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CORRESPONDENCE

Association between fentanyl vial size and dose given: an interrupted time series analysis of intraoperative opioid administration

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Editor—Increased intraoperative opioid administration has been associated with increased length of stay and risk of readmission.[1] Despite the ongoing opioid epidemic, there were shortages of injectable opioids in the USA in 2018.[2] Owing to supply chain limitations, our hospital was forced to switch from 2 ml prefilled syringes of fentanyl to 5 ml vials of fentanyl of the same concentration. We assessed the effect of the change in vial size on the amount of fentanyl and total opioids administered to patients in our operating rooms.

Data were collected retrospectively from all patients undergoing surgery at a single academic hospital (Brigham and Women's Hospital, Boston, MA, USA). Institutional review board approval was obtained, and the requirement for informed consent was waived. Data were extracted from pharmacy records and electronic health records. Our study included three periods: period 1 (14 weeks), when 2 ml fentanyl syringes were available; period 2 (12 weeks), during which only 5 ml fentanyl vials were available; and period 3 (10 weeks), after the 2 ml fentanyl syringes returned. Data were collected from July 1, 2018 through March 22, 2019, and the study period included consecutive weeks with no interruptions.

The primary outcomes were mean dose of fentanyl administered to the patient per case and the total morphine milligram equivalents (MME) of all opioid boluses administered to the patient per case (fentanyl, morphine, and hydromorphone). The primary outcomes were compared between periods 1 and 2 and between periods 2 and 3 using an interrupted time series (ITS) approach with weighted segmented linear regression.[3] The primary analysis estimated model parameters using ordinary least squares with robust standard errors, and a sensitivity analysis used MM estimation to account for outliers.[4,5] Regression models were weighted by the odds to account for variability in age, sex, ASA physical status, emergency status, patient class, anaesthesia type, service, and anaesthesiologist distribution across periods.[6] The Supplementary Methods file contains details about the assessment of covariate balance between periods and the weighting methodology. The Durbin–Watson test did not detect any autocorrelation of weighted model residuals. All statistical hypothesis tests were two-sided, with alpha set at 0.025. Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

A total of 17,695 cases were included in our analysis. Patient and procedural characteristics for all periods can be found in Supplementary Table S1. The mean (standard deviation, SD) dose of fentanyl per case increased from 110 (115) μg (median quartile 1 [Q1], quartile 3 [Q3]: 100 [50, 125] μg) to 164 (160) (median [Q1, Q3]: 150 [100, 250] μg) μg after the change to 5 ml vials, corresponding to a weighted percent difference in mean fentanyl administration of 32% (weighted difference in means [97.5% confidence interval, CI]: 38 [26, 50]; $P<0.001$) (Supplementary Table S2 and Fig. 1). After the 2 ml syringes returned, the mean (SD) dose of fentanyl decreased to 120 (129) μg (median [Q1, Q3]: 100 [100, 150] μg) with a weighted percent difference of −37% (weighted difference in means [97.5% CI]: −62 [−75, −50]; $P<0.001$) (Supplementary Table S2 and Fig. 1). The mean (SD) total intraoperative opioids administered per case increased from 40 (38) MME (median [Q1, Q3]: 30 [22.5, 50] MME) to 55 (52) MME (median [Q1, Q3]: 45 [30, 75] MME) with 5

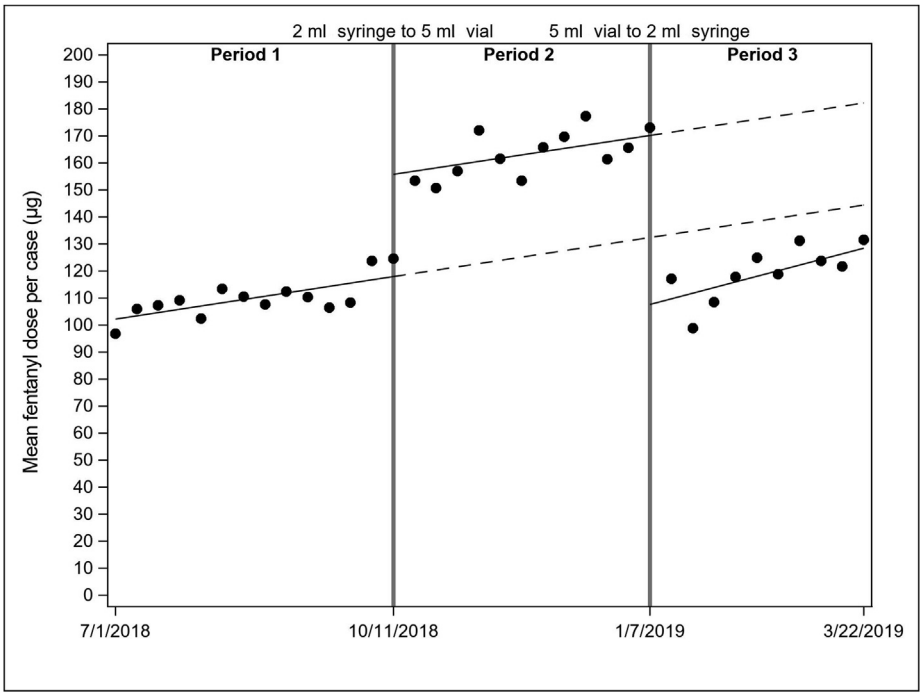

Fig 1. Change in mean fentanyl dose administered per case associated with change in vial size. Circles represent the mean fentanyl dose administered per case per week. Solid lines show the observed temporal trends in mean fentanyl dose administered per case per week within each study period, estimated from a weighted segmented linear regression model. The vertical distance between adjacent trend lines represents the difference in mean fentanyl dose per case associated with the corresponding change in vial size. Dashed lines show the projected temporal trend in mean dose of fentanyl administered per case, predicted based on data from prior periods using weighted linear regression models.

ml vials, and returned to 42 (42) MME (median [Q1, Q3]: 35 [30, 55] MME) after 2 ml syringes were reintroduced. The weighted percent difference in mean total opioid administered was 25% (weighted difference in means [97.5% CI]: 10 [6.6, 14]; $P<0.001$) with the vial size increase and −31% (weighted difference in means [97.5% CI]: −18 [−22, −14]; $P<0.001$) when the vial size was returned to 2 ml (Supplementary Table S2). Regression parameter estimates were similar between the primary ordinary least squares and sensitivity MM estimation regression analyses (Supplementary Table S2).

We observed a temporary increase in intraoperative fentanyl administration associated with an increase in the fentanyl package size provided to anaesthesiologists from 2 to 5 ml. Availability of larger fentanyl vials was also associated with greater overall opioid administration. Medication vial size is a modifiable environmental factor that appears to influence how anaesthesiologists dose medications in the operating room. One possible explanation is that anaesthesiologists are motivated to reduce intraoperative medication waste. Although we do not report data on waste in this article, prior studies have shown that smaller vial sizes of propofol and midazolam have been associated with reduced medication waste.[7,8]

The limitations of our study include the fact that the data are from a single centre and that the observational ITS design may be confounded by secular changes, such as changes in dosing patterns related to progression of anaesthesia residents over the academic year. This study was not designed to qualitatively investigate what drove this change in dosing practice.

Although our study was a natural experiment made possible by a local opioid shortage, it suggests that careful selection of vial size has the potential to modify perioperative dosing practices and possibly reduce opioid use.

Declaration of interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.03.006.

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