

1 **Table S1. Rescue medication**

Variables	Placebo group (N=20)	Study group (N=15)	p value
Total dose			
Remifentanil (mg)	16.54±16.92	9.81±17.66	0.261
Dexmedetomidine (mcg)	1784.03±2354.07	1482.83±3325.28	0.755
Midazolam (mg)	168.93±428.59	74.87±191.58	0.435
Average dose			
Remifentanil (mg/day)	2.75±2.40	2.30±3.40	0.652
Dexmedetomidine (mcg/day)	304.57±358.54	367.22±646.43	0.717
Midazolam (mg/day)	25.21±61.34	11.89±27.73	0.440
Other sedative drugs			
Haloperidol	3 (15.0)	0 (0.0)	0.117
Other drugs for delirium ^a	6 (30.0)	3 (20.0)	0.503

2 Note: Data are expressed as number (percentage) or mean ± standard deviation

3 ^aOther drugs for delirium included lorazepam or oral anti-psychotics

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Table S2. Previous randomized controlled trials of pharmacologic delirium prophylaxis in ICU

Drug	Country	Study design	Setting	Cases	Primary outcome	Main results
Risperidone [19] 2007	Thailand	Prospective, double-blind, RCT	Cardiac surgery patient	Study: 63 Placebo: 63	Incidence of postoperative delirium	Reduced (11.1% vs. 31.7%, p=0.009, RR=0.35)
Rivastigmine [18] 2009	Swiss	Prospective, Double- blind, RCT	Cardiac surgery patient	Study: 59 Placebo: 61	Postoperative delirium within 6 days	Failed (30% vs. 32%, p=0.8)
Haloperidol [15] 2005	Netherland	Prospective, Double- blind, RCT	Hip surgery Patients	Study: 212 Placebo: 218	Incidence of postoperative delirium	No efficacy (15.1% vs. 16.5%, RR=0.91)
Haloperidol [14] 2012	China	Prospective, Double- blind, RCT	Non-cardiac Surgery patients	Study: 229 Placebo: 228	Incidence of delirium within 7 days after surgery	Decreased (15.3% vs. 23.2%, p=0.031)
Haloperidol Ziprasidone [16] 2010	USA	Prospective, Double- blind, RCT	Medical ICU Surgical ICU Trauma ICU	Haloperidol: 35 Ziprasidone: 30 Placebo: 36	Number of days without delirium or coma	Feasible (14.0 vs. 15.0 vs. 12.5 days, p=0.66)
Haloperidol [39] 2017	Japan	Prospective, open-label randomized trial	Postoperative elderly patients (>75yrs)	Study: 101 Placebo: 100	Incidence of severe postoperative delirium	Reduced (18.2% vs. 32.0%, p=0.002)
Haloperidol	Netherlands			1 mg haloperidol: 350	28 days survival	No difference

[17]2018		Prospective, Double- blind, RCT	Medical ICU Surgical ICU Trauma ICU	2 mg haloperidol: 732 Placebo: 707		
Dexmedetomidine [20] 2016	China	Prospective, Double- blind, RCT	Non-cardiac Surgery patients	Study: 350 Placebo: 350	Incidence of postoperative delirium	Decreased (9% vs. 23%, p<0.001, RR=0.35) Reduced delirium
Dexmedetomidine [21] 2018	Canada, US	Prospective, double-blind, RCT	medical-surgical ICU	Study:50 Placebo: 50	Proportion of patients who remained free of delirium	Greater proportion of patients who remained delirium-free during the ICU stay (80% vs 54%, p=0.006 RR, 0.44)

Abbreviations: ICU, intensive care unit; RCT, randomized controlled trial; RR, relative risk