



PHARMA SCRIPT

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Nighttime medication administration and sleep quality in the intensive care unit

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Purpose: To determine if nighttime medication administration in the intensive care unit (ICU) has an impact on subjective sleep scores.

Methods: Records for chart review included patients screened for a multicenter ICU sleep assessment. Between January 6, 2020, and March 31, 2020, ICU patients were asked to rate their sleep using the Richard's Campbell Sleep Questionnaire (RCSQ). Patients with a RCSQ >50 (good sleep) were compared with patients with RCSQ ≤50 (poor sleep). Baseline characteristics were collected and compared between groups. Data on nighttime medication administration (between 22:00 – 6:00) was collected to determine the association between nighttime medication administration and sleep quality in the ICU. Multiple logistic regression analysis was used to correct for factors with a $p < 0.1$ on bivariate analysis.

Results: 117 patients were included in the study. Results revealed patients with a median age of >60 years old reported better sleep than those ≤60 years old ($p = 0.02$). Additionally, patients receiving >3 medications overnight reported poorer sleep. However, this finding was not statically significant ($p = 0.3$).

Conclusions: Sleep in the ICU may not be impacted by nighttime medication administration. The RCSQ includes questions on sleep depth, latency, awakenings, returning to sleep, sleep quality, and noise. Although the cumulative score may not be impacted by nighttime medication administration, it is possible specific components are impacted. Further research is needed to determine if the RCSQ is an accurate measurement to quantify subjective sleep ratings. Study limitations included retrospective study design, small sample size, and RCSQ is not the gold standard for sleep assessment.

Does COVID-19 exacerbate macroglossia in critically ill patients: A case study analysis

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Purpose: Critically ill patients that are hospitalized with COVID-19 are subject to a number of symptoms throughout their course of infection. Macroglossia is a rare side effect that has been recently observed in these patients without an understood pathophysiology, which can cause a number of functional and aesthetic problems. It is not only important to understand the causative factor of macroglossia, but also to treat it successfully to prevent further complications (airway obstruction, obstructive sleep apnea, etc.). The purpose of this case analysis was to identify the reason for developing macroglossia in critically ill patients to help future clinician diagnoses and ultimately expedite treatment.

Methods: A search strategy using PubMed through May 26th, 2021 was completed. Titles, abstracts, and full texts were screened independently by two reviewers with any conflicts resolved by a third reviewer. Case studies written in English that referenced macroglossia were included. All case report findings/results were then interpreted to the third reviewer and compiled.

Results: 1 pertinent case study was identified and screened. This included a 40 y.o. African American woman who was intubated and admitted to the ICU after worsening respiratory function. In order to improve oxygenation, she underwent prone positioning for 11 days (16 hours of prone positioning followed by 8 hours of supine positioning). At the end of her treatment, she was experiencing severe macroglossia. Typical first line treatment for this is methylprednisolone and a bite block but was ineffective in this patient. However, a lingual compress schedule of 12 hours for 8 days and then 8 hours for 3 additional days proved to be effective. The lingual compress consisted of saline moisturized gauze that was loosely wrapped around the tongue, followed by a Coban wrap layer.

Conclusions: Findings suggest that COVID-19 cannot directly cause a macroglossia event without an underlying etiology. The prone positioning should be interrupted if a patient starts to develop macroglossia. First-line treatment is the combination of steroids and bite blocks, then lingual compression if refractory to avoid partial glossectomy. Non-operative management strategies are likely a desirable alternative given the potential for postoperative morbidity.

Characterization of sleep aid medication prescribing during transitions of care for hospitalized patients

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Purpose: Factors related to hospitalization can disrupt sleep, resulting in the frequent prescription of neuropsychiatric medications to induce sleep. Data suggest that medications prescribed in the inpatient setting are frequently continued unnecessarily across transitions of care. The purpose of this study was to identify the current practices for prescribing sleep aid medications across transitions of care for hospitalized medical patients at a large academic medical center.

Methods: Electronic medical records of adult patients (≥ 18 years old) admitted to an internal medicine service between September 2019 to November 2019 were reviewed. In addition to primary demographic data, sleep aid prescriptions before, during, and after hospitalization were also collected. Descriptive statistics were used for data analysis.

Results: 891 charts were originally reviewed, 134 patients were eliminated as the discharging team was not an internal medicine team, leaving 757 patients remaining for inclusion. Nearly a third of medical patients were prescribed sleep aids during hospitalization, and only half of those patients were prescribed sleep aids prior to admission. Additionally, only 39 patients were prescribed a sleep aid at discharge. Overall, the agents prescribed prior to admission and during hospitalization differ. Although melatonin was the most prescribed sleep aid during both care periods, prescribing was increased 2-fold during hospitalization.

