Hyperoxia influences cancer growth and metastasis. A pilot experimental model

Ristescu Irina[1,2], Tiron Adrian[3], Tiron Crina[3], Iliescu Radu[1,3,4], Zugun-Eloae Florin[1,3], Carasevici Eugen[3], *Grigoraș Ioana[1,2]

[1]Grigore T. Popa University of Medicine and Pharmacy, Iași, România
[2]Regional Institute of Oncology, Anaesthesia and Intensive Care Department, Iași, România
[3]Regional Institute of Oncology, Department of Molecular Biology, TRANSCEND, Iași, România
[4]CEMEX Research Center, Grigore T. Popa University of Medicine and Pharmacy, Iași, România
*Corresponding author: ioana.grigoras.ro@gmail.com

Introduction: Perioperative care of cancer patients is under scrutiny. Among many factors promoting cancer recurrence and metastasis, high oxygen concentration exposure is underevaluated. While oxygen toxicity is documented in several circumstances, its implication in tumor cell growth and progression is poorly understood.
Objective: To characterize high oxygen concentration exposure effects on tumor progression using a breast cancer murine model.
Material and methods: A highly aggressive breast tumor cell line 4T1 (ATCC®) was injected in mammary gland in 8 week old females BALB/c mice. We divided the animals into 3 groups, each including 6 individuals: G1 – tumor bearing mice with no intervention post inoculation; G2 – primary tumor removal at 2 weeks post inoculation; G3 - primary tumor removal at 2 weeks post inoculation followed by 6 hours of 75% oxygen exposure. In all groups cancer evolution was assessed at 6 weeks by standard pathomorphological evaluation: specimens from the primary tumor, locally recurrent tumor and target organ metastasis were assessed by hematoxylin-eosin staining, and digital microscopy.
Results: Surgically removed primary tumors in G3 group had similar characteristics with those in G2 group and previously described models. At study endpoint, compared with both G2 and G1 groups, G3 animals showed significantly higher tumor burden: larger local recurrence and more metastasis (larger number and dimensions) in liver and lungs, associated with significantly enlarged spleen.
Conclusions: Short term (6 hours) high oxygen (75%) concentration exposure results in significantly more aggressive progression of a 4T1-BALB/c murine breast cancer model.
Key words: hyperoxia, cancer growth, metastasis.

Effects of different sevoflurane concentrations on Akt isoforms in normal and cancer breast cells. An experimental model

Patrașcanu Emilia[1,2], Ristescu Irina[1,2], Tiron Crina[3], Tiron Adrian[3], Postu Paula[3], Carasevici Eugen[3], *Grigoraș Ioana[1,2]

[1]Grigore T. Popa University of Medicine and Pharmacy, Iași, România
[2]Regional Institute of Oncology, Anaesthesia and Intensive Care Department, Iași, România
[3]Regional Institute of Oncology, Department of Molecular Biology, TRANSCEND, Iași, România
*Corresponding author: ioana.grigoras.ro@gmail.com

Introduction: Multiple perioperative factors influence cancer patient evolution and outcome. Microenvironmental factors activate different gene programs that enable tumor cell to invade, survive and promote drug resistance and metastasis. The effects of anesthetic drugs on cancer progression is under scrutiny, but published data are controversial and the involved mechanisms unclear. Tumor development implies PI3K/AKT pathway activation. Akt isoforms (1,2,3) are frequently amplified in various malignant tumors and associated with malignant cell survival, proliferation and invasion. Their activation is often observed in human cancers and is associated with decreased survival rate.
Objective: Identification of Akt isoforms activated in sevoflurane exposed breast tumor cells.
Material and methods: Normal breast cells MCF10A (ATCC®) and breast cancer cells MDA-MB-231 (ATCC®) were cultured 2D (standard adhesive culture plastic plates) and 3D (matrigel). Study groups were exposed to different sevoflurane concentrations

(0.5, 2, 3, 4 mM) compared to control unexposed groups. Unexposed and sevoflurane exposed cells (2D and 3D) were evaluated by optic microscopy and viability tests. Akt isoforms were assessed by immunofluorescence.
Results: Sevoflurane alters tumor cell proliferation and Akt isoforms expression in a dose-dependent manner. The phenotype of 3D 2mM sevoflurane exposed cells show an increased migration capacity which indicates increased aggressivity.
Conclusions: Sevoflurane exposure of breast cancer cells influences cell proliferation, phenotype and Akt isoform expression. Increased sevoflurane concentrations activate different Akt isoforms, putatively related to epithelial-mesenchimal transition and promote cancer cell invasion, migration and metastasis.
Key words: sevoflurane, Akt isoforms.

Changes of heart vegetative tonus after intravenous administration of three different agents for induction of general anesthesia

Feghiu Iuliana, Cobîlețchi Sergiu, *Baltaga Ruslan, Șandru Sergiu

Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova
*Corresponding author: rbaltaga@yahoo.com

Background: Aim of the study. Evaluation of heart vegetative tonus changes after intravenous administration of propofol, midasolam or tiopental for induction of general anesthesia.
Material and methods: The study was performed within Institute of Emergency Medicine and was approved by the Ethic Committee of the "Nicolae Testemițanu" SUMPh. In the study groups were involved 141 patients scheduled for elective general surgery. With TLC 5000 Holter ECG there were registered LFun (Low Frequency) – marker of sympathetic heart tonus, HFun (High Frequency) – marker of parasympathetic heart tonus and the HFun/HFun ratio – marker of sympathetic-parasympathetic heart balance. The heart vegetative tonus was registered 5 minutes in baseline and 5 minutes after intravenous administration of 2,5 mg/kg propofol with 2,0 mkg/kg fentanyl (group 1); 0,2-0,3 mkg/kg midasolam with 2,0 mkg/kg fentanyl (group 2) or 7-8 mg/kg tiopental with 2,0 mkg/kg fentanyl (group 3).
Results: Group 1: LFun enhanced from 66,8(95%CI62,6-70,9) to 72,0(95%CI 67,9-76,1) (p=0,004); HFun reduced from 33,2 (95%CI29,0-37,4) to 26,4(95%CI 20,4-34,3) (p=0,007) and the LFun/HFun ratio enhanced from 2,7(95%CI2,1-3,2) to 3,9(95%CI2,9-4,8) (p=0,003).
Group 2: LFun reduced from 67,7(95%CI 62,9-72,5) to 52,4(95%CI 62,9-70,0) (p=0,14); HFun enhanced from 27,4(95% CI21,4-37,0) to 47,5(95%CI 30,4-37,4) (p=0,01) and the LFun/HFun ratio reduced from 3,1(95%CI2,4-3,8) to 1,1(95%CI0,6-1,8) (p=0,02).
Group 3: LFun enhanced from 65,5(95%CI 60,8-70,1) to73,5(95%CI 68,4-78,6)(p=0,001); HFun reduced from 34,5(95%CI29,8-39,2) to 24,5(95%CI20,3-28,7)(p=0,001) and the LFun/HFun ratio enhanced from 2,7(95%CI 2,1-3,3) to 4,4(95%CI3,5-5,2) (p<0,001).
Conclusions: Administration of propofol or tiopental for induction of general anesthesia is associated with enhanced heart sympathetic vegetative tonus. Administration of midasolam for induction of general anesthesia leads to the development of heart parasympathicotonia.
Key words: vegetative cardiac tonus, LFun, HFun, LFun/HFun.