Reduction of post-operative morbidity following patient-controlled morphine

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The present study examined the impact of two methods of pain management on recovery in 38 women undergoing hysterectomy. One group received IV morphine in the recovery room and IM morphine on the ward on a PRN basis (PRN group). In the other group, a loading dose of morphine 8 mg IV was given when the patient first complained of pain and patient-controlled IV morphine (PCA) was initiated and continued for 48 h (PCA group). Both groups received similar amounts of morphine overall, differently distributed over time. The PCA patients received 8 mg · h^{-1} in the recovery room (approximately 2.5 hrs) and less thereafter. The PRN patients received approximately 2 mg · h^{-1} for the entire 48-hr period. Pain control was better throughout convalescence and less variable across time with PCA management. Minute ventilation also recovered faster and by day four was 25 per cent above the preoperative baseline in the PCA group. In addition, oral temperature became normal one day earlier, ambulation recovered more rapidly and patients were discharged from hospital earlier. The data suggest that early treatment with relatively high, self-titrated morphine doses may alter the course of the metabolic response to surgery.

Nous avons mesuré l'impact de deux méthodes d'analgésie sur la récupération post-hystérectomie de 38 patientes. A celles du groupe PRN, on injectait de la morphine IV à la salle de réveil puis de la morphine IM au besoin. Aux autres (groupe PCA), on donnait 8 mg de morphine IV dès l'avènement des douleurs et on les laissaient ensuite elles-mêmes contrôler l'injection de la morphine IV pendant 48 hre. Les patientes des deux groupes utilisèrent des quantités semblables de morphine quoique vec des profils temporels différents soit 8 mg · h^{-1} en salle de réveil (~2,5 hre) et moins par la suite pour celles du groupe PCA contre approximativement 2 mg · h^{-1} pendant 48 hre pour celles du groupe PRN. L'analgésie était plus stable et de meilleure qualité pendant la convalescence chez le groupe PCA. La ventilation/minute remontait aussi plus vite dans ce groupe, dépassant même les valeurs pré-opératoires de 25 pour cent au quatrième jour post-opératoire.De plus la température orale s'y normalisait un jour plus tôt, la mobilisation y était plus rapide et le congé y survenait plus précocement. Il semble donc que l'auto-injection précoce de doses relativement importantes de morphine puisse modifier la réponse métabolique au stress chirurgical.

Key words
ANALGESIA: patient controlled, postoperative;
ANALGESICS: morphine;
COMPLICATIONS: morbidity;
PAIN: postoperative.

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Postsurgical pain management is complicated by the fact that there are large individual differences in both pain and analgesic requirements.[1] Patient-controlled analgesia (PCA) allows doses to be individually titrated and maintained without extensive investment of nursing time.[2,3] The fluctuations in serum concentration of analgesic agents that follow intramuscular administration are avoided[4] and patients are allowed to compensate for individual differences in metabolism and elimination, which are substantial for morphine.[5] It has been proposed that, where post-surgical pain contributes to restriction of movement or breathing, appropriate management reduces morbidity.[1,6] However, the effects of PCA on postsurgical morbidity have not been investigated directly and an editorial in the Lancet concluded that reduction of suffering is the major justification for appropriate use of analgesics.[7]

The present study undertook to examine the effects of early establishment of pain control using PCA morphine on functional recovery from abdominal surgery. To this end, patients were given a loading dose of morphine when they first complained of pain and then encouraged to use the PCA device. Pain, respiratory function, ambulation, body temperature and discharge day were assessed in

TABLE Agents used during anaesthesia

Premedication	*PCA*	*PRN*	*Analgesics*	*PCA*	*PRN*	*Agents*	*PCA*	*PRN*
None	5	2	Morphine $0.15 \pm 0.02\ mg \cdot kg^{-1}$	4	1	Isoflurane	4	4
Glycopyrrolate	1	0	Fentanyl $2.73 \pm 1.26\ \mu g \cdot kg^{-1}$	7	4	Isoflurane + N_2O	3	7
Meperidine*	7	6	Fentanyl + droperidol $2.36 \pm 1.01\ \mu g \cdot kg^{-1}$ + 1.25–2.5 mg	4	10	Enflurane + N_2O	12	7
Diazepam	7	5	Sufentanil $0.30 \pm 0.08\ \mu g \cdot kg^{-1}$	5	3[b]			
Lorazepam	0	3						
Morphine†	0	2						

Anaesthesia was induced with thiopentone. Patients were paralyzed with pancuronium and lungs were ventilated to a normal $PaCO_2$. Other agents used are listed by group.

