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Hydrogen sulfide induces hyperpolarization and decreases the exocytosis of secretory granules of rat GH3 pituitary tumor cells

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ABSTRACT

The aim of the present study was to evaluate the effects of hydrogen sulfide (H_2S) on the membrane potential, action potential discharge and exocytosis of secretory granules in neurosecretory pituitary tumor cells (GH3). The H_2S donor – sodium hydrosulfide (NaHS) induced membrane hyperpolarization, followed by truncation of spontaneous electrical activity and decrease of the membrane resistance. The NaHS effect was dose-dependent with an EC_{50} of 152 μM (equals effective H_2S of 16–19 μM). NaHS effects were not altered after inhibition of maxi conductance calcium-activated potassium (BK) channels by tetraethylammonium or paxilline, but were significantly reduced after inhibition or activation of ATP-dependent potassium channels (K_{ATP}) by glibenclamide or by diazoxide, respectively. In whole-cell recordings NaHS increased the amplitude of K_{ATP} currents, induced by hyperpolarizing pulses and subsequent application of glibenclamide decreased currents to control levels. Using the fluorescent dye FM 1–43 exocytosis of secretory granules was analyzed in basal and stimulated conditions (high K^+ external solution). Prior application of NaHS decreased the fluorescence of the cell membrane in both conditions which links with activation of K_{ATP} currents (basal secretion) and activation of K_{ATP} currents and BK-currents (stimulated exocytosis). We suggest that H_2S induces hyperpolarization of GH3 cells by activation of K_{ATP} channels which results in a truncation of spontaneous action potentials and a decrease of hormone release.

1. Introduction

Hydrogen sulfide (H_2S), a member of the gasotransmitter family, is endogenously synthesized and participates in the regulation of a great variety of physiological and pathophysiological processes [1–8]. In the central nervous system H_2S induces long-term potentiation in the hippocampus [9], and modulates neuronal excitability and transmitter release in the central and peripheral nervous system [10–15].

Ion channels are a main target of H_2S action in excitable cells [3], among which are NMDA-receptors [9], K^+ and Ca^{2+} channels [1,5,7,8,16–19]. Endocrine pituitary cells are neurosecretory cells, expressing Na^+ Ca^{2+}, K^+ and Cl^- channels which are involved to establish the membrane resting potential, modulate the electrical discharge activity and generate spontaneous activity, which is observed not only in cell lines *in vitro* but also in rat pituitary slices *in situ* [20].

The fluorescent dye FM1-43 has been used extensively to study secretory activity [21] and provides the ability to label selectively those structures that are undergoing exocytosis and endocytosis in living cells in real time [22].

The aim of this study was to evaluate the effects of H_2S on membrane potential and exocytosis of secretory granules in neurosecretory pituitary tumor GH3 cells using electrophysiological and fluorescent techniques.

Abbreviations: H_2S, hydrogen sulfide; TEA, tetraethylammonium; BAPTA AM, 1,2-bis(o-aminophenoxy)ethane-N,N,N′,N′-tetraacetic acid; DMSO, dimethyl sulfoxide; NaHS, sodium hydrosulfide; BK-channels, maxi conductance calcium-activated potassium channels; K_{ATP}, ATP-dependent potassium channels.

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