

ity of anesthetic agents could be caused by inhibition of the electron transport system. In this study, using high-resolved respirometry of human blood cells, the objective was to evaluate the influence of commonly used anesthetic agents in a wide concentration range on mitochondrial oxygen consumption in platelets.

#### [Materials and methods]

Platelets samples were isolated from healthy volunteers and were rapidly analyzed by high-resolution respirometry using an Oroboros-2k Oxygraph. Platelets were exposed to propofol (5-150 microg/ml), sevoflurane (0.4-8 mmol/L) and midazolam (0.1-20 microg/ml). Mitochondria were stimulated with complex-specific substrates and inhibitors.

Statistical analysis were performed using one way ANOVA with post hoc Dunnett's test and were compared to a separate control group ( $n=20$ ). Informed consent was received from all participants and the study was approved by the ethical committee of Tokyo Medical University.

#### [Results and discussion]

Within the therapeutic concentration-range of the investigated agents, no apparent inhibition of respiratory capacity was noted. Rather, at therapeutic concentrations, significant increases in mitochondrial respiratory parameters were detected for sevoflurane and propofol. Dose-dependent inhibition of respiration was found in the presence of high doses of propofol (30 microg/ml and above) and sevoflurane (1.6 mmol/L and above). The respiratory inhibition was more prominent for complex I respiration as compared to complex II-supported respiration. For midazolam no significant effects were noted at the concentration range investigated.

#### [Conclusion]

In freshly isolated and permeabilized human platelets, the commonly used anesthetics sevoflurane and propofol stimulate mitochondrial respiratory capacity at clinically relevant concentrations. At higher concentrations, these agents displayed a dose-dependent inhibition of complex I and II-supported respiration. The increased respiratory capacity induced by sevoflurane and propofol might be beneficial and the inhibition of respiration could be relevant to situations of prolonged or excessive exposure, especially in situations of tissue accumulation of these anesthetics.

### P3-47.

#### メトホルミン服用中の糖尿病患者でのピオグリタゾン併用効果—高分子量アディポネクチンの推移—

(八王子：糖尿病・内分泌・代謝内科)

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【目的】 メトホルミン服用中の2型糖尿病患者において、ピオグリタゾンの併用もしくはメトホルミンの増量を行い、高分子量アディポネクチンを含む各種臨床データの推移を比較検討した。

【方法】 HbA1c  $\geq$  6.9% (NGSP 値)、BMI  $\geq$  22 でメトホルミンを 250 mg~750 mg 服用中の2型糖尿病患者 18 名を、ピオグリタゾン (7.5 mg~30 mg) 併用群 8 名と、メトホルミン増量 (最大投与量 1,000 mg/日) 群 10 名に分け、治療方針の変更前、変更後 3 ヶ月、変更後 6 ヶ月で HbA1c、グリコアルブミン、空腹時血糖値、随時血糖値、総コレステロール、中性脂肪、LDL コレステロール、HDL コレステロール、空腹時 IRI、HOMA-IR、AST、ALT、BUN、Cr、随時尿中アルブミン定量 (クレアチニン換算値)、高分子量アディポネクチン (変更前と変更後 6 ヶ月のみ)、体脂肪率、体水分量、BMI、ウエスト周囲径、血圧を測定。また、既往歴、調査期間中の心血管イベント出現を含む合併症の有無を調査し、両群間で比較した。

【成績】 変更前と変更後 6 カ月の比較において、ピオグリタゾン併用群の高分子量アディポネクチン、HbA1c、HDL コレステロール、ピオグリタゾン併用群とメトホルミン増量群のグリコアルブミンに有意な改善を、メトホルミン増量群の HbA1c に改善傾向を認めたが、ピオグリタゾン併用群のウエスト周囲径は増加傾向を認めた。

【結論】 すでにメトホルミンを服用中の2型糖尿病患者において、ピオグリタゾンの併用により高分子量アディポネクチンの増加を認めた。