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Heart rate reduction through lifestyle modification: reply

In their letter, Drs Michalsen and Dobos correctly highlight the influence that several lifestyle-related factors may have on heart rate. Indeed, sedentary habits, unhealthy diet, excessive stress, smoking, high alcohol, and coffee consumption increase the sympathetic nervous system activity with consequent effects on resting heart rate. Therefore, improvement of unhealthy lifestyle might be an effective therapeutic approach in subjects with high heart rate. Among the non-pharmacological measures mentioned by Drs Michalsen and Dobos, regular endurance exercise appears to be the most effective one. Physical training causes a reduction of the sympathetic tone with beneficial effects not only on heart rate but also on abdominal visceral fat, blood pressure, and the other components of the metabolic syndrome. Recent data have shown that exercise programmes can be fruitfully followed also by elderly individuals and heart rate has been shown to be a strong predictor of mortality in the old. Thus, at any age, sedentary subjects should be advised to start walking, jogging, swimming, or other types of aerobic exercise for 30–45 min, three to four times a week. Adoption of one such programme could reduce heart rate by 5–10 beats/min, avoiding the use of pharmacological therapy in subjects with mild elevations of heart rate. As mentioned by Drs Michalsen and Dobos, stress management in persons exposed to high level of occupational, ecological, or social stress is another potential mechanism through which a decrease in heart rate can be obtained. In this respect, various therapeutic approaches such as relaxation or biofeedback techniques, group support, individualized advice, yoga, meditation, and nutrition have been proposed. Although these behavioural techniques proved effective in subjects with anxiety disorders and symptoms of high sympathetic arousal, their effect on heart rate in unselected samples is less known. In the last decade, the protective cardiovascular effect of n-3 polyunsaturated fatty acids has been firmly established. One possible mechanism by which n-3 fatty acids may prevent sudden death and fatal cardiovascular events is by reducing heart rate. In support of this hypothesis, clinical evidence has been accumulated showing a significant impact of n-3 fatty acids on parameters of heart rate variability. Recent results have shown that regular consumption of fish can cause a 2–3 beats/min reduction in resting heart rate in a general male population. A greater effect may be expected in subjects with fast resting heart rate. In keeping with the remarks by Drs Michalsen and Dobos, adoption of healthy lifestyle including regular physical activity, healthy dietary habits, and stress management in subjects exposed to high levels of stress could revert to normal mild to moderate heart rate elevations without using pharmacological treatment. However, although this approach might represent the most physiological way to prevent cardiovascular events in subjects with tachycardia, long-term studies have shown that adherence to programmes of non-pharmacological measures is often poor and that in many subjects pharmacological therapy is finally instituted.

References


Paolo Palatini
Department of Clinical and Experimental Medicine
University of Padova
Padova
Italy
Tel: +39 049 8212278
Fax: +39 049 8754179
E-mail address: palatini@unipd.it

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Drug-induced sudden cardiac death

We have read with great interest the paper which was recently published by Strauss et al. on the association between the use of non-cardiac QTc-prolonging drugs and the risk of sudden cardiac death (SCD). On the basis of their findings, which were drawn from a large population-based case-control study, the authors concluded that the use of certain non-cardiac drugs that prolong myocardial repolarization is indeed associated with an increased risk of SCD.

This study seems to represent an extension of a methodologically almost identical study published in 2004 by the same group. This previous study reviewed all cases of death in the Integrated Primary Care Information study between 1 January 1995 and 1 April 2001 (in the recently published paper, the time of observation was extended to 1 September 2003) and concentrated on the association between current use of antipsychotics and SCD. The results of the studies are similar. In the earlier paper, the current use of an antipsychotic drug was associated with a three-fold increase in risk of SCD. In the present article, current use of non-cardiac QTc-prolonging drugs was associated with a similar increase in risk of SCD (adjusted OR: 2.7), although gastrointestinal drugs and antibiotic drugs were included in the analysis. In their final conclusion, the authors extrapolate their results by emphasizing that 320 cases of sudden death per year can be attributed to the use of non-cardiac QTc-prolonging medication in the Netherlands. The authors stress the role of regulatory authorities in the evaluation of the clinical significance of QTc prolongation induced by drugs.

We believe that extrapolation of these findings has to be made with greatest caution. The authors themselves extensively discuss some of the potential limitations of their study (e.g. the chance of misclassification of events and also misclassification of drug exposure). In addition, the cases occurring during treatment with antipsychotics seem to have made a significant contribution to the study results obtained. The finding that conventional antipsychotics may increase mortality is not new. Epidemiological studies have confirmed a direct relationship between the conventional antipsychotics and the risk of sudden death. The newer, so called atypical antipsychotics (e.g. clozapine, risperidone, olanzapine) are considered to be safer.

