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Factors influencing the time course of noradrenaline-induced Contractions of the porcine isolated splenic artery

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Introduction: In our early study, we reported that contractions of the porcine isolated splenic artery (PSA) to selective α_1-adrenoceptors agonists, phenylephrine and L-erythromethoxamine, declined over 30 min, but were enhanced and better maintained in the presence of lithium[1]. During our studies, we noted that contractions to noradrenaline (NA) were similarly labile. Since catecholamines are subject to auto-oxidation[2], we investigated whether lithium or known antioxidants can influence the time course (TC) of response to NA in the PSA *in vitro*.

Methods: The PSA was dissected from spleens obtained from a local abattoir. Vessels were stored overnight at 4^{o}C in closed universal tube. On the next day 5mm segments prepared for isometric tension recording in Krebs-Henseleit solution gassed with either 95%O_2/5%CO_2 or 95%Air/5%CO_2 and maintained at 37^{o}C. Responses to 60mM KCl were used to compare NA contractions. Cumulative concentrations of NA were added to the PSA in the presence and absence of 1mM lithium, EDTA 10µM, ascorbic acid (AA) 50µM or pargyline 1µM and the TC followed up to 120 min thereafter. Student's t-test used for data analysis.

Results: Maximal contractions to NA declined by more than 50% over 60 min, from 228.5±17.4 % (n=8) to 114.8±26.1%. Neither lithium1mM, EDTA10µM, AA 50µM not 1µM pargyline influenced the potency (pD_2) of NA in the PSA or the maximum response. In separate experiment, lithium 1mM failed to alter in the decline in response to NA 30µM over 60 min (17.3±6.5% (Li) and 16.7±8.9% (Con) of KCl 60mM, n=4). Neither AA 50µM nor EDTA 10µM altered the TC of responses to NA, but pargyline 1µM and 95%Air/5%CO_2 significantly enhanced response to NA over time, contraction after 120 min was 9.4±2.7% (Con) in compare with 27.7±4.1% for pargyline 1µM, (n=14), and the contraction was 10.7±1.8% in 95%O_2/5%CO_2 in compare with 80.5±8.9% in 95%Air/5%CO_2, n=8.

Discussion: Since lithium did not alter the TC of responses to NA, the basis of the decline in responses in the PSA is different from that noted for other α_1-adrenoceptor agonists[1]. The failure of AA or EDTA to increase the potency of NA, or to limit the decline in responses, differs from that accepted for antioxidant and metal-chelating agents[2] and highlights the major detrimental effect of hyperoxia on catecholamines during *in vitro* experiments.

References:

1. Yahya *et al*., (2016) BPS Winter Meeting. http://www.pa2online.org/abstract/abstract.jsp?abid=33241&kw=Lithium&cat=-1&period=64
2. Maxwell LC *et al.,* (1983). *Microvascular Research.* **26,** 81-88