INFLUENCE OF THE CALCIUM ANTAGONIST BAY K 8644 ON MECHANICAL RESPONSES OF SKELETAL MUSCLE FROM NON SUSCEPTIBLE PATIENTS AND PATIENTS SUSCEPTIBLE TO MALIGNANT HYPERTHERMIA

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Transverse tubule Ca2+ regulation has been implicated in the abnormal Ca2+ induced-Ca2+ release (CICR) mechanism which is thought to be the principal defect in malignant hyperthermia (MH) (1). In order to determine if changes in Ca2+ flux through the sarcolemma may modify the halothane (H)-induced contracture, we monitored the influence of the Ca2+ agonist BAY K 8644 on normal and MH susceptible (MHS) human muscle in the presence or in the absence of extracellular Ca2+.

METHOD : Fifteen MHS patients and 20 MH non susceptible (MHN) patients were investigated with informed consent and approval by the Research Comittee (Univ. of Lille). The contracture methods have been previously described for the MH diagnostic procedures (2). In addition to the usual halothane and caffeine contracture tests, other muscle strips were exposed to 10 µM. BAY K 8644 in the presence of increasing concentration of halothane. In another series of experiment, the same protocol was performed in the absence of extracellular Ca2+.

Results : BAY K 8644 significantly reinforced the H contracture at 0.5,1 and 1.5 % of H in MHS muscle strips and had no significant influence on H effects in normal muscle. However, when the same experiment was performed in Ca2+ free solution, no contracture was observed in the presence of BAY K 8644.

Discussion : These results on muscle strips are in agreement with the hypothesis of an abnormal CICR release of the sarcoplasmic reticulum in MH skinned muscle fibers(3). Hence, the BAY K 8644-induced increase in Ca2+ flux through the sarcolemma enhanced the H induced contractures only in MHS muscle strips. This study also suggest that extracellular Ca2+ may play a role for the CICR mechanisme involved in MH

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MHS

H %	H alone n=15	H + BAY K n=15	H + BAY K + zero Ca2+ n=10
0.5	0.15 (±0.07)	1.01* (±0.17)	0
1	0.38 (±0.14)	1.02* (±0.14)	0
1.5	0.6 (±0.17)	0.86* (±0.12)	0
2	0.77 (±0.17)	0.77 (0.11)	0

MHN

H %	H alone n=20	H + BAY K n=20	H + BAY K + zero Ca2+ N=10
0.5	0	0	0
1	0	0.01 (±0.01)	0
1.5	0	0.06 (±0.03)	0
2	0	0.11 (±0.08)	0

Changes in tension (g) with H, H+BAY K an H+BAY K=zero Ca2+ in MHS and MHN muscle strips (n) ; values are means ±SEM ; *p<0.05 compared with H alone

TITLE: INTRAVENOUS CLONIDINE DOES NOT PROMOTE HYPOXEMIA AND PLATELET AGGREGATION IN MAN.

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Controversial reports exist concerning hypoxemia following systemic administration of Clonidine (CL).[1,2] Animal studies show dose dependant hypoxemia ascribed to platelet aggregation with pulmonary microembolism.[3] In vitro, Cl shows a great affinity for human platelets.[4] The aim of this study was to evaluate hypoxemia and platelet aggregation in man following intravenous administration of Cl.

Methods: With institutional approval and after informed consent, 20 patients (ASA I-II) without spontaneous or drug-induced coagulation disorder undergoing total hip replacement were studied. They were randomly divided into 2 groups: group A (n=10) received an IV loading dose of 4 µg/kg of Cl in 30 min. followed by an infusion of 1 µg/kg/h till the end of the procedure and group B (n=10) received saline. Platelet aggregation was assessed before infusion (P1), after the loading dose (P2) and at the end of infusion (P3). PaO2 was measured before anesthesia (FiO2 21%)(I), before femoral cementation (FiO2 40%)(II), 2 min. after prosthesis implantation (FiO2 100%)(III), before the end of the procedure (FiO2 40%)(IV) and in the recovery room (spontaneous breathing with FiO2 40% and 21%)(V-VI). Statistical analysis was done with Student t-test. Results are expressed as means ± SD.

Results: Both groups were comparable in terms of population , duration of procedure, perioperative blood losses and fluid replacement. PaO2 and platelet aggregation are presented in tables 1 and 2 respectively. No statistical differences were noted between the groups.

Table 1.

	I	II	III	IV	V	VI
Group A	84 ± 12	168 ± 44	311 ± 105	158 ± 40	110 ± 36	61 ± 10
Group B	82 ± 11	191 ± 37	341 ± 84	170 ± 38	104 ± 36	66 ± 15

Table 2.

	Group A	Group B
P1 - ADP	68.0 ± 18.4	51.7 ± 14.7
Collagen	77.9 ± 12.9	73.3 ± 12.3
Arach.Acid	94.5 ± 8.1	87.5 ± 11
Ristocetin	82.1 ± 15.9	82.3 ± 12.8
P2 - ADP	71.7 ± 14	60.3 ± 14.3
Collagen	74.7 ± 9.1	78.4 ± 12.3
Arach.Acid	95.6 ± 9	104.7 ± 17
Ristocetin	51.7 ± 23.5	39.8 ± 31.2
P3 - ADP	66.8 ± 13.1	56.9 ± 16.4
Collagen	76.5 ± 6.5	72.8 ± 27.3
Arach.Acid	86.8 ± 17.6	88.8 ± 24.7
Ristocetin	41.1 ± 33.2	71.1 ± 22.5

Conclusion: During total hip replacement, Cl did not promote hypoxemia nor additional platelet aggregation. Animal studies can be explained by inter species variations in platelet aggregation.

References:
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