RAPID AND PERMANENT HEARING LOSS IN CATS FOLLOWING CO-ADMINISTRATION OF
KANAMYCIN AND ETHACRYNIC ACID
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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, ethacrynate 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 adminis-
tration 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
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.

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Marcel Dekker.

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