A further limitation may result from the methodology of case-control matching. Patients were matched for age, gender, and practice, but the severity of disease was not included. The data of this study suggest that patients who died suddenly had more frequent co-morbidities and usually more frequent use of concomitant cardiovascular drugs. Also, patients on antipsychotics may...
have been sicker than control patients. Patients with schizophrenia are at higher risk for medical illnesses than people in the general population. The risk of atherosclerosis and cardiac death in these patients is markedly higher and parallels the severity of the disease.6

Last but not least, one should mention the role of the treating physician in the unwanted occurrence of abnormal QTc prolongation and SCD, mostly resulting from torsade de pointes (TdP). There is no question that the most effective way of preventing complications due to drug-induced QTc prolongation is to avoid the use of these drugs. However, there are many QTc-prolonging drugs which have certain therapeutic advantages which the physician usually does not want to miss. In these cases, a systematic approach seems advisable. First of all, the physician prescribing such a drug must be familiar with the problem of drug-induced TdP. Moreover, the physician should also know that the risk for abnormal QTc prolongation and TdP varies between patients: although some patients may have a high propensity to the development of drug-associated TdP, the risk may be low in others. Risk factors for the occurrence of the arrhythmia have been identified (e.g. female gender, bradycardia, and hypokalaemia). Thus, although the role of regulatory authorities in pharmacology is crucial, we should not forget the role of the prescribing physician.

References


Wilhelm Haverkamp
Department of Cardiology
Charité—Campus Virchow Clinic
Augustenburger Platz 1
13353 Berlin
Germany
E-mail address: wilhelm.haverkamp@charite.de

Günter Breithardt
Department of Cardiology and Angiology
Hospital of the University of Münster
Münster
Germany

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Drug-induced sudden cardiac death: reply

We would like to thank Dr Haverkamp and colleagues for their interest in our work. In the first analysis, we focused on the association between antipsychotics and sudden cardiac death. We agree that patients with schizophrenia are at higher risk for medical illnesses than people in the general population. Therefore, we adjusted for indication and showed that the risk of sudden cardiac death was also increased in patients receiving antipsychotics for other indications than schizophrenia.1 In addition, we had in our study complete access to the full medical records of all participants, including hospitalizations and specialists information. Therefore, we were able to gather complete information on known risk factors for sudden cardiac death and other co-variates. These risk factors and co-variates were included in our analysis [cerebrovascular and cardiovascular ischaemia (history of myocardial infarction, stroke, and angiina pectoris), heart failure, hypertension, diabetes mellitus, arrhythmia, hypercholesterolaemia, smoking, and alcohol abuse] and we feel that we have accounted for many of the factors that might increase the risk of sudden cardiac death. In the second study, we investigated the association between all QTc-prolonging drugs from a website and sudden cardiac death to study their clinical relevance. Indeed, the contribution of antipsychotics to this problem was relatively substantial and therefore we referred to this earlier study.

We fully agree with Dr Haverkamp and colleagues that the role of the treating physician is crucial in weighing risk benefit of the drugs prescribed. It is crucial that the treating physician is aware of the possible adverse effects of the treatment and we do hope that our study will enable the physicians to choose optimal therapy for their patients.

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S. M. J. M. Straus
Pharmaco-Epidemiology Unit
Department of Epidemiology and Biostatistics and Internal Medicine
Erasmus Medical Center
PO Box 1738
3000 DR Rotterdam
The Netherlands

Bruno H. Ch. Stricker
Pharmaco-Epidemiology Unit
Department of Epidemiology and Biostatistics and Internal Medicine
Erasmus Medical Center
PO Box 1738
3000 DR Rotterdam
The Netherlands
Tel.: +31 10 4088229
E-mail address: b.stricker@erasmusmc.nl

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Complete myocardial revascularization: between myth and reality

We read with great interest the article by Zimarno et al.1 focusing on the complex issue of complete vs. incomplete myocardial revascularization in patients submitted to percutaneous or surgical coronary intervention. We believe that the authors correctly pointed out some caveats of available literature in this regard, resulting mainly from the lack of prospective randomized investigation specifically designed to address this controversial topic. However, the authors failed to acknowledge that the benefit of early intervention when compared with the conservative approach in patients with non-ST segment elevation acute coronary syndrome (NSTEACS) known to be at medium or high-risk for future cardiovascular events, as mainly supported by the results of FRISC II,2 TACTICS-TIMI 18,3 and RITA 34 trials, was obtained following a complete revascularization strategy, either accomplished through