*Plus phenergan, atropine or glycopyrrolate.

†Plus atropine or glycopyrrolate.

[b]Two patients also received droperidol.

patients receiving PCA morphine or well managed intramuscular morphine on a PRN basis.

Methods

The study was approved by the Hospital Ethics Committee. Thirty-eight women aged 30 to 55 yr (mean = 42), ASA physical status I or II, who were scheduled for abdominal surgery (total hysterectomy (14), total hysterectomy plus bilateral salpingo-oophorectomy (20), total hysterectomy plus omentectomy (1) and myomectomy (3)) participated in the study. The women were randomly assigned to one of two groups. The first group received IV morphine according to recovery room protocol (2 mg IV, given as judged necessary) and IM morphine, 5–20 mg plus phenergan, 25 mg, Q4-6H PRN on the ward. The other group received a loading dose of IV morphine, 4 mg × 2, when the patient first indicated pain in the recovery room. Morphine was delivered by a patient-controlled analgesia system (PCA; Abbott Laboratories) thereafter. The PCA device was set to deliver $2\ mg \cdot 5\ min^{-1}$ in the recovery room and $1\ mg \cdot 10\ min^{-1}$ on the ward. Phenergan, 25 mg IM, was prescribed PRN to PCA patients but it was only necessary in one case. Approximately 48 hr after surgery, most patients were transferred to oral codeine-acetaminophen, 60/650 mg, PRN, Q4-6H. Drug equivalents[8] were used to calculate approximate analgesic consumption during the period when patients were transferred from parenteral to oral medication.

Anaesthesia was given by 11 anaesthetists. The premedication and anaesthetic agents used are listed in the Table. Despite considerable variability, there were no systematic differences between groups. Surgery was performed by ten gynaecologists. The groups were not different in regard to surgeon, procedure, incision (midline or Pfannenstiel), operative blood loss (PCA: 339 ± 228 ml, PRN: 256 ± 180 ml; mean ± SD), time of day of surgery, time in the operating room or in the recovery room.

Respiratory function was measured using a Wright respirometer with patients reclining in bed except for measures in the recovery room which were done with the patient supine. Vital capacity, resting respiratory rate and minute ventilation were measured on the evening before surgery, in the recovery room 30–90 min after admission, 2–5 hr later and in the evening of the first four days after surgery. Ambulation was assessed by attaching magic markers to slippers and asking the patient to walk as normally as possible down an 18 m strip of paper. Performance on the middle 6 m of the paper strip was used to determine ambulatory ability. Stride length and width were obtained by measuring the marks on the paper and velocity by means of a stopwatch. Ambulation measurements were done on the evening before surgery and the second to the fifth days after surgery. Pain was assessed using the McGill Pain Questionnaire Short Form[9] and a Visual Analog Scale[10] on the evening prior to surgery, in the morning of the first five days after surgery, prior to each respiratory measurement and at the time of discharge from hospital. In addition, patients were contacted by telephone two weeks after discharge to administer an oral questionnaire on pain and functional status. Other information was obtained by chart review.

Respiratory and ambulation variables were analyzed using repeated measures ANOVA's on scores after surgery using the preoperative score as a covariate. (This reduced variance and removed the complex interaction produced by the change from baseline.) The absolute values, however, are shown in the Figures. Postoperative

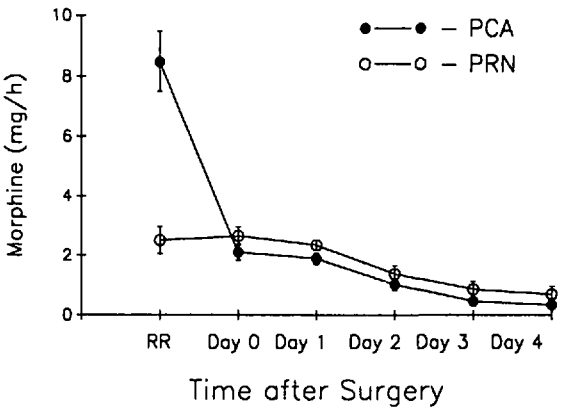

FIGURE 1 Morphine doses (mean ± SEM) received to control postsurgical pain. RR indicates recovery room period (2–3 hr). Day 0 extends form RR discharge to 24:00 hr.

pain scores were also treated by repeated measures ANOVA. The PRN and PCA scores at specific time points were compared using t tests. Chi square and Fisher exact tests were performed on categorical data.

