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| **Supplementary Table 1. Differences between faster titration group, slower titration group, and ultra-slower titration group** | | | | | | |
|  | Total | Faster titration group | Slower titration group | Ultra-slower titration group | Statistical test | p |
| Number of patients, n (%) | 512 | 129 (25) | 270 (53) | 113 (22) |  |  |
| Age, years, mean (SD) |  | 43.2 (12.6) | 43.9 (12.4) | 44.9 (13.6) | F (2, 509) = 0.506 | 0.60 |
| Male, n (%) | 295 (57) | 79 (61) | 155 (57) | 61 (54) | Fisher's exact test | 0.53 |
| BMI, kg/m2, mean (SD) |  | 23.6 (4.1) | 24.0 (4.5) | 24.0 (4.5) | F (2, 509) = 0.387 | 0.68 |
| CP equivalent of concomitant antipsychotics at start of clozapine, mg, mean (SD) |  | 702 (613) | 490 (539) | 419 (398) | Kruskal-Wallis test | <0.001 a |
| Diazepam equivalent of concomitant benzodiazepines at start of clozapine, mg, mean (SD) |  | 12.7 (18.6) | 12.3 (15.0) | 11.2 (10.8) | Kruskal-Wallis test | 0.31 |
| CTR |  | 0.93 (0.13) | 0.54 (0.09) | 0.29 (0.07) | Kruskal-Wallis test | <0.001 b |
|  |  |  |  |  |  |  |
| Number of febrile patients, n (%) |  |  |  |  |  |  |
| Fever duration 1 day or more | 141 (28) | 52 (41) | 60 (22) | 29 (26) | Fisher's exact test | <0.001 c |
| Fever duration 2 days or more | 96 (19) | 44 (34) | 37 (14) | 15 (14) | Fisher's exact test | <0.001 d |
| Fever duration 4 days or more | 60 (12) | 32 (25) | 19 (7) | 9 (8) | Fisher's exact test | <0.001 e |
|  |  |  |  |  |  |  |
| Clozapine discontinuation due to fever, n (%) | 17 (3.3) | 7 (5.4) | 7 (2.6) | 3 (2.7) | Fisher's exact test | 0.33 |
| Abbreviations: BMI, body mass index; CI, confidence interval; CP, chlorpromazine; CTR, clozapine titration rate; OR, odds ratio; SD, standard deviation. | | | | | | |
| a: Faster titration group―Group A, p = 0.0023; Faster titration group―Group B, p = 0.0023; Group A―Group B, p = 1 (Bonferroni) | | | | | | |
| b: Faster titration group―Group A, p<0.00001; Faster titration group―Group B, p<0.00001; Group A―Group B, p = p<0.00001 (Bonferroni) | | | | | | |
| c: Faster titration group―Group A, p = 0.00061; Faster titration group―Group B, p = 0.05973; Group A―Group B, p = 1.000 (Bonferroni) | | | | | | |
| d: Faster titration group―Group A, p = 0.000014; Faster titration group―Group B, p=0.00049; Group A―Group B, p = 1.000 (Bonferroni) | | | | | | |
| e: Faster titration group―Group A, p < 0.00001; Faster titration group―Group B, p = 0.0015; Group A―Group B, p = 1.000 (Bonferroni) | | | | | | |

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| **Supplementary Table 2. Logistic regression analysis for the risk of clozapine-associated fever: Sensitivity analysis based on smoking status** | | | |
|  | OR | 95％CI | p |
| Titration group (Slower)a | 1.21 | 0.61-2.43 | 0.59 |
| Titration group (Faster)a | 4.42 | 2.13-9.15 | < 0.001 |
| Sex (Male) | 1.82 | 1.09-3.02 | 0.021 |
| Obesity (BMI > 30) | 1.13 | 0.55-2.33 | 0.75 |
| Hospitals that allow smoking | 0.48 | 0.29-0.80 | 0.0050 |
|  |  |  |  |
| **Concomitant drugs at start of clozapine** |  |  |  |
| Valproic acid | 2.09 | 1.19-3.66 | 0.011 |
| Lithium | 1.26 | 0.69-2.29 | 0.45 |
| Olanzapine | 0.84 | 0.47-1.49 | 0.55 |
| Quetiapine | 2.44 | 1.02-5.84 | 0.046 |
| Suvorexant | 0.65 | 0.29-1.45 | 0.29 |
| Lemborexant | 0.85 | 0.29-0.80 | 0.70 |
| Abbreviations: BMI, body mass index; CI, confidence interval; CP, chlorpromazine; OR, odds ratio. | | | |
| a: Ultra-slower is the reference. |  |  |  |