

How do detrusor responses to clinical antimuscarinic medications vary between differently aged porcine bladders?

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Objective: Antimuscarinics are the first line medications for overactive bladder (OAB) patients,¹ with a mechanism involving the inhibition of detrusor spontaneous contractions during the filling phase.² However, 70% of OAB patients discontinue their antimuscarinic treatments due to lower-than-expected treatment benefits or adverse side effects. With an increasing prevalence of OAB with age, there is a benefit to identifying whether the influence of antimuscarinics on bladder tissue alters due to ageing.³ This study aims to find the variations in the ability of common clinical antimuscarinics to inhibit contractions of the detrusor and compare these responses in juvenile and adult porcine tissues.

Methods: Strips of detrusor tissue from juvenile and adult pigs were mounted in carbogen-gassed Krebs-bicarbonate solution at 37°C. The tissues were paired with carbachol concentration-response curves performed in the absence or presence of oxybutynin (1µM), solifenacin (1µM), darifenacin (100nM), tolterodine (1µM), trospium (100nM) and fesoterodine (100nM). Concentrations were chosen to ensure complete concentration-response curves in response to carbachol. EC50 values for each curve were analysed and estimated affinities calculated. Ethical approval was not required for this study as tissues were sourced from the local abattoir after slaughter for the routine commercial provision of food.

Results: All antimuscarinics induced a consistent rightward shift from the control in both juvenile and adult detrusor tissues. Estimated affinities were calculated for oxybutynin (7.47, n=10), solifenacin (6.73, n=8), darifenacin (7.58, n=11), tolterodine (8.09, n=8), trospium (8.69, n=8) and fesoterodine (8.67, n=8) in juvenile detrusor tissues. Estimated affinities were calculated for oxybutynin (7.44, n=9), solifenacin (6.63, n=8), darifenacin (7.95, n=9), tolterodine (7.93, n=8), trospium (9.30, n=9) and fesoterodine (8.54, n=8) in adult detrusor tissues. Comparisons of estimated affinities for each antimuscarinic between juvenile and adult tissues revealed no differences in each tissue's functional response to the six antimuscarinics (p>0.05).

Conclusions: This ongoing study suggests that there are no significant differences between detrusor functional responses to antimuscarinics of differently aged porcine samples. Further suggesting that these medications can assist in the treatment of OAB and differences in compliance may be due to lifestyle or behavioral changes with age, rather than alterations in the tissues ability to respond to the prescribed medication themselves.

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References

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