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EFFECTS OF TAK-802 AND DISTIGMINE ON THE PRESSURE FLOW STUDIES IN DECEREBRATED CATS

Hypothesis / aims of study

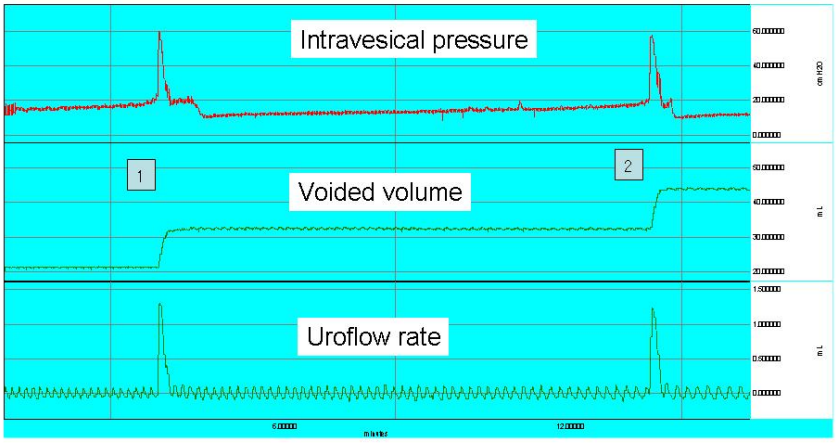
Cholinomimetic drugs have been used for the treatment of voiding dysfunction associated with detrusor underactivity, but their efficacy remains controversial. We investigated the effects of TAK-802, a novel non-carbamate acetylcholinesterase inhibitor, by performing a pressure flow study in decerebrated cats and compared these results with those seen with Distigmine used clinically.

Study design, materials and methods

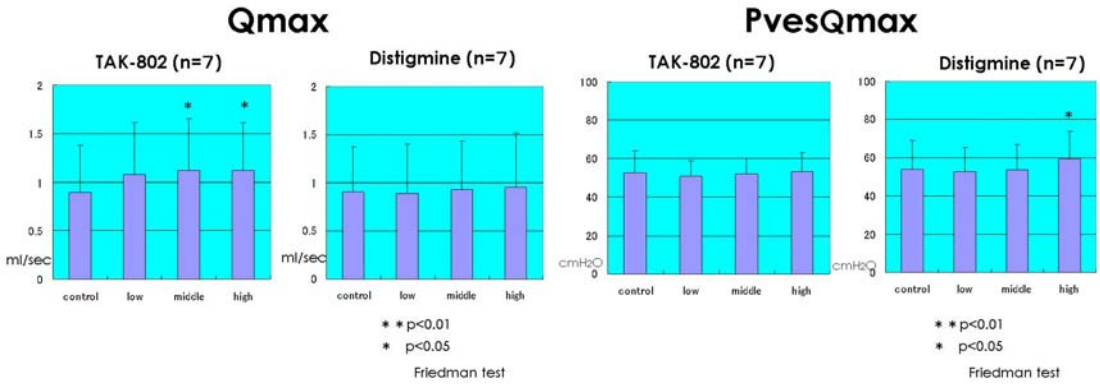
In this study we used 14 male adult cats (2.6-3.4kg). Tracheotomy was performed using general anesthesia with halothane inhalation. 4Fr double lumen catheter was inserted into the bladder dome. The brain was decerebrated by cutting between the anterior margin of diencephalon and mesencephalon. The cats were fixed on a streotaxic puncture apparatus and started after they awakened from anesthesia. The intravesical pressure were measured using a pressure transducer. And physiological saline was injected into bladder at the rate of 1ml/min. Voided volume were measure using an electronic balance. Each single was concomitantly recorded using a multiple-channel data acquisition system (MP-100A,Biopac systems). The voided volume was differentiated to obtain the flow rate. Each urodynamic parameter were measured, TAK-801 or Distigmine were administered intravenously. TAK-801(0.0003, 0.001, 0.003mg/kg) and Distigmine (0.003, 0.01, 0.03mg/kg).

Results

TAK-802 increased the voided volume and the maxiumum flow rate without affecting either intravesical pressure Distigmine while not increasing the Qmax, increased the intravesical pressure at Qmax.



	Qmax ml/sec	Qave ml/sec	volume ml	Pvesmax cmH2O	PvesQmax cmH2O
1	1.34	0.52	12.36	61.29	59.02
2	1.25	0.54	12.63	58.81	57.50



Interpretation of results

These results suggest that TAK-802 reinforces bladder-voiding function by increasing bladder contractility without a deterioration of the storage function. On the other hand, Carbamate AChE inhibitors not only deteriorate the voiding function by inducing contraction of the external urethral sphincter muscle resulting in urethral resistance, but they also cause a deterioration in storage function.

Concluding message

TAK-802 may therefore be a more useful drug than either carbamate AChE inhibition for the treatment of voiding dysfunction associated with detrusor interactivity.