RAPID AND PERMANENT HEARING LOSS IN CATS FOLLOWING CO-ADMINISTRATION OF KANAMYCIN AND ETHACRYNIC ACID

S.A. Xu, R.K. Shepherd and G.M. Clark, Department of Otolaryngology, University of Melbourne, Parkville, Victoria, 3052, Australia.

A safe, simple and effective technique for producing profound-totally deaf animal models in both young and adult cats is required for auditory prosthesis related research. Exposure to loud noises can result in a partial hearing loss, the degree of which varies significantly among animals. Long-term systemic injection of an aminoglycoside ototoxic drug frequently results in renal dysfunction and can show significant variation in response among animals (Shepherd & Clark, 1985). Finally, direct infusion of ototoxic drugs produces extensive and highly variable cochlear pathology, unsuitable for auditory prosthesis research. Brummett & Fox (1982) described a technique to permanently deafen guinea pigs by co-administration of the aminoglycoside kanamycin (KA 400 mg kg$^{-1}$) and the loop diuretic, ethacrynic acid (EA 40 mg kg$^{-1}$). We have investigated and developed this technique for use in cats.

In this study, seven normal hearing cats ranging in age from 1 to 12 months were anaesthetized with saffan (9 mg kg$^{-1}$) and maintained with halothane and methoxyflurane. Click-evoked auditory brainstem responses (ABRs) were recorded to monitor the animals' hearing status. KA (300 mg kg$^{-1}$ kanamycin monosulfate, Sigma) dissolved in sterile normal saline, was injected subcutaneously. Thirty minutes later EA (ethacrynate sodium, MSD) dissolved in sterile normal saline, was administered intravenously via a slow infusion apparatus at a rate of 1 mg per minute until the ABR threshold was elevated 70dB above the pre-drug level. The animals were sacrificed by overdose of anaesthetic (pentobarbitone sodium i.m.) 2 to 6 months following the deafening procedure. Cochleas and kidneys were processed for histology.

All the cats had a profound hearing loss following the deafening procedure. Typical hearing loss is illustrated in the figure. Click-evoked ABR thresholds are plotted against time (minutes) following the administration of KA for two representative cats. The administration of EA commenced 30 minutes after the KA (arrow). ABR thresholds remained stable until the dose of EA was in the range 15 to 25 mg kg$^{-1}$, whereupon the thresholds rose rapidly to levels in excess of 90dB peak-equivalent SPL. This profound hearing loss was bilateral and permanent. All the animals made a routine recovery from the anaesthetic and resumed a normal diet. There was no evidence of vestibular disturbance. Although blood urea and creatinine levels were slightly to moderately elevated following the procedure, these levels returned to normal values within a week. No animal exhibited renal failure and there was no evidence of renal histopathology. Histology of the 14 cochleas consistently showed a total hair cell loss throughout all cochlear turns.

We have described a safe, effective and reliable technique for producing deaf animal models. By monitoring hearing status and accordingly varying the dose of EA, the technique can compensate for individual variations in response to the drugs, thereby routinely producing a profound-totally deaf animal model. The technique also has the potential to produce controlled partial hearing losses in experimental animals.


This study was supported by NIH Contract NO1-NS-7-2342.
Author/s:
Xu, Shi-Ang; Shepherd, Robert K.; Clark, Graeme M.

Title:
Rapid and permanent hearing loss in cats following co-administration of kanamycin and ethacrynic acid [Abstract]

Date:
1990

Citation:

Persistent Link:
http://hdl.handle.net/11343/26843