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SEVOFLURANE MAY NOT INDUCE LONG-TERM TOXICITY ON SPINOCEREBELLAR ATAXIA TYPE 3 TRANSGENIC DROSOPHILA MODEL

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Abstract:

Introduction:

Spinocerebellar ataxia type 3 (SCA3) is a rare inherited neurodegenerative disease and it is incurable. Sevoflurane is one of the most commonly used volatile anesthetics for general anesthesia during surgery. Sevoflurane has previously been shown to be toxic effects on some neurodegenerative diseases, but the neurologic relationship with sevoflurane and SCA3 was still unknown. However, there is no study for the effects of inhalational anesthetics on long-term outcome. One of the advantages of Drosophila model in researches is more than 77% of known human genes are recognizably matched in the genome of Drosophila1-2.Therefore, we investigate the long-term effects of sevoflurane, currently the most commonly used inhalational anesthetic, on the overall survival in SCA3 transgenic Drosophila.

Methods:

We used five strains of Drosophila: elav-Gal4, w1118; P{UAS-SCA3.fl-Q84.myc}7.2/MKRS (UAS-Q84), w1118; P{UAS-SCA3.fl-Q27.myc}46.2 (UAS-Q27), and w1118 (wild type). All flies were obtained from Bloomington Drosophila Stock Center. Virgin female flies carrying the driver elav-Gal4 on X chromosome were crossed to males carrying the UAS-Q27 or UAS-Q84. All F1 offspring expressed Q27 or Q84 separately in the nervous system, giving us a model for SCA3. The virgin female flies carrying the driver elav-Gal4 were crosses to w1118 male flies and their F1 offspring were used as control. SCA3-transgenic and control flies were exposed to sevoflurane with 2.1% or 3.0% plus 100% oxygen for 4 times (1 hour per time per day) and observed survival rate of flies. Flies were exposed to sevoflurane at 6th days after eclosion and anesthetic and oxygen concentrations were measured continuously (Dräger Medical AG & Co., Germany). The flies were maintained at a density of 35 per vial, at 25℃ in 50 to 60% relative humidity under a 12-h light:12-h dark (LD) cycle, and transferred to new food every 3 or 4 days until all SCA3 transgenic flies dead3.

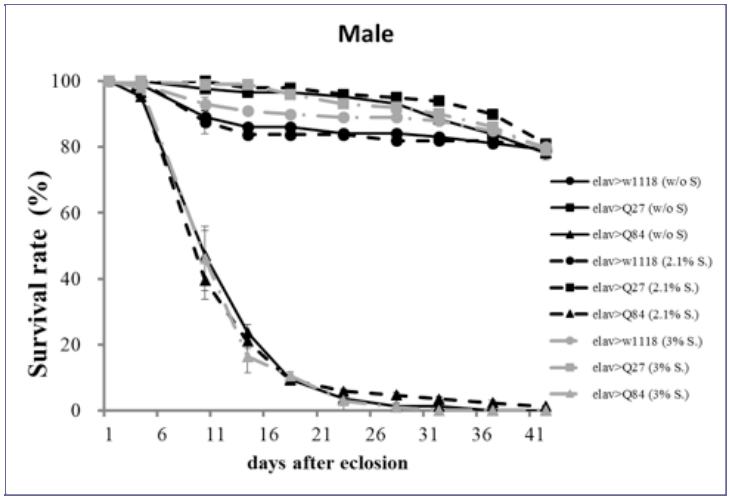
Results:

The survival rate of anesthetized SCA3-transgenic flies (2.1% or 3.0% sevoflurane) had no significant difference compared with control. The survival curves of SCA3 disease male flies, which were exposed to different concentration of sevoflurane (2.1% or 3.0%) were similarity with SCA3-transgenic flies which were not exposed (Figure 1).

Conclusions: This finding indicated that sevoflurane might not attenuate the neurologic abnormality in SCA3 transgenic Drosophila Model. We found that sevoflurane in clinically relevant concentrations might not affect the overall survival of control and SCA3-transgenic flies. This suggests that sevoflurane might not have long-term neurotoxic effects and general anesthesia with sevoflurane might be still effective and safe in clinical practices including the elderly and patients with SCA3. Future studies are necessary to determine whether inhalational anesthetics may induce neurotoxic or neuroprotective effects, which may eventually lead to safer anesthesia care for patients.

References:

1. Neurobiol Dis 40:29-39 (2010)
2. Exp Gerontol 46:335-9 (2011)



3. J Nutr Biochem 19:376-83 (2008)

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