CONFIRMATION OF SUBTYPE OF ALPHA-1 ADRENERGIC RECEPTOR PRODUCING RELAXATION IN GOAT ARTERY STRIP

ABSTRACT

Phenylephrine (PE) is an alpha adrenergic agonist and is known to produce constriction of vascular smooth muscle. It has been recently demonstrated from our department that PE can also induce vasorelaxation under certain circumstances in a nitric oxide (NO)-dependent manner. It was also demonstrated that such vasorelaxation is mediated through alpha adrenergic receptors and is not an alpha adrenoceptor-independent effect of PE. In this study, we have delineated the roles of four different subtypes of alpha receptors (α_{1A}, α_{1B}, α_{1D} and α_2) in mediating responses to PE on spiral strips of goat arteries, from which tension recordings were made.

Aim:

To identify the subtype of alpha adrenergic receptor producing relaxation in goat artery strip

Objectives:

1. To induce vasorelaxation in goat artery strip by incubating with L-Arginine (NO donor), followed by phenylephrine
2. To test if such vasorelaxation induced by L-Arginine/PE combination is preventable with specific α_1 blocker (prazosin), specific α_{1A} blocker(RS 17053), specific α_{1B} blocker (chloroethylclonidine dihydrochloride), specific α_{1D} blocker (BMY 7378 dihydrochloride) and specific α_2 blocker (Yohimbine)

3. To test the response produced by phenylephrine with specific α_{1A} blocker(RS 17053), specific α_{1B} blocker (chloroethylclonidine dihydrochloride), specific α_{1D} blocker (BMY 7378 dihydrochloride) and specific α_2 blocker (Yohimbine), in the absence of L-Arginine
4. To test the response produced by phenylephrine with combinations of subtype selective blockers, in the absence of L-Arginine

Methods:

Artery isolated from fresh goat leg was cut into spiral strip and suspended in an organ bath (25 ml), filled with physiological salt solution at 37ºC, aerated with carbogen. One end of the strip was connected to a force transducer and recorded using a data acquisition system (powerlab). Drugs were added to the organ bath and the change in tension was recorded & analyzed using Igor pro software.

Results:

Both contractile response under control conditions (without high NO environment) and relaxant response to PE in a high NO environment are mediated through alpha 1D receptor. Blockade of alpha 1D receptor renders the tissue unresponsive to PE. Contractile response mediated through alpha 1D receptor under control conditions requires coactivation of the other three receptor subtypes. Even if one of the other three receptor subtypes is blocked, only a relaxant response will occur with PE even under conditions where NO levels are expected to be normal.

Conclusion:

Alpha-1D receptor is required for the contractile or relaxant response with PE and coactivation of other three receptor subtypes is required for preventing relaxation and for contraction to occur under control conditions. The results suggest that each receptor subtype has a specific role to play in mediating the effects of PE and are not redundant mechanisms acting through the same pathway.

Keywords: NO-dependent vasorelaxation, Phenylephrine, Alpha adrenergic receptor, Vascular smooth muscle