated at 30–50%,⁷ for which there are a variety of reasons, including the efforts and strategies used by the physician, the individual characteristics of the patient, and the type, complexity and cost of the therapeutic regimen.⁸

In this systematic review we aimed to assess the impact of dosing frequency (single vs. two or more daily doses) on adherence to drug treatment in patients with chronic CVD.

Methods

The electronic databases MEDLINE and the Cochrane Library were searched in November 2013. The search strategy (shown in Supplementary Data Table 1, available online) was adapted from other studies in this area and was extended to searches of references in other systematic reviews and the studies obtained.⁹

The inclusion criteria were randomized controlled trials comparing different daily dosing regimens (single vs. two or more daily doses) in patients with chronic CVD (coronary disease, hypertension, dyslipidemia or persistent arrhythmia) that provided data on adherence to drug therapy. We arbitrarily set a minimum 5-month follow-up period when selecting trials to assess rates of long-term adherence. Placebo-controlled and double-dummy trials were excluded

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