Results

The two groups were similar with respect to education, marital status, parity, employment, smoking status, age, height, weight and preoperative haematocrit. Pain scores were marginally, but not significantly, higher for the PRN group on the evening prior to surgery due to four patients reporting pre-existing pain on the VAS measure (P = 0.06). When these individuals were deleted from the analyses, no substantial differences were observed in the results. They were, therefore, included in the sample.

Total intake of morphine for the first 48 hr was virtually identical for the PRN and PCA groups (117.0 ± 52.5 and 109.8 ± 50.8 mg; mean ± SD). However, as Figure 1 indicates, the pattern of analgesic intake was markedly different ($P < 0.001$). During the recovery room stay (approximately 2½ hr), PCA patients self-administered a mean of 12 mg of morphine (min 2 mg; max 25) after receiving the 8 mg loading dose. Thereafter, there was a consistent trend for the analgesic intake to be lower, even after most patients were transferred to oral codeine/acetaminophen on Day 2.

The respiratory rate was reduced to a greater extent in the PCA group ($P < 0.05$) (Figure 2a) but the lowest rate recorded was 10 breaths·min^{-1}. The reduction in vital capacity (Figure 2b) was similar for the two groups and recovery occurred at the same rate. However, in the case of minute ventilation (Figure 2c), the initial reduction was similar but recovery was more rapid in the PCA group and was associated with an overshoot above preoperative level ($P < 0.001$). The overshoot represents a 25 per cent increase in ventilatory function from the preoperative

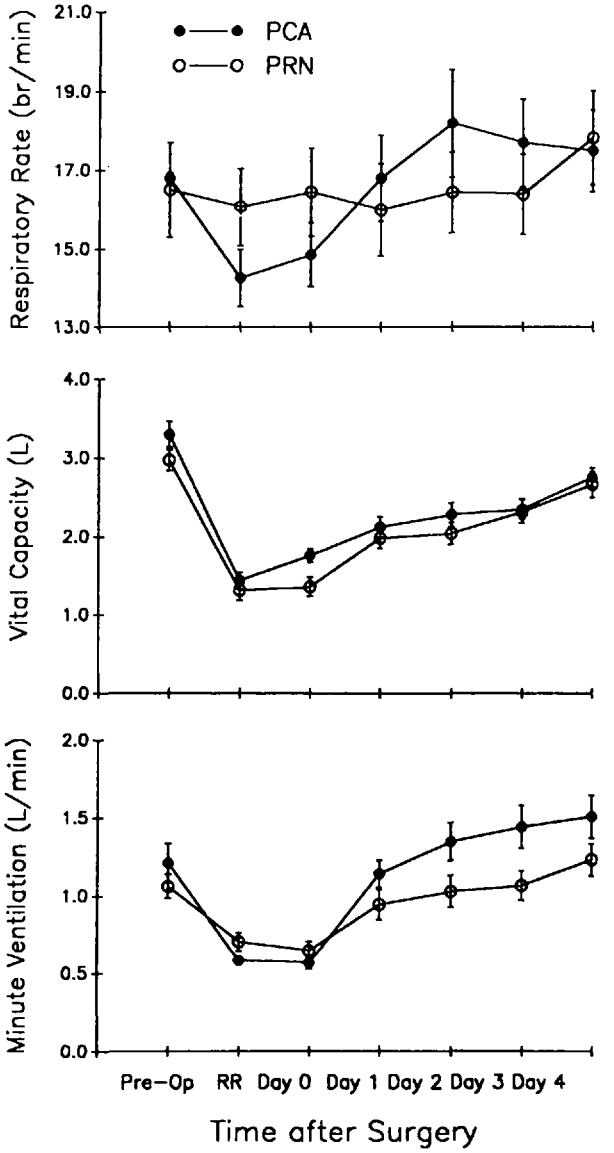

FIGURE 2 Respiratory rate (top), forced vital capacity (middle) and minute ventilation (bottom) preoperatively and during postsurgical recovery (means ± SEM).

level by Day 4. The increase in minute ventilation was not associated with an increase in body temperature. The maximum temperatures (Figure 3) recorded were lower on days two and three for the PCA group ($P < 0.05$) and this difference was maintained when patients who received antibiotic medication on clinical grounds were excluded ($P < 0.05$). Vital signs, blood pressure and heart rate were similar for the two groups throughout the hospital stay.

Ambulation was impaired on Day 2 and gradually returned toward baseline levels by Day 5 (Figure 4). Stride length ($P < 0.05$) and velocity ($P < 0.05$) increased significantly faster in the PCA patients. Other

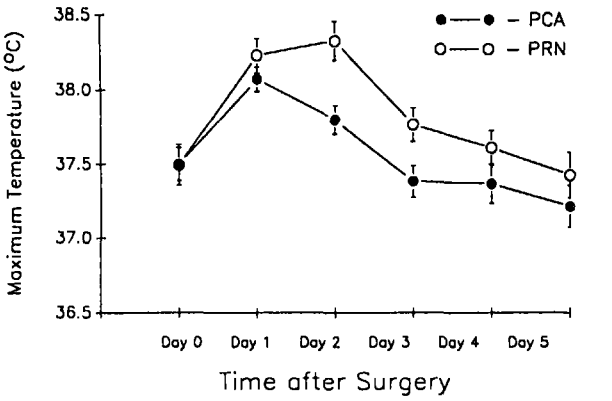

FIGURE 3 Maximal temperatures recorded for each postoperative day (means ± SEM).

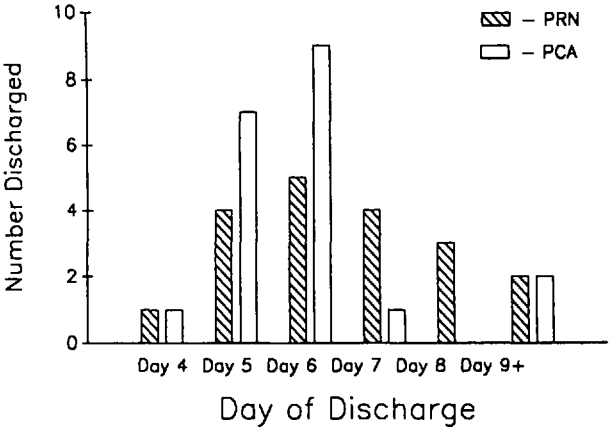

FIGURE 5 Distribution of the duration of hospital stays.

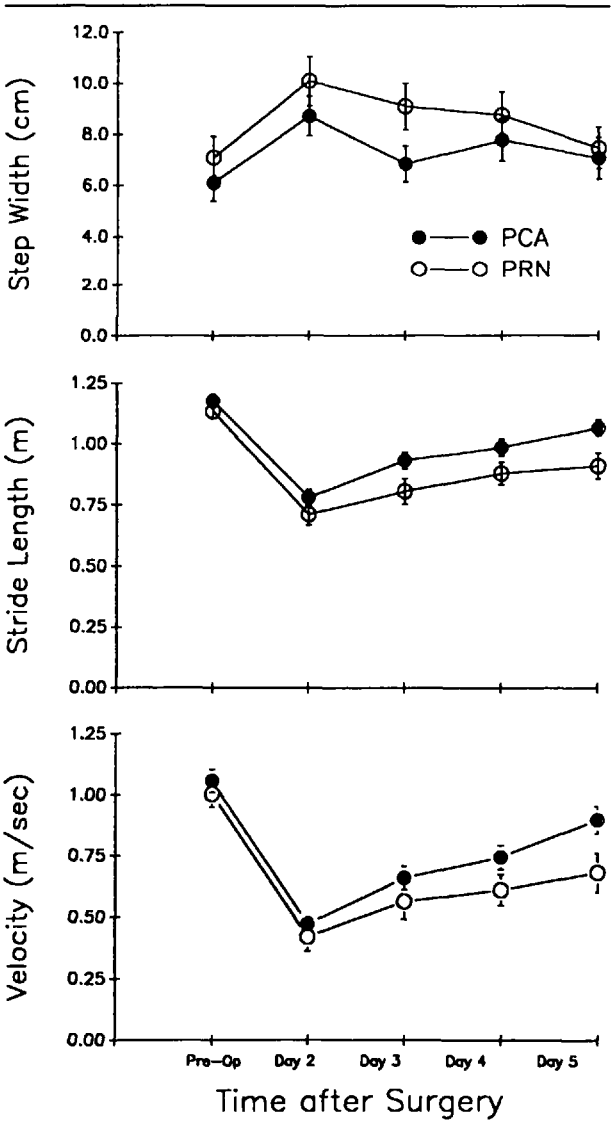

FIGURE 4 Step width, stride length (mean of left and right) and velocity during postoperative recovery (means ± SEM).

indices of post-surgical recovery also indicated that PCA management produced beneficial effects. Antibiotics were administered to 1/20 patients in the PCA group and 7/18 in the PRN group (Fisher exact p = 0.013). The day on which nursing notes in the charts indicated introduction of solid food ("diet as tolerated") was earlier ($P < 0.05$). Figure 5 shows the duration of hospitalization after surgery. On this index, PCA patients also did better (median split, Fisher exact $P < 0.05$).

Figure 6 shows pain scores obtained on the evening prior to surgery, in the recovery room after surgery, later the same day, the mean of morning and evening pain assessments on Days 1–5, at discharge and two weeks after discharge. Repeated measures ANOVA's across recovery room to the two-week post-discharge scores indicated that PCA management reduced pain scores on both measures (VAS, $P < 0.05$; MPQ, $P < 0.01$). The interaction terms were not significant which implied that the difference between groups was maintained despite the fact that PCA was discontinued around 48 hr and pain management was identical for the two groups from that time on. In addition to mean pain levels of PCA patients being lower, the standard deviations of pain scores for each patient were also reduced ($P < 0.05$) indicating that pain fluctuated less over time. The PCA patients not only reported less discomfort two weeks after discharge,but also that pain interfered less with activity around the house ($P < 0.05$) and with food intake ($P < 0.05$). Effects of pain on anxiety, concentration, sleep and distress were low and not different for the two groups.

When subjects were classified on the basis of a median split of pain scores on day 1, there was no relationship with hospital stay (Fisher exact $P = 0.276$). The peak body temperature on days 2 and 3 were also not correlated with pain on day 1. The reduction of minute ventilation on days 1 to 4 was only weakly predicted by pain on day 1 (NS). The correlations between pain on day 1 and the

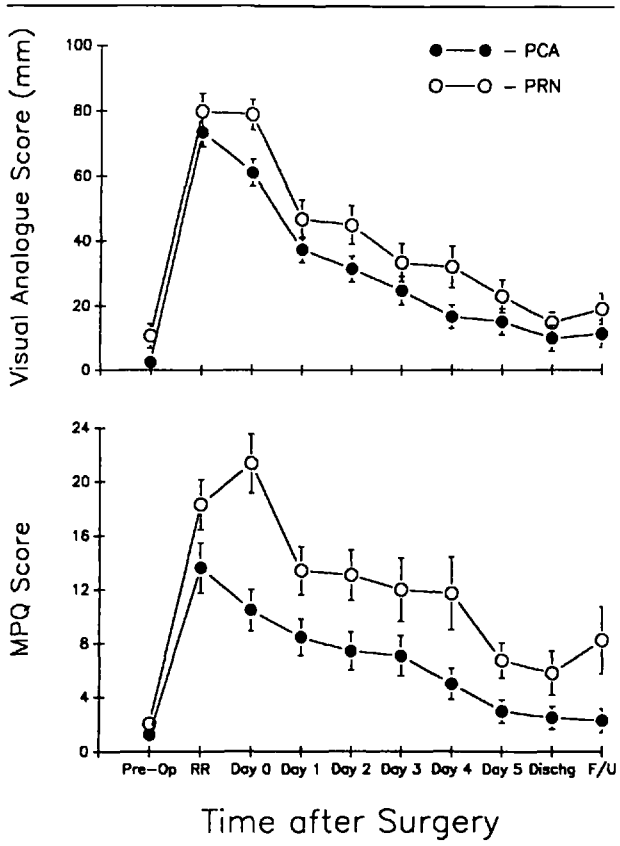

FIGURE 6 Pain levels reported by patients on the evening prior to surgery and at the indicated times (means ± SD).

magnitude of the impairment of walking velocity and stride length on days 2 to 5 were also weak ($P = 0.10$ to < 0.02). When the two groups were examined separately, stronger correlations between ambulation and pain in the PRN group suggest that pain may be a limiting factor in these patients (mean $P \leq 0.05$ for velocity and stride length, respectively). In contrast, there was no reliable correlation between ambulatory impairment and pain in PCA patients.

