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Title: Can post-operative pain be predicted by the response to pre-operative intervention?
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Introduction: Part of anaesthesia is managing patients' post-operative pain. This is important for reducing both patient suffering and the likelihood of chronic post-operative pain. The cold pressor test, where the patient's hand is immersed in ice water and changes in their heart rate and blood pressure are measured, can be used to predict individuals' post-operative pain, but this is impractical in the clinical context.

Aim: We wished to determine whether the amount of pain patients felt in response to two routine, painful pre-operative stimuli – intravenous cannulation and injection of a small dose of propofol, which is often used to reduce pre-operative anxiety – would predict how much pain they experienced after the operation.

Impact: Having a pre-operative measurement tool to predict how much pain individual patients are likely to experience post-operatively would allow anaesthetists and other personnel to optimise patient outcomes via individualised intra- and post-operative pain management strategies.

Method: We recruited patients undergoing laparoscopic and minor bony procedures, as these patient groups have historically high levels of post-operative pain. Patients were asked to rate their pain from "no pain" to "worst possible pain" on a non-segmented visual analogue scale (VAS) of 100mm immediately following both cannulation and injection of 30mg of propofol. We then recorded administration of fentanyl both during and after the operation. Fentanyl is a pain relief agent that often has a dominant role in both intra- and post-operative pain relief. By recording fentanyl doses we could use computer modelling to predict a patient's fentanyl levels as they entered recovery and observe how much additional fentanyl they required for their pain to be tolerable. Average post-operative fentanyl effect site concentration (Ce) was hence used as a proxy measure of post-operative pain.

Results: We recruited 48 patients, of ASA (a physical status classification) I – III and varied ethnicities. Upon graphing the results we could not find the hypothesised observable correlation between VAS score and average post-operative fentanyl Ce, as indicated by a correlation coefficient of 0.139. We did observe a pattern linking VAS score and recovery (post-operative) pain scores. Most patients gave low scores on the VAS and had a wide range of recovery pain scores. However, as VAS scores increased above approximately 40mm, recovery pain scores shifted upwards. This group of patients with high VAS scores, who we termed "pain responders," had predictably high recovery pain scores – indicating that their responses to painful stimuli were distinct from the rest of the patient population. One obstacle we faced in the course of the study was that many patients arrived in theatre with a cannula already in situ, so pain on cannulation could not be measured. Another was that pain of injection of propofol appeared to be less useful as a measurement tool, as patient responses were drastically affected by variables such as cannula size and location.

Conclusion: This study enabled us to identify the pain responder subgroup, whose distinct responses to painful stimuli recommend alternate approaches to their pain management. This would be of great clinical relevance when anaesthetising or otherwise attending to these individuals. Another outcome of this study was determining the clinical applicability of measuring pain on cannulation. It could be done quickly and informally by anaesthetists or other personnel to identify pain responders. The lack of correlation between VAS and our original variable, average post-operative fentanyl Ce, is related to the fact that administration of opioids such as fentanyl has decreased

gradually since similar studies five years ago. Anaesthetists are increasingly turning to multi-modal, non-opioid forms of pain relief, suggesting that fentanyl Ce alone may not fully communicate a patient's pain relief needs. In fact, our observation that average post-operative fentanyl Ce does not appear to be elevated for pain responders serves to further highlight that they require alternate pain management strategies.

This study may pave the way for a larger future study, possibly only open to patients undergoing elective procedures, so pain of cannulation can reliably be obtained in theatre. Future studies could also involve further investigation of pain responders. This might include exploring identifying characteristics of the group and incidence of chronic post-operative pain – an identified problem for responders to the cold pressor test.

The next step would be to begin applying the findings of this study in practice. Anaesthetists could assess pain of cannulation and individualise pain management strategies for pain responders. This may involve use of pain relief adjuncts such as ketamine and lignocaine and proactive post-operative management by informing recovery nurses of increased pain relief requirements.