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SHORT COMMUNICATION

Effect of Isoproterenol on ^{85}Sr Accumulation in the Myocardium of the Rat during Postnatal Ontogeny

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Summary

The aim of this study was to establish whether administration of toxic doses of isoproterenol (IPRO) increases the accumulation of strontium – a homologue element of calcium – in the rat heart during postnatal development. It has been shown that in 14-day-old animals ^{85}Sr uptake was not increased; starting from the 30th day of postnatal life this parameter increases significantly up to adulthood.

Key words

Isoproterenol – Strontium – Rat heart – Development

Administration of large doses of the beta-mimetic synthetic catecholamine isoproterenol (IPRO) to adult experimental animals produces necrotic lesions in their myocardium (for review see Rona 1985). According to Fleckenstein (1971), the main pathogenetic mechanism of cardiac damage in adults is an excess of intracellular calcium followed by depletion of high energy phosphates and injury of the mitochondria. IPRO-induced cardiac lesions can be quantified by the measurement of ^{45}Ca uptake into myocardial cell (Fleckenstein 1971, Mráz *et al.* 1980).

Recently, we reported (Ošťádalová and Ošťádal 1988) that the administration of IPRO to adult rats also increases cardiac accumulation of the homologue element of calcium, i.e. strontium. The reason of the use of strontium is a methodological advantage: ^{45}Ca is a source of beta radiation and biological samples must be modified before they can actually be measured. ^{85}Sr is measurable as a gamma emitter; the samples need no modification and work with them is, therefore, quicker and simpler.

There are many discrepancies in the literature dealing with responsiveness of the developing mammalian heart to beta-mimetic catecholamines (for review see Driscoll 1987, Ošťádal *et al.* 1989). The situation seems to be even more complex with respect to the possible age-related changes in cardiotoxicity. The information in this respect is insufficient even though catecholamines are used in clinical practice, both during pregnancy and just after birth. We have found (Ošťádal *et al.* 1973, Ošťádal *et al.* 1989) that from birth up to the end of the 4th postnatal week the rat heart is resistant to the effect of IPRO. The first microscopic changes were observed on the 30th day of postnatal life and the incidence of changes increased with the age of animals. We were therefore interested in whether the ontogenetic changes of IPRO-induced cardiotoxicity in rats coincides with the developmental changes in IPRO-induced myocardial accumulation of the homologue element of calcium, i.e. strontium.

Experiments were performed on 64 male laboratory rats (Wistar strain) 14, 30, 60 and 120 days old. The experimental males were given IPRO ($1 mg.kg^{-1}$), the controls received the same volume of distilled water. Two hours later, $^{85}SrCl_2$ was administred subcutanously to 60- and 120-day-old control and experimental rats in a dose of 0.56 MBq ($15 \mu Ci).kg^{-1}$ and to all 14- and 30-day-old animals in a dose of 3.73 MBq ($100 \mu Ci).kg^{-1}$ (specific activity 57 $MBq.mg^{-1}Sr$). After futher three hours the animals were decapitated. Blood and heart samples were weighted and ^{85}Sr content was measured with

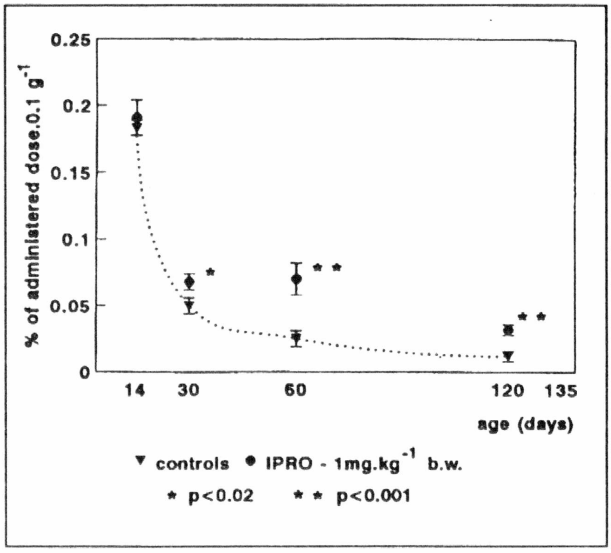

Fig. 1
Effect of isoproterenol on myocardial concentration of ^{85}Sr. Values (means±S.E.M.) are expressed as percentage of administered dose.0.1 g^{-1}.