Discussion

The present data show that establishment of early self-titrated pain control improved recovery from routine abdominal surgery when compared with PRN management. Pain was less, from the immediate postoperative period until two weeks after discharge (approximately 20 days after surgery), in patients who received morphine by PCA after a loading dose. Ambulation and respiratory function also recovered more rapidly, complications were reduced, and there were significantly fewer long-stay patients. The reduction in the duration of hospitalization was an average of 0.29 days for the 20 PCA patients. This is an underestimation of the reduction in hospital stays since four PCA patients were ready for discharge on day five but could not leave until day six because home care had been planned on an estimated stay of six days.

It should be emphasized that the ward staff who cared for the patients in this study were very aware of the importance of adequate pain management and the amount of morphine dispensed to the PRN group was higher than that reported in the literature.[11–13] Thus, PCA was compared with well-managed routine care. None of the investigators was directly or indirectly involved in any aspect of patient care on the ward so that decisions regarding administration of antibiotics, and readiness for discharge were conducted independently. It is unlikely that bias contributed to the present data, although the results may well influence judgments in future studies. A double-blind design was not attempted because the purpose was to examine the influence of different pain management strategies on recovery.

It has been suggested that pain control might improve recovery from surgery by reducing stress and improving pulmonary function.[1,6] If pain control was the most important intervening variable, then it would be expected that pain levels should be stronger predictors of recovery than the method of analgesic administration since there was considerable overlap in pain scores between the PCA and PRN groups. However, discharge day, return of body temperature to normal, and rapid increase in minute ventilation are best predicted by the method of pain management rather than by pain scores. This suggests that factors associated with the schedule of analgesic administration other than better control of pain accelerated recovery.

The increase in minute ventilation beginning 48 hr after surgery implies that either pulmonary dead space was increased or oxidative metabolism increased above preoperative resting baseline in PCA patients. Because the PCA patients' ambulation and body temperature returned to normal rapidly, it is unlikely that the high minute ventilation indicated pulmonary dysfunction. It is, therefore, possible that the course of metabolic recovery was altered in PCA patients. A mechanism whereby this could occur is that relatively high doses or morphine were administered during the period that hormonal indices of surgical stress are still rising (first six hours).[14,16] Epidural analgesia (bupivicaine) maintained into the post-surgical period abolishes the corticosteroid and catecholaminergic response to lower abdominal surgery.[17] Epidural morphine[18] or systemic fentanyl (25 $mg \cdot kg^{-1}$)[19] moderate these indices of surgical stress. The present doses of morphine may have been high enough to dampen the stress response leading to alterations in function late in recovery and only detected two to five days after surgery.

An alternative explanation is that PCA avoids the high peaks in serum morphine concentrations that are produced by IM administration, thereby reducing the deleterious effects of opioids. In support of this, only one of the PCA patients required antiemetic medication and the improved performance on functional measures could reflect decreased sedation. All PRN patients received antiemetic medication routinely. Opiates can also suppress the immune system,[20] an effect that could be important in surgical patients. Because the differences between the PCA and PRN groups emerged in the latter part of the hospital stay, this also implies lasting or delayed effects of the method of analgesic management in the first 48 hr.

In summary, the present study suggests that early control of postsurgical pain with PCA morphine after a generous loading dose produces physiological and functional effects that are not apparent until 48 hr later. These effects are associated with earlier discharge from hospital, more rapid ambulation and lower pain and disability scores throughout convalescence. A better understanding of which aspects of the schedule of morphine administration are beneficial and the mechanisms of action of morphine on the process of recovery from surgery are necessary, particularly to extend the present findings to more seriously ill patients.

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