**Additional File 2**

**The effects of salbutamol on epithelial ion channels depend on the etiology of acute respiratory distress syndrome but not the route of administration**

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**Additional Results**

Figure 3 W_D-ratio.tif

Figure S1: Wet-to-dry (W/D) ratio. All values are expressed as mean and standard deviation. Differences between groups (SALB vs. CTRL; SALB-iv vs. SALB-it) were tested separately for ARDSp and ARDSexp using one-way ANOVA followed by Bonferroni correction. Statistical significance was accepted at α = 0.05. CTRL = control; SALB = salbutamol; i.t. = intratracheally; i.v. = intravenously; ARDSp = pulmonary acute respiratory distress syndrome; ARDSexp = extrapulmonary acute respiratory distress syndrome.

**Table S2** Body weight, anesthesia and fluid therapy

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **ARDSp** | | | | **ARDSexp** | | | |  |
| CTRL-it | SALB-it | CTRL-iv | SALB-iv | CTRL-it | SALB-it | CTRL-iv | SALB-iv |  |
|  |  |  |  |  |  |  |  |  |  |
| **Body weight [kg]** | 0.300 ± 0.027 | 0.299 ± 0.029 | 0.290 ± 0.032 | 0.301 ± 0.035 | 0.294 ± 0.027 | 0.298 ± 0.036 | 0.295 ± 0.029 | 0.295 ± 0.015 | ns |
|  |  |  |  |  |  |  |  |  |  |
| **Midazolam [mg]** | 1.08 ± 0.24 | 1.12 ± 0.18 | 1.06 ± 0.26 | 1.05 ± 0.10 | 1.04 ± 0.20 | 1.05 ± 0.12 | 0.91 ± 0.29 | 0.98 ± 0.13 | ns |
|  |  |  |  |  |  |  |  |  |  |
| **Ketamine [mg]** | 54.1 ± 12.3 | 56.4 ± 9.5 | 53.5 ± 13.3 | 52.5 ± 5.0 | 52.3 ± 9.9 | 55.5 ± 8.7 | 45.8 ± 14.7 | 49.4 ± 6.8 | ns |
|  |  |  |  |  |  |  |  |  |  |
| **Crystalloid [mL]** | 4.3 ± 0.7 | 4.1 ± 0.4 | 4.3 ± 0.3 | 4.1 ± 0.5 | 4.3 ± 0.6 | 4.2 ± 1.0 | 4.5 ± 0.9 | 4.3 ± 4.5 | ns |
|  |  |  |  |  |  |  |  |  |  |
| **Colloid [mL]** | 1.1 ± 0.2 | 1.2 ± 0.3 | 1.6 ± 0.9 | 1.6 ± 0.7 | 1.4 ± 0.6 | 1.6 ± 0.6 | 1.1 ± 0.2 | 1.6 ± 0.7 | ns |
|  |  |  |  |  |  |  |  |  |  |

All values are expressed as mean and standard deviation. Differences between groups were tested separately for ARDSp and ARDSexp using one-way ANOVA followed by Bonferroni correction. Statistical significance was accepted at α = 0.05. ns = non-significant; CTRL = control; SALB = salbutamol; it = intratracheally; iv = intravenously; ARDSp = pulmonary acute respiratory distress syndrome; ARDSexp = extrapulmonary acute respiratory distress syndrome.

**Table S3** Ventilator parameters and respiratory mechanics

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | | | **ARDSp** | | | | **ARDSexp** | | | |
| CTRL-it | SALB-it | CTRL-iv | SALB-iv | CTRL-it | SALB-it | CTRL-iv | SALB-iv |
| **VT [mL]** |  | |  |  |  |  |  |  |  |  |
|  | BL2 | | 6.02 ± 0.32 | 6.01 ± 0.45 | 6.01 ± 0.43 | 6.99 ± 0.46 | 6.08 ± 0.45 | 6.13 ± 0.33 | 5.94 ± 0.25 | 5.78 ± 0.32 |
|  | T30 | | 5.86 ± 0.28 | 6.04 ± 0.85 | 6.10 ± 0.52 | 6.27 ± 0.48 | 6.10 ± 0.35 | 6.10 ± 0.50 | 5.96 ± 0.62 | 6.02 ± 0.32 |
|  | T60 | | 6.19 ± 0.38 | 5.68 ± 0.37 | 6.60 ± 0.63 | 6.11 ±0.40 | 5.99 ± 0.51 | 6.31 ± 0.41 | 5.89 ± 0.81 | 6.02 ± 0.46 |
|  | Time effect | | Ns | | | | ns | | | |
|  | Interaction | | p<0.05 | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |
| **RR [1/min]** |  | |  |  |  |  |  |  |  |  |
|  | BL2 | | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 0 | 79 ± 1 | 79 ± 1 | 79 ± 1 |
|  | T30 | | 79 ± 1 | 80 ± 0 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 80 ± 0 | 79 ± 1 | 79 ± 2 |
|  | T60 | | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 | 79 ± 1 |
|  | Time effect | | Ns | | | | ns | | | |
|  | Interaction | | Ns | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |
| **MV [L/min]** |  | |  |  |  |  |  |  |  |  |
|  | BL2 | | 0.143 ± 0.011 | 0.142 ± 0.019 | 0.143 ± 0.016 | 0.147 ± 0.017 | 0.139 ± 0.012 | 0.136 ± 0.010 | 0.136 ± 0.019 | 0.141 ± 0.010 |
|  | T30 | | 0.144 ± 0.022 | 0.149 ± 0.015 | 0.140 ± 0.020 | 0.150 ± 0.020 | 0.136 ± 0.015 | 0.145 ± 0.021 | 0.137 ± 0.011 | 0.141 ± 0.014 |
|  | T60 | | 0.152 ± 0.028 | 0.138 ± 0.017 | 0.140 ± 0.012 | 0.152 ± 0.021 | 0.136 ± 0.016 | 0.147 ± 0.021 | 0.137 ± 0.017 | 0.143 ± 0.008 |
|  | Time effect | | Ns | | | | ns | | | |
|  | Interaction | | Ns | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |
| **Pawpeak [cmH2O]** | | |  |  |  |  |  |  |  |  |
|  | BL2 | | 11.8 ± 5.5 | 10.0 ± 5.1 | 12.0 ± 3.5 | 14.6 ± 2.3 | 13.1 ± 3.6 | 13.8 ± 3.1 | 10.3 ± 3.3 | 11.8 ± 3.6 |
|  | T30 | | 14.6 ± 4.5 | 15.0 ± 5.3 | 12.6 ± 3.3 | 13.0 ± 3.1 | 11.6 ± 3.7 | 17.8 ± 4.1 | 14.5 ± 3.4 | 13.1 ± 2.7 |
|  | T60 | | 15.7 ± 4.3 | 13.8 ± 5.4 | 14.9 ± 2.8 | 14.7 ± 1.9 | 13.0 ± 1.5 | 16.1 ± 3.8 | 13.8 ± 3.5 | 12.5 ± 2.2 |
|  | Time effect | | p<0.05 | | | | p<0.05 | | | |
|  | Interaction | | Ns | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |
| **Pawmean [cmH2O]** | | |  |  |  |  |  |  |  |  |
|  | | BL2 | 7.1 ± 5.4 | 8.1 ± 2.7 | 7.9 ± 1.6 | 9.5 ± 1.7 | 8.1 ± 2.8 | 9.0 ± 2.8 | 5.9 ± 2.2 | 7.0 ± 3.0 |
|  | | T30 | 8.0 ± 4.0 | 9.1 ± 4.9 | 8.0 ± 2.3 | 7.5 ± 2.3 | 7.1 ± 2.5 | 11.6 ± 4.0 | 9.1 ± 3.0 | 7.6 ± 2.2 |
|  | | T60 | 9.2 ± 5.0 | 8.0 ± 5.1 | 9.3 ± 2.3 | 8.4 ± 2.0 | 7.2 ± 1.5 | 9.8 ± 3.7 | 8.1 ± 3.2 | 6.8 ± 2.2 |
|  | | Time effect | Ns | | | | ns | | | |
|  | | Interaction | Ns | | | | ns | | | |
|  | | Group effect | Ns | | | | ns | | | |
| **Ers [mL/cmH2O]** | | |  |  |  |  |  |  |  |  |
|  | BL2 | | 4.44 ± 0.88 | 3.56 ± 1.55 | 4.03 ± 1.09 | 4.62 ± 1.44 | 4.78 ± 0.91 | 4.53 ± 1.38 | 4.58 ± 1.25 | 4.03 ± 0.59 |
|  | T30 | | 5.48 ± 0.65 | 5.26 ± 1.25 | 4.83 ± 0.83 | 5.22 ± 1.76 | 5.19 ± 1.11 | 6.31 ± 1.81 | 6.13 ± 0.83 | 5.69 ± 1.63 |
|  | T60 | | 5.94 ± 1.27 | 5.73 ± 0.83 | 5.84 ± 1.13 | 6.48 ± 1.75 | 6.37 ± 1.28 | 6.56 ± 1.40 | 6.67 ± 0.83 | 5.93 ± 0.59 |
|  | Time effect | | p<0.001 | | | | p<0.001 | | | |
|  | Interaction | | Ns | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |
| **Rrs [cmH2O/L/s]** | | |  |  |  |  |  |  |  |  |
|  | BL2 | | 152.0 ± 21.9 | 181.0 ± 109.5 | 148.3 ± 66.5 | 151.3 ± 72.6 | 172.3 ± 50.8 | 194.0 ± 94.2 | 143.4 ± 57.8 | 161.8 ± 59.2 |
|  | T30 | | 177.3 ± 32.8 | 269.5 ± 109.1 | 163.3 ± 44.5 | 185.9 ± 122.9 | 205.3 ± 85.5 | 265.7 ± 139.1 | 262.6 ± 129.4 | 236.3 ± 92.8 |
|  | T60 | | 168.9 ± 58.8 | 265.2 ± 161.7 | 195.9 ± 74.2 | 236.3 ± 108.4 | 275.3 ± 168.1 | 226.7 ± 75.5 | 278.1 ± 168.9 | 252.4 ± 114.6 |
|  | Time effect | | p<0.05 | | | | p<0.001 | | | |
|  | Interaction | | Ns | | | | ns | | | |
|  | Group effect | | Ns | | | | ns | | | |

All values are expressed as mean and standard deviation. Differences between and within groups (*group and time effects, BL2-T60 as well as their interactions*) were tested with two-way ANOVA and adjusted for repeated measures according to the Bonferroni method for ARDSp and ARDSexp separately. Statistical significance was accepted at α = 0.05. ns = non-significant; CTRL = control; SALB = salbutamol; it = intratracheally; iv = intravenously; ARDSp = pulmonary acute respiratory distress syndrome; ARDSexp = extrapulmonary acute respiratory distress syndrome; BL2 = baseline 2; T30 and T60 = 30 and 60 min after initiation of therapy; VT = tidal volume; RR = respiratory rate; MV = minute ventilation; Pawpeak = peak inspiratory airway pressure; Pawmean = mean inspiratory airway pressure; Ers = elastance of the respiratory system; Rrs = resistance of the respiratory system.