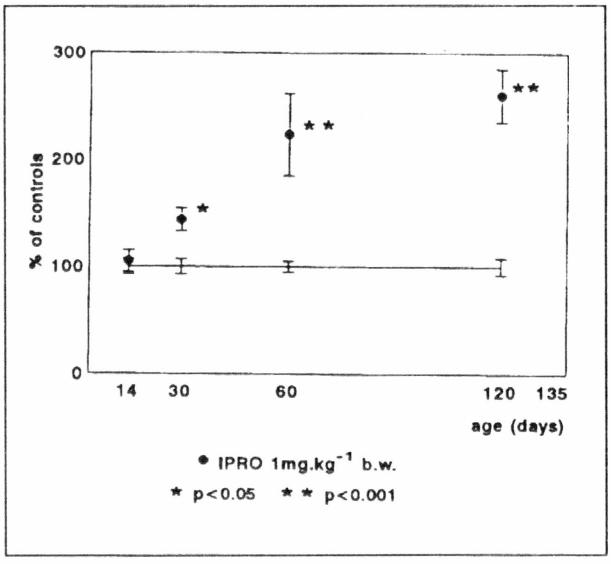

Fig. 2
Effect of isoproterenol on myocardial content of ^{85}Sr (% of administered dose). Values (means±S.E.M.) are expressed as percentage of the controls.

an automatic gamma system (Searle Nuclear Chicago model 1185). ^{85}Sr incorporation into the tissues was expressed as percentage of the administered dose.

The ability of the heart to accumulate ^{85}Sr decreases significantly during postnatal ontogeny (Fig. 1). In 14-day-old animals which were resistant to the necrogenic action of IPRO, the content as well as

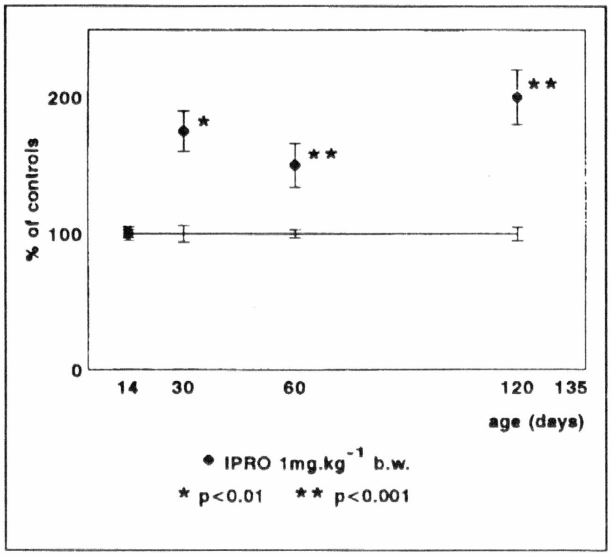

Fig. 3
Effect of isoproterenol on heart/blood ratio of ^{85}Sr uptake. Values (means±S.E.M.) are expressed as percentage of the controls.

the concentration of ^{85}Sr was not increased, whereas in 30- to 120-day-old hearts these values were significantly increased by IPRO (Fig. 1, 2). Similar developmental changes were obtained with heart/blood ratio; the control values of heart/blood ratio were 0.47±0.01, 0.42±0.04, 0.43±0.03 and 0.42±0.02 in 14-, 30-, 60- and 120-day-old rats, respectively (Fig. 3).

The age-dependent decrease of myocardial ^{85}Sr uptake is in good agreement with the data of Elz and Nayler (1987), who showed that the Ca content in the rat heart decreases during postnatal ontogeny. This fact may be at least partly due to maturation of the systems involved in calcium (strontium) handling.

The IPRO-induced increase in ^{85}Sr accumulation in the myocardium of adult rats is comparable to the repeatedly described analogous changes in radioactive calcium uptake (Fleckenstein 1968, 1983, Mráz *et al.* 1980). It can be assumed that IPRO-stimulated uptake of strontium by myocardial cells is effected by voltage-dependent calcium channels (Kohlhardt *et al.* 1973). This possibility is supported by the findings of Luchowski *et al.* (1984) showing that the transport of strontium across the membranes of smooth muscle cells can be blocked by nitrendipine, a calcium antagonist.

It may be assumed that IPRO-induced stimulation of ^{85}Sr uptake in the rat myocardium is strictly age dependent and is connected with the development of necrotic lesions. This concept is supported by the finding that IPRO-induced non-necrotic changes in the chick embryonic heart are not followed by significant elevation of ^{85}Sr accumulation (Ošťádalová and Ošťádal 1992 a,b).

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