Supplementary material

Supplementary Table 1. Patient characteristics.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Daytime Group  (n = 145) | | | | |  | Nighttime Group  (n = 145) | | | | |  |
| Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value | Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value |
| Age (yr) | | 30.0 ±5.7 | 32.1 ± 4. 2 | 31.2 ± 3.7 | 30.6 ± 5.6 | 32.1 ± 5.3 | 0.418 | 29.9 ± 6.0 | 31.3 ± 5.0 | 29.0 ± 6.0 | 31.9 ± 6.2 | 30.7 ± 5.6 | 0.185 |
| Height (cm) | | 160.9 ± 5.8 | 159.9 ± 4.4 | 159.9 ± 5.6 | 160.6 ± 6.0 | 160.3 ± 7.1 | 0.959 | 160.9 ± 4.0 | 162.5 ± 6.9 | 159.0 ± 6.7 | 160.0 ± 6.4 | 158.9 ± 5.5 | 0.132 |
| Weight (kg) | | 56.5 ± 9.2 | 54.8 ± 6.0 | 55.8 ± 7.3 | 57.1 ± 6.1 | 55.1 ± 6.3 | 0.717 | 58.2 ± 7.8 | 57.5 ± 6.6 | 55.0 ± 7.0 | 56.3 ± 6.1 | 54.5 ± 5.5 | 0.111 |
| BMI (kg·m−2) | | 21.7 ± 2.4 | 21.4 ± 2.0 | 21.7 ± 2.1 | 22.1 ± 2.0 | 21.5 ± 2.2 | 0.758 | 22.5 ± 2.2 | 21.7 ± 1.5 | 21.8 ± 2.4 | 22.0 ± 2.1 | 21.6 ± 2.1 | 0.495 |
| Type of hysteroscopic surgery | | | | | | | | | | | | | |
|  | Polypectomy | 18 (62.1) | 20 (69.0) | 19 (65.5) | 18 (62.1) | 21 (72.4) | 0.902 | 19 (65.5) | 17 (58.6) | 20 (69.0) | 18 (62.1) | 20 (69.0) | 0.905 |
| Lysis of adhesion | 11 (37.9) | 9 (31.0) | 10 (34.5) | 11 (37.9) | 8 (27.6) | 10 (34.5) | 12 (41.4) | 9 (31.0) | 11 (37.9) | 9 (31.0) |
| Surgery duration (min) | | 22.2 ± 6.0 | 24.1 ± 8.9 | 21.7 ± 7.1 | 23.1 ± 8.7 | 24.1 ± 7.2 | 0.220 | 23.4 ± 7.4 | 21.6 ± 6.8 | 23.2 ± 9.4 | 22.4 ± 7.5 | 22.9 ± 6.6 | 0.738 |

Data are presented as mean ± SD or N (%).

BMI: Body mass index.

Supplemental Table 2. Efficacy outcomes.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Daytime Group  (n = 145) | | | | |  | Nighttime Group  (n = 145) | | | | |  |
| Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value | Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value |
| Primary outcome | | | | | | | | | | | | | |
|  | Effective number of patients (%) | 17 (58.6) | 9 (31.0)† | 17 (58.6)‡ | 22 (75.9)†‡§ | 25 (86.2)†‡§ | **<0.001** | 21 (72.4) | 16 (55.2)† | 22 (75.9)‡ | 25 (86.2)†‡ | 26 (90.0)†‡§ | **0.020** |
| Secondary outcomes | | | | | | | | | | | | | |
|  | One rescue dose of ciprofol | 11 (37.9) | 16 (55.2)† | 10 (34.5)‡ | 7 (24.1)†‡§ | 3 (10.3)†‡§|| | **0.005** | 7 (24.1) | 10 (34.5) | 8 (27.6) | 4 (13.8) | 3 (10.3) | 0.155 |
| Two rescue doses of ciprofol | 1 (3.4) | 3 (10.3) | 0 (0) | 0 (0) | 1 (3.4) | 0.184 | 0 (0) | 3 (10.3) | 0 (0) | 0 (0) | 0 (0) | 0.016 |
| Three rescue doses of ciprofol | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Other outcomes | | | | | | | | | | | | | |
|  | Induction requirements of ciprofol (mg/kg) | --- | 0.40 (0.30, 0.50) | 0.40 (0.40, 0.60) | 0.50 (0.50, 0.60) | 0.60 (0.60, 0.60)‡§ | **<0.001** | --- | 0.32 (0.30, 0.50) | 0.40 (0.40, 0.55) | 0.50 (0.50, 0.50)‡ | 0.60 (0.60, 0.60)‡§|| | **<0.001** |
| Total requirements of ciprofol (mg/kg) | --- | 0.95 (0.85, 1.95) | 0.92 (0.80, 1.19) | 1.09 (0.91, 1.23) | 1.00 (0.93, 1.15) | 0.404 | --- | 0.89 (0.80, 1.03) | 1.15 (0.83, 1.28) | 1.02 (0.83, 1.11) | 0.98 (0.88, 1.12) | 0.058 |
| Total requirements of ciprofol (mg/kg/min) | --- | 0.05 (0.04, 0.05) | 0.05 (0.04, 0.06) | 0.05 (0.04, 0.06) | 0.05 (0.04, 0.06) | 0.148 | --- | 0.04 (0.04, 0.05) | 0.04 (0.04, 0.06) | 0.04 (0.04, 0.06) | 0.04 (0.04, 0.05) | 0.788 |
| Time to anesthesia emergence (min) | 7.0 (6.0, 8.0) | 5.0 (4.0, 6.0)† | 6.0 (6.0, 7.0)‡ | 6.0 (5.0, 8.0)‡ | 6.0 (5.0, 8.0)†‡ | **<0.001** | 8.0 (8.0, 9.0) | 8.0 (6.0, 9.0) | 8.0 (7.0, 9.0) | 8.0 (7.0, 9.0) | 8.0 (7.0, 9.0) | 0.482 |
| Length of PACU stay (min) | 30.0 (27.5, 32.0) | 29.0 (26.5, 30.0) | 28.0 (27.0, 30.0) | 29.0 (27.0, 30.0) | 28.0 (26.5, 32.0) | 0.228 | 30.0 (27.5, 31.0) | 30.0 (26.5, 32.0) | 29.0 (27.0, 31.0) | 30.0 (27.0, 31.0) | 30.0 (28.0, 32.0) | 0.802 |
| Intraoperative adverse events\* | 22 (75.9) | 12 (41.4)† | 12 (41.4)† | 15 (51.7) | 16 (55.2) | **0.045** | 21 (72.4) | 12 (41.4)† | 14 (48.3) | 16 (55.2) | 22 (75.9)‡§ | **0.029** |
| Postoperative adverse events\* | 17 (58.6) | 6 (20.7)† | 3 (10.3)† | 2 (6.9)† | 3 (10.3)† | **<0.001** | 15 (51.7) | 4 (13.8)† | 5 (17.2)† | 4 (13.8)† | 6 (20.7)† | **0.003** |

Data are presented as median (interquartile range) or N (%) or mean (95% CI). *p* values in bold indicate < 0.05.

Data are presented as mean ± SD or N (%) or median (interquartile range).

\*Included hypertension, hypotension, [bradycardia](file:///C:/Users/Administrator/AppData/Local/youdao/dict/Application/8.9.3.0/resultui/html/index.html#/javascript:;), tachycardia, desaturation, injection pain, nausea and vomiting, and shivering.

†*p* < 0.005, compared with Propofol 2 mg/kg after Bonferroni correction in Daytime group or Nighttime group.

‡*p* < 0.005, compared with Ciprofol 0.3 mg/kg after Bonferroni correction in Daytime group or Nighttime group.

§*p* < 0.005, compared with Ciprofol 0.4 mg/kg after Bonferroni correction in Daytime group or Nighttime group.

||*p* < 0.005, compared with Ciprofol 0.5 mg/kg after Bonferroni correction in Daytime group or Nighttime group.

PACU: post-anesthesia care unit.

Supplemental Table 3. Postoperative numeric rating scale score of pain and Ramsay sedation scale score.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Daytime Group  (n = 145) | | | | |  | Nighttime Group  (n = 145) | | | | |  |
| Propofo  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value | Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value |
| Numeric rating scale of pain, median (IQR), point\* | | | | | | | | | | | | | |
|  | 1 h after surgery | 2 (1, 2) | 1 (1, 2) | 2 (1, 2) | 1 (1, 2) | 2 (1, 2) | 0.363 | 2 (1, 2) | 1 (1, 2) | 1 (1, 2) | 1 (1, 2) | 2 (1, 2) | 0.168 |
| 6 h after surgery | 0 (0, 1) | 1 (0, 2) | 0 (0, 1) | 0 (0, 1) | 1 (0, 2) | 0.384 | 1 (0, 2) | 1 (0, 2) | 1 (0, 2) | 1 (0, 1) | 0 (0, 1) | 0.266 |
| 12 h after surgery | 0 (0, 1) | 0 (0, 1) | 0 (0, 1) | 0 (0, 1) | 0 (0, 1) | 0.648 | 0 (0, 1) | 0 (0, 1) | 0 (0, 1) | 1 (0, 1) | 0 (0, 1) | 0.769 |
| 1 d after surgery | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0.940 | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0 (0, 0) | 0.969 |
| Ramsay sedation scale, median (IQR), point† | | | | | | | | | | | | | |
|  | 1 h after surgery | 3 (3, 3) | 2 (2, 2)§ | 2 (2, 2)§ | 2 (2, 2)§ | 2 (2, 2)§ | **<0.001** | 3 (3, 3) | 2 (2, 2)§ | 2 (2, 2)§ | 2 (2, 2)§ | 2 (2, 3)§ | **<0.001** |
| 6 h after surgery | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 0.320 | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 0.966 |
| 12 h after surgery | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | >0.999 | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | >0.999 |
| 1 d after surgery | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | >0.999 | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | 2 (2, 2) | >0.999 |

Data are median (interquartile range). *p* values in bold indicate < 0.05.

\*Score ranges from 0 to 10, where 0 = no pain and 10 = the worst pain.

†Ramsay sedation score ranges from 1 (restlessness) to 6 (deeply asleep and does not respond) and 2 indicates completely awake, quiet and cooperative.

§*p* < 0.005, compared with Propofol 2 mg/kg after Bonferroni correction in Daytime group or Nighttime group.

Supplemental Table 4. Intraoperative and postoperative data and side effects.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Daytime Group  (n = 145) | | | | |  | Nighttime Group  (n = 145) | | | | |  |
|  | | Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value | Propofol  2 mg/kg  (n = 29) | Ciprofol  0.3 mg/kg  (n = 29) | Ciprofol  0.4 mg/kg  (n = 29) | Ciprofol  0.5 mg/kg  (n = 29) | Ciprofol  0.6 mg/kg  (n = 29) | *p-*value |
| Postoperative data | | | | | | | | | | | | | |
|  | Use of NSAIDs | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Use of opioids | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Use of other painkillers | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Overall satisfaction score (point)\* | 10 (9.5, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 0.056 | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 0.351 |
| Modified Aldrete score | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 0.371 | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 10 (10, 10) | 0.850 |
| Length of hospital stay after surgery (d) | 1 (1, 2) | 1 (1, 2) | 1 (1, 2) | 1 (1, 1) | 1 (1, 1.5) | 0.789 | 1 (1, 2) | 1 (1, 1) | 1 (1, 1) | 1 (1, 1) | 1 (1, 2) | 0.827 |
| Postoperative complications† | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Intraoperative adverse events | | | | | | | | | | | | | |
|  | Tachycardia‡ | 1 (3.4) | 1 (3.4) | 1 (3.4) | 1 (3.4) | 2 (6.9) | 0.952 | 1 (3.4) | 2 (6.9) | 1 (3.4) | 0 (0.0) | 1 (3.4) | 0.723 |
| [Bradycardia](file:///C:/Users/Administrator/AppData/Local/youdao/dict/Application/8.9.3.0/resultui/html/index.html#/javascript:;)§ | 1 (3.4) | 0 (0.0) | 1 (3.4) | 1 (3.4) | 1 (3.4) | 0.587 | 1 (3.4) | 0 (0.0) | 1 (3.4) | 1 (3.4) | 2 (6.9) | 0.723 |
| Hypertension|| | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Hypotension¶ | 7 (24.1) | 6 (20.7) | 5 (17.2) | 6 (20.7) | 5 (17.2) | 0.963 | 8 (27.6) | 7 (24.1) | 7 (24.1) | 9 (31.0) | 9 (31.0) | 0.952 |
| Desaturation\*\* | 11 (37.9) | 3 (10.3) | 3 (10.3) | 6 (20.7) | 7 (24.1) | 0.055 | 11 (37.9) | 3 (10.3) | 5 (17.2) | 6 (20.7) | 10 (34.5) | 0.070 |
| Nausea and vomiting | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Shivering | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Injection pain | 11(37.9) | 1 (3.4)†† | 0 (0.0)†† | 0 (0.0)†† | 0 (0.0)†† | **<0.001** | 10 (34.5) | 0 (0.0)†† | 0 (0.0)†† | 0 (0.0)†† | 0 (0.0)†† | **<0.001** |
| Postoperative adverse events | | | | | | | | | | | | | |
|  | Tachycardia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| [Bradycardia](file:///C:/Users/Administrator/AppData/Local/youdao/dict/Application/8.9.3.0/resultui/html/index.html#/javascript:;) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Hypertension | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Hypotension | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Desaturation | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | >0.999 |
| Nausea and vomiting | 4 (13.8) | 4 (13.8) | 2 (6.9) | 2 (6.9) | 2 (6.9) | 0.763 | 3 (10.3) | 4 (13.8) | 4 (13.8) | 3 (10.3) | 4 (13.8) | 0.984 |
| Shivering | 2 (6.9) | 1 (3.4) | 1 (3.4) | 0 (0.0) | 1 (3.4) | 0.584 | 2 (6.9) | 0 (0.0) | 1 (3.4) | 1 (3.4) | 2 (6.9) | 0.656 |

Data are presented as median (interquartile range) or N (%). *p* values in bold indicate < 0.05.

PACU: post-anesthesia care unit; NSAIDs: Nonsteroidal Antiinflammatory Drugs.

\*Scale range from 0 to 10 (0 represents the worst satisfaction and 10 represents the best satisfaction).

†Generally deﬁned as new-onset medical conditions that were harmful to patients’ recovery and required medical intervention, *i.e.*, grade II or higher on the Clavien-Dindo classiﬁcation.

‡Defined as heart rate >100 beats per minute or an increase of >20% from baseline.

§Defined as heart rate <60 beats per minute or a decrease of >20% from baseline.

||Defined as systolic blood pressure >160 mmHg or an increase of >30% from baseline.

¶Defined as systolic blood pressure <90 mmHg or a decrease of >30% from baseline.

\*\*Defined as pulse oxygen saturation less than 90% or a decrease of more than 5% (absolute value) from baseline.

††*p* <0.005, compared with Propofol 2 mg/kg after Bonferroni correction in Daytime group or Nighttime group.