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Title: Peri-operative Analgesic Requirements and Quality of Recovery
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## Introduction:

Painful stimuli cause arousal of the central nervous system (CNS), which the brain then interprets as pain. Analgesia (pain-relief) can reduce arousal of the CNS through a number of different mechanisms. As every person is unique, analgesic agents have different potency and side effects in different individuals, which makes pain management complex. This is further complicated as there is no direct relationship between dose and effect. The concept of effect-site concentration has been developed to estimate the pain-relieving effect.

Previous research indicates a relationship between intra-operative and post-operative analgesic requirements (as represented by effect-site opioid levels) and that there is variation in modelled opioid levels when comparing laproscopic and orthopaedic surgery. We also know that suboptimal treatment of acute pain is a significant predictor of chronic pain.

## Aim:

This study explored two surgical groups: orthopaedic and laproscopic. The primary purpose was investigating peri-operative pain where fentanyl was the primary opioid. As pain relief beyond PACU (the post-anaesthetic care unit) is important we also employed a standard questionnaire as a marker of recovery, which simultaneously allowed investigation of possible situations where acute pain from an operation could develop into chronic pain.

## Method:

With Ethics Committee approval, suitable subjects were identified and verbal consent acquired from the consulting anaesthetist. Written consent was obtained from 47 subjects aged 15 to 65 with an American Society of Anaesthesiologists (ASA) physical status of I, II, or III scheduled for orthopaedic or laproscopic surgery. Subjects in the laproscopic study group were scheduled for abdominal surgery, hysterectomy, or a diagnostic procedure. Orthopaedic subjects were scheduled for any bony surgery excluding total hip replacements and operations involving the neck of the femur.

Effect-site opioid levels were calculated at one minute intervals from the start of surgery to PACU discharge from doses and times of opioids administered using standard models. For analysis we used the mean intra-operative, PACU arrival, mean PACU and PACU discharge ready values.

Subject quality of recovery was derived from Postoperative Quality of Recovery Scale (PQRS) questionnaires, designed to assess quality of recovery in a variety of different domains (physiological, nociceptive, emotional, activities of daily living and cognitive) over an extended period. Subjects completed a baseline questionnaire before the operation, which was then repeated post-operatively at 30 minutes, one day, one week, and one month. This was either face-to-face or over the phone. We assessed recovery by calculating the percentage of subjects who had recovered to baseline at each assessment timepoint.

Data was compared using paired, two-tailed t-tests with 95% confidence intervals. Statistically significant results had a p-value $<0.01$, to correct for multiple comparisons.

## Results:

47 subjects were included in the study; 20 in the orthopaedic group and 27 in the laproscopic group. There was no significant difference between the two surgical groups for any of the derived values. Mean intra-operative opioid levels for the orthopaedic group were 1.19ng/mL and for the laproscopic group were 1.31ng/mL, with a difference of -0.12ng/mL (95% CI, -0.34 – 0.086; p-value 0.24). PACU arrival values were 0.91ng/mL (orthopaedic), 0.79ng/mL (laproscopic) with a difference of 0.12ng/mL (CI, -0.073 – 0.31; p 0.22). PACU mean 0.93, 0.91, difference 0.025 (CI, -0.13 – 0.18; p 0.75). PACU discharge ready 0.82, 0.87, difference -0.046 (CI, -0.25 – 0.16; p 0.65). In the laproscopic group the slope of the regression line for the relationship between mean intra-operative and mean PACU opioid levels was 0.31, with a correlation co-efficient of 0.15, while the orthopaedic regression line was essentially flat; slope of 0.004, correlation co-efficient of 3.29e-005.

The percentage of subjects who had recovered to baseline PQRS at 30 minutes post-operatively were: physiological 45%, nociceptive (pain) 34%, emotional 93%, and cognitive 26%. 6% had recovered in all domains. At one month, recovery by domain was: nociceptive (pain) 90%, emotional 100%, activities of daily living 85%, and cognitive 57%. 54% had recovered in all domains. Physiological recovery was better in the laproscopic group: 52% recovered at 30 minutes and 100% recovered at day one, where orthopaedic had 36% and 83% recovery. The orthopaedic group had better nociceptive results for late and long-term recovery; 79% recovery at one week and 94% at one month, compared to 57% and 86% in the laproscopic group. Emotional recovery decreased in the orthopaedic study group between 30 minutes, one day, and one week (84%, 83%, 79%), then increased at one month (100%), while the laproscopic study group maintained 100% recovery after 30 minutes. Activities of daily living were comparable between the surgical groups, except at day one – the laproscopic group was significantly worse (35%) compared to orthopaedic (67%). Cognitive recovery was more stable in the orthopaedic group – 30 minutes 24%, one day 69%, one week 69%, one month 71% – compared to the laproscopic group (27%, 75%, 89%, 55%).

## Conclusion:

The surgical groups had no significant difference in modelled opioid levels at any of the four chosen points of comparison. In laproscopic subjects the correlation between intra-operative and PACU needs of 0.3 is less than seen in previous summer research and the literature (0.7). The lack of relationship between intra-operative and PACU needs in the orthopaedic group could be due to the variation in anaesthetic and surgical technique.

Most subjects had fully recovered by one month, with no significant difference between the surgical groups. Between 30 minutes and one month, the laproscopic group had better physiological and emotional recovery, while the orthopaedic group had better nociceptive recovery. The longer recovery time experienced by the orthopaedic subjects may have affected their emotional recovery.

The PQRS questionaires appear to be a good measure of recovery, although variation in overall subject health when the baseline measurement was taken may have affected results; the orthopaedic subjects tended to have been injured for the preceding weeks and the laproscopic were a mix of individuals with acute, chronic or no symptoms. I would recommend more research into the different kinds of anaesthetic technique used within the orthopaedic group, as it may aid predictions of post-operative needs for those patients.