Conclusion: Prescribing of sleep aids in hospitalized medical patients is prevalent, but routine sleep assessment in this setting is less common. The results of this study identified an opportunity for pharmacist-led quality improvement in prescribing sleep aids across transitions of care.

Comparison of PharmD dual degree programs offering provider status

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Purpose: As of 2021, the American Association of Colleges of Pharmacy officially recognizes a total of 110 institutions that offer Doctor of Pharmacy (PharmD) dual degree programs, including Business Administration (MBA), Doctor of Medicine (MD), Physician Assistant (PA), and Master of Public Health (MPH) among many others. Pharmacy dual degree programs offering prescribing authority are on the rise, including those for medicine, physician assistant, and nurse practitioner. With a PharmD dual degree, there are several benefits, such as the potential to reduce total time spent in school and reduce total tuition compared to earning the two degrees independently, increasing networking opportunities, and the possibility of gaining prescribing power depending on the dual degree obtained.¹ Specifically, programs that offer provider status provide a broader perspective on healthcare and support the individual with more tools when providing patient care, affording students with an alternative track to attaining prescribing power upon graduation. The purpose of this research is to assess the various programs that offer a PharmD dual degree with provider status and evaluate potential benefits associated.

Methods: Pharmacy school programs were assessed using the Pharmacy College Application Service (PharmCAS), which is a centralized application service for individuals interested in pursuing a PharmD degree. All programs that offer either a “PharmD/MD”, “PharmD/PA”, or “other” were filtered. Once all applicable programs were screened, research on each program was done either by looking at the information provided on their website or by contacting the program directors through phone and/or email. Main domains of interest include the name of the program, dual degree offered, name of the affiliated dual degree school, year the program was established, total duration to obtain the dual degree, year in pharmacy school to apply to the program, cost of the dual program, scholarships offered, number of dual degree students per year, curriculum, and number of years saved if an individual were to obtain the two degrees independently.

Results: Four PharmD dual programs met inclusion criteria based on PharmCAS results. One was PharmD/MD, two were PharmD/PA, and one was PharmD/NP. Upon closer inspection of the programs, one of the two PharmD/PA programs is no longer offered at the institution that was listed on PharmCAS and was excluded from the review. Rutgers established a PharmD/MD dual program in 2014 in affiliation with the Robert Wood Johnson Medical School, University of Arizona established a PharmD/Masters of Science in Nursing with Family Nurse Practitioner Certificate (PharmD/MSN/FNP Cert) dual program in 2019, and University of Washington established a PharmD/PA dual program in affiliation with MEDEX Northwest. The PharmD/MD program at Rutgers is a full eight-year program where pharmacy students apply in their second or third year of pharmacy school for the dual program, obtain their PharmD, and then matriculate into the MD program to complete the full four-year MD curriculum prior to graduating with a PharmD/MD. Approximately ten students matriculate into the MD program a year. There is no overall reduction in tuition for the dual degree which averages a total of \$57,662 per year. On the other hand, interested students are waived from taking the Medical

College Admission Test (MCAT). The University of Arizona's PharmD/MSN/FNP Cert program can be completed in five and a half years, decreasing the total duration by two and a half years of school. Interested applicants apply to the dual program simultaneously, and with the program initiating in 2019, only four students are currently in the program and no maximum has been established. The total cost of the dual program is approximately \$39,109 per year but a scholarship of \$10,000 per year is available for individuals interested in this dual program. The PharmD/PA program at the University of Washington spans over five years, saving students one year and interested students are eligible to apply in their second year of pharmacy school. The estimated total cost of this dual program is approximately \$49,685.

Evaluation of pharmacist-led direct oral anticoagulation management service in a community teaching hospital

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Background: Direct oral anticoagulant (DOAC) use has impressively increased for various approved indications. There are several advantages of DOACs over vitamin K antagonists including less frequent monitoring and fewer drug interactions. However, the safe and effective use of DOAC therapy still remains challenging as dosing errors can still occur. In April 2021, MedStar Harbor Hospital (MHH) inpatient pharmacy implemented a pharmacist-led DOAC management service. Providers order pharmacy to manage apixaban, rivaroxaban, or dabigatran consults for hospitalized patients. Upon receiving DOAC-pharmacy to manage consults, pharmacists initiate DOAC therapy. Pharmacists monitor DOAC therapy during patient hospitalization and complete monitoