There are numerous studies showing that sustained treatment with morphine can produce supersensitization of adenylyl cyclase (AC) in different cell lines as well as in brain tissue. However, there is lack of information about the potential effect morphine on the myocardial AC signaling system. In the present study we investigated the impact of prolonged (10 or 28 days) administration of different doses of morphine (0.1-10 mg/kg per day) on β-adrenergic receptor-mediated AC signaling in rat heart. For the most part, morphine did not affect the number and affinity of β-adrenergic receptors and expression of selected G protein subunits (G\textsubscript{s} alpha, G\textsubscript{i/o} alpha, G\textsubscript{z} alpha, G\textsubscript{q/11} alpha and Gbeta), but it markedly elevated (almost doubled) the amount of AC type V/VI. These changes were accompanied by considerable supersensitization of AC: the enzyme activity stimulated by Mn\textsuperscript{2+}, NaF, forskolin or isoprenaline was increased by about 50-100 % in samples of myocardium from morphine-exposed rats. On the contrary, the ability of opioid agonists (DADLE and U-50488) to inhibit forskolin-stimulated AC activity was rather decreased. We also observed that morphine reduced the incidence of ischemia- provoked ventricular arrhythmias and infarct size under certain experimental conditions. The effects of morphine on myocardial signaling and susceptibility to ischemic injury were dose- and time-dependent and lasted for several days. These data indicate that prolonged morphine treatment may substantially alter functioning of the myocardial AC signaling system and induce cardioprotection against ischemia-induced arrhythmias.