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Clinical Investigation

CLINICAL INVESTIGATION

Diurnal variations in recovery times after general anaesthesia in children

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Background: Circadian rhythms coordinate almost all physiological functions and are implicated in major disease development. Even though circadian rhythms have a major impact on human health, little is known about how they affect general anaesthesia. The purpose of this study was to understand if the time of day affects the length of time a child needs to achieve readiness for discharge after general anaesthesia for brain MRI.
Methods: A retrospective analysis over a 3 yr period (2013–5) on the length of stay in the postanaesthesia care unit (PACU) before discharge was performed for children (age <18 yr) undergoing brain magnetic resonance imaging as outpatients. PACU duration was correlated to either morning *vs* afternoon or to time clusters for discharge times (<9 AM, >9 AM <12 PM, >12 PM <3 PM, >3 PM <6 PM, >6 PM).
Results: Data from 2340 procedures in children, with median age [inter-quartile range (range)] of 4.7 [2.3–7.25 (0.5–17.8)] yr were available for analysis. The length of stay in the PACU significantly increased over the course of the day with an observed maximum increase of 18 or 19 min (<9 AM *vs* >6 PM) in children older than 3 or 5 yr, respectively. Subgroup analysis suggested time of day dependent PACU time increase was independent of sex, co-medications, or obstructive sleep apnoea.
Conclusion: The time of day significantly affects PACU recovery times in children of both genders having brain imaging under general anaesthesia. Children younger than 3 yr might not be affected. Further validation of these findings may guide future strategies to reduce discharge times.

Keywords: ambulatory surgical procedures; anaesthesia, general; paediatric anaesthesia; circadian rhythm; length of stay

Editor's key points

- Circadian rhythms are biological processes showing an endogenous diurnal oscillation.
- Most physiological and pharmacological processes show diurnal variations.
- The authors investigated the influence of time of day on discharge readiness among children who had undergone imaging under general anaesthesia.
- A strong correlation between time of day and time until PACU discharge readiness was found.

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The earth's 24 h rotational cycle, with its light and dark periods, has existed for more than 4 billion years and has led to the evolution of circadian rhythms in humans. The impact of circadian rhythms on health beyond mental well-being is currently an area of intense investigation.[1–11] Its disruption is implicated in the pathogenesis of a spectrum of diseases such as diabetes, hypertension, sepsis, and cardiovascular disease.[4] General anaesthetics and a variety of adjunct medications given during surgery have the potential to disrupt the circadian cycle.[12,13] While this is a well-recognised phenomenon, the underlying mechanisms are not yet well understood, so research to understand the impact of anaesthesia on circadian rhythms and health is highly desirable.

Another important aspect of circadian biology is the influence of the timing of drug administration during different time points during the day. In fact, many drugs have significant different effects at different times during the day,[14] so not only might anaesthetics disrupt circadian rhythms, but their side-effects or efficacies might differ at certain times during the day.

Patients can only be discharged home after surgery once they meet all discharge criteria, including being appropriately alert, as assessed using a validated scoring system. Thus 'sleepiness' after a general anaesthetic for same day surgery can delay discharge. To further understand daily variations of general anaesthesia potentially effecting PACU readiness and discharge times, we sought to investigate the effects of propofol general anaesthesia on PACU discharge readiness in children after brain MRI in an outpatient setting. We performed a retrospective chart review from 2340 anaesthetics in children over a 3 yr time period to determine if the PACU time was different in children who were anaesthetised in the morning *vs* the afternoon, irrespective of drug dose. Subgroup analyses accounted for sex, age, prescribed medications, or the presence of obstructive sleep apnoea (OSA).

Methods

We collected data on children from 6 months to 18 yr of age who underwent general anaesthesia for brain MRI at the Children's Hospital Colorado (CHCO) between January 1, 2013 and December 31, 2015. The anaesthetic for brain MRI patients is quite standardised at our institution and consists of no premedication, inhalation indication with sevoflurane, followed by i.v. cannula placement. Maintenance consists solely of a continuous propofol infusion delivered at 200–250 $\mu g\ kg^{-1}\ min^{-1}$ and an unsecured airway. No opioids or other sedative hypnotics are administered. Supplemental oxygen is delivered, and capnography measured via a nasal cannula. Approval was obtained, and waiver of written informed consent was granted from the Institutional Review Board (Colorado Multiple Institutional Review Board) at the University of Colorado Denver, Denver, CO, USA.

Data were derived from Epic™ anaesthesia charts and PACU flowsheets. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Colorado School of Medicine, Anschutz Medical Campus.[15]

The time points for anaesthetic induction, end of procedure, and meeting Phase 1 PACU discharge criteria ('PACU time') were collected along with total propofol dose administered, normalised for weight and duration, scoring for the presence of sleep-disordered breathing pattern [Snoring, Trouble Breathing, Un-Refreshed (STBUR) score],[16] diagnosis of OSA, and home and facility administered medications grouped by pharmacological classification. To mark 'Phase I complete' strict criteria have to be met, the most relevant to this study being achieving a modified Aldrete score of 9 or higher that signals an awake patient.[17] Patients were only included in the study if this 'Phase I complete' time was recorded. Details on timeliness/latency of PACU charting, nurse:patient ratios, PACU admissions, or PACU census can be found in the discussion.

Exclusion criteria included inpatients, MRI studies performed in conjunction with anaesthesia for another study or procedure, patients with vagus nerve stimulators, inhalation anaesthetic only patients, or anaesthetics with i.v. inductions. Children younger than 6 months were excluded as their circadian rhythms are not fully developed yet.[18] Subjects 18 yr and older were excluded based on current National Institutes of Health definitions of a child. Our initial search resulted in 3081 anaesthetics. Incomplete data sets (missing PACU times) were removed and the remaining 2340 records were analysed. Ages and time of day distributions were similar in the excluded and analysed records {median [interquartile range (range)]}: age excluded data set 4.5 [2.5–7.0 (0.5–17.8)] *vs* age included data set: 4.7 [2.3–7.25 (0.5–17.8)], time of day excluded data set: 11:24 AM [9:22 AM–2:12 PM (7:44 AM–6:41 PM)] *vs* time of day included data set: 12:14 PM [10:04 AM–2:52 PM (7:40 AM–7:12 PM)].

For multiple comparisons, one-way analysis of variance (ANOVA) with Bonferroni adjustment, and for single comparison, the unpaired Student's *t*-test were applied. For five-time cluster group comparisons we used ANOVA with Bonferroni adjustment (alpha/10), resulting from 10 comparisons made for all pairwise comparisons among the five-time groups. The number of groups was determined based on high resolution sequencing data indicating that smaller time intervals are superior in detecting a circadian pattern.[14] Values are expressed as mean [standard deviation (SD)], or as median [inter-quartile range (IQR)]. Correlation analysis was performed using liner regression. SPSS automated linear regression modelling was performed using the best subsets criterion and the Akaike information criterion correction. The SPSS analysis software computes a predictor importance value for a target (*target*: length of stay in PACU) that represents the percent of explainable variation, explained by that predictor (*included predictors*: PACU Phase 1 discharge time, propofol start time, propofol stop time, case duration, age, propofol dose, STBUR score, OSA, and anticonvulsive and antihistamine drugs). The predictor importance is the portion of the coefficient of determination that is attributable to the inclusion of that predictor. The value is calculated by taking the reduction in the sum of squares of the residuals that results from including the predictor, and then normalises all the values against each other such that the sums equal 1. A P-value <0.05 was considered statistically significant for all tests. Initial statistical power analysis using an alpha error of 0.05, a beta error of 0.1 (power of 0.9), and an assumed SD of 16 min and minimal relevant difference of 5 min revealed that at least 120 patients per group were needed to reach statistical significance. We chose 5 min, as even small but consistent differences of recovery time add up in a busy unit. An active paediatric centre will routinely perform 20 or more imaging cases a day. Even if the difference was only 5 min for each afternoon case, these can easily add considerable time to the schedule of the PACU by early evening. For all statistical analysis, GraphPad Prism 5.0 (La Jolla, CA, USA), GraphPad