Recurrent Pericarditis: Can Anakinra Offer a Promising Therapy in Adults With Refractory Symptoms? Response

Pericarditis recurrente: ¿la anakinra puede aportar un tratamiento prometedor para adultos con síntomas refractarios? Respuesta

To the Editor,

I have read with interest the correspondence by Chhabra et al. on the issue of refractory recurrent pericarditis.[1] A small but significant subset of patients (overall 5% or less in my experience) may develop several recurrences despite polypharmacy and may become corticosteroid-dependent, since each attempt to taper or withdraw corticosteroids is followed by a recurrence.

Alternative treatments could be immunosuppressive drugs (especially azatioprine) or human intravenous immunoglobulins (hIVIgs). Such drugs are used in 2 broad disease categories: immunodeficiency and autoimmunity. Case reports and small series of patients with idiopathic recurrent pericarditis support the use of hIVIgs at doses of 400 to 500 mg/kg iv for 5 days and a possible repeated therapeutic cycle in cases of disease recurrence.

Anakinra, a recombinant human interleukin-1β receptor antagonist, is a promising new biologic agent for the treatment of autoinflammatory diseases such as cryopyrinopathies, tumor necrosis factor receptor-associated periodic syndrome, and hyperimmunoglobulinemia D with periodic fever syndrome, especially in the pediatric setting. The main issue is that this drug requires prolonged subcutaneous administration and the exact length of treatment is unknown. Moreover, withdrawal of these agents is frequently followed by a relapse.

Biological agents are considered a possible new therapeutic frontier in the care of idiopathic recurrent pericarditis but, as correctly pointed out, their usefulness needs to be demonstrated in new randomized studies. As a last resort, pericardiectomy has been proposed especially by US experts from the Mayo Clinic, but such an intervention is controversial and is not recommended by all pericardial experts. Moreover, as pointed out, some patients may still have recurrent chest pain and symptoms after the surgery. Last but not least, pericardiectomy is a long procedure and requires the involvement of a skilled cardiac surgery team.

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Is Cocaine-associated Acute Myocardial Infarction the Same as Myocardial Infarction Associated With Recent Cocaine Consumption?

¿Los trastornos por cocaína asociados al infarto agudo de miocardio son lo mismo que el infarto de miocardio asociado al consumo reciente de cocaína?

To the Editor,

We read with great interest the article published recently by Gili et al,[1] who studied the relationship between cocaine use disorder and the incidence and outcome of acute myocardial infarction by analyzing the Minimum Basic Data Set (MBDS) of 87 hospitals in Spain. The study concluded that cocaine use disorders increased the risk of myocardial infarction 3-fold, thereby extending hospital stay and increasing costs.

As the authors themselves note, the study design could be limited by MBDS coding, which may underestimate the prevalence of cocaine use. If we compare the data with a prospective registry run by our group of consecutive patients younger than 50 years, admitted with acute coronary syndrome, who underwent a structured interview on their history of chronic cocaine use and a cocaine metabolites urine test, the prevalence of cocaine use was 11.7% and recent use as demonstrated by the urine test results was 5.2%.[2] These figures are much higher than those reported by Gili et al[1] and are in line with other studies that systematically measured metabolites in urine.[3] We should also

remember that large biases may be present in the way patients with chest pain are questioned about cocaine use in clinical practice. In 44% of patients, the physician taking the medical history does not ask about cocaine, with obvious differences according to the individual's sociodemographic profile.[4] Likewise, patients themselves are also a source of bias as a nonnegligible proportion do not admit to cocaine use even after a positive urine test result.[2,3]

In cases of acute myocardial infarction, recent cocaine use is an important prognostic factor in young patients, as it increases the complications of the acute myocardial infarction itself,[5] as well as in-hospital mortality.[2] In view of the importance of cocaine use as a prognostic factor and the difficulty of detecting such use in the initial contact, the European guideline on acute coronary syndrome recommends specific questions about cocaine use as part of the medical history and systematic measurement of cocaine metabolites in urine as part of the work-up.[6]

Assessment of the extent of cocaine use and myocardial infarction through the MBDS may be an interesting initial approach. However, we wonder whether the authors think that the prevalence of myocardial infarction associated with recent cocaine use may be underestimated, given the differences in the detection of cocaine use among studies. Could this underestimation and the greater age of patients with myocardial infarction at inclusion also have led to an underestimation of the prognostic effect of recent cocaine use on acute myocardial infarction? From our standpoint, we think it is important to differentiate between

disorders arising from chronic cocaine use, which triples the risk of acute myocardial infarction, and acute cocaine use, which increases the complications and in-hospital mortality of infarction. We are therefore of the opinion that it is essential to specifically question patients with suspected myocardial infarction about chronic cocaine use and measure drug metabolites in urine.

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To the Editor,

We agree with Carrillo et al with regard to the importance of the information bias when dealing with cocaine use. Nevertheless, other factors also explain the differences between our results[1] and the findings reported in their study,[2] carried out in a coronary critical care unit (CCCU). In a study by Gupta et al[3] involving 102 952 acute myocardial infarction patients in 364 hospitals participating in the American College of Cardiology Registry of the United States, only 924 patients (0.9%) of all ages were cocaine-positive, defined as use of the drug within the preceding 72 hours or its presence in urine.

Extrapolation of the results of a study involving 87 hospitals (Spain) or 364 hospitals (United States)—in patients with confirmed acute myocardial infarction from different geographical areas, treated in different types of hospitals and departments, and of different ages—to the findings in a single CCCU in which acute coronary syndrome was studied in patients under 50 years of age is problematic. It would also be risky to extrapolate the results of a single CCCU to all the patients hospitalized for acute myocardial infarction.

We were surprised by the high mortality rate among cocaine-positive patients in the CCCU. There were no statistically significant differences between the study by Gupta et al[3] and ours.[1] Hollander et al[4] reported a 0% mortality rate among cocaine-positive patients, which could be due to 2 different circumstances:

1. In their study, Carrillo et al[2] performed a simple analysis based on 2 deaths among 24 cocaine-positive patients and 3 deaths among 379 patients with a cocaine-negative urine test. If we calculate the odds ratio (OR) and use an exact method to determine its 95% confidence intervals (CI), we obtain an OR = 11.4 (95% CI, 0.89-103.3). These authors only evaluated the statistical significance (P = .03), but overlooked the imprecision of the OR which, with a 95% CI, indicates that a cocaine-positive urine test can be associated with an increased risk of death, with no effect at all (OR = 1) or, surprisingly, with a reduced risk of death (OR = 0.89-0.99).

2. Our study[1] and that of Gupta et al[3] (but not that of the abovementioned authors) involved a multivariate analysis that included important prognostic variables (age, sex, other addictive disorders, comorbidities, complications, analytical findings, and treatments, depending on the study).

For all these reasons, we consider that, to calculate the risk of mortality attributable to cocaine use in patients with acute coronary syndrome admitted to a CCCU, the sample should be large enough to guarantee the statistical power of the study, the accuracy of the estimators of the effect size, and control of confounding bias by means of a multivariate analysis of the results.

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