Supplementary Material 1. Morphine/Morphine Milligram Equivalent Use Among Participants During Hospitalization

| Authors | Design; no. of participants; study length | Pain rating on admission | Opioid, dose | Pain response | Major findings |
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| Al-Anazi et al, 2017[1] | Retrospective cohort studyn = 99Observation period: 3 days | Mean ± SD where 0 = no pain and 10 = severe pain5.43 ± 1.73 | Cumulative daily dose of morphine ± SDDay 1: 215 ± 128 mg (PCA group); 44 ± 25 mg (intermittent IV group)Day 2: 331 ± 101 mg (PCA group); 45 ± 28 mg (intermittent IV group)Day 3: 230 ± 84 mg (PCA group); 50 ± 31 mg (intermittent IV group) | Intermittent IV vs. PCA IV groupsDay 1 (P < 0.0004)2.7% vs. none: no pain24.3% vs. none: mild pain60.8% vs. 84%: moderate pain 12.1% vs. 16%: severe painIntermittent IV vs. PCA IV groupsDay 2 (P < 0.0008)8.1% vs. none: no pain29.7% vs. 12%: mild pain59.5% vs. 76%: moderate pain 2.7% vs. 12%: severe painIntermittent IV vs. PCA IV groupsDay 3 (P < 0.0032)12.1% vs. 4%: no pain22.9% vs. 12%: mild pain60.8% vs. 72%: moderate pain4.2% vs. 12%: severe pain | Participants in the intermittent IV group experienced a significant reduction (P < 0.0004) in pain compared to those in the PCA group. Participants in the PCA group were administered significantly higher amounts (P < 0.000003) of mean total morphine over 3 days. |
| Ballas et al, 2010[2] | Randomized, double-blind, placebon= 299Observation period in days:Treatment groupHU: 7.6 ± 6.7Placebo: 7.8 ± 6.5HU response groupResponders: 5.9 ± 2.6Non-responders: 7.7 ± 6.8 | Not reported | Mean daily dose of IV MME (SE)Treatment groupHU: 42.7 (1.1)Placebo: 41.3 (1.1)HU response groupResponders: 54.8 (1.4)Non-responders: 42.3 (1.1)Mean daily dose of oral MME ± SETreatment groupHU: 34.0 (1.1)Placebo: 34.2 (1.1)HU response groupResponders: 50.5 (1.4)Non-responders: 32.6 (1.1) | Mean number of painful crisesTreatment groupHU: 6.4 ± 8.5Placebo: 8.5 ± 10.1HU response groupResponders: 2.1 ± 4.1Non-responders: 7.2 ± 8.8 | Groups did not differ significantly regarding total opioid amounts used to treat pain. |
| Desai et al, 2013[3] | Randomized, double-blind, placebon = 13Observation period: 7 days | Not reported | Median total dose of MME typically via PCA: 400.2 mg (treatment group); 1,471 mg (placebo group) | Two participants from the treatment group were without pain crisis resolution after 7 days. | There were no significant differences between groups regarding time to crisis resolution, pain intensity, or time to discharge. |
| Lagas et al, 2010[4] | Case reportn = 1Observation period: 6 days | “Severe” bone pain | Cumulative daily dose of morphineDays 1 to 5: about 100 mg subcutaneouslyDay 6: 10 mg subcutaneously, 29 mg intravenously | No pain resolution | Participant died on day 6 while receiving treatment. |
| van Beers et al, 2007[5] | Randomizedn = 19Observation period: 12 days  | Median pain score (IQR) where 0 = no pain, 100 = worst pain72 (63 - 84) (PCA group)59 (51 - 85) (CI group) | Mean daily morphine consumption medians (interquartile ranges)0.5 (0.3 - 0.6) mg/h (PCA group)2.4 (1.4 - 4.2) mg/h (CI group) | Mean daily pain where 0 = no pain and 10 = worst pain4.9 (PCA group)5.3 (CI group) | During VOC, the median cumulative dose of morphine given to participants in the PCA group was significantly lower (P < 0.018) compared to participants in the CI group. |

SD: standard deviation; SE: standard error; intermittent IV: intermittent intravenous opioid administration; PCA: patient-controlled analgesia; HU: hydroxyurea; MME: morphine milligram equivalent; CI: continuous infusion; IQR: interquartile range.

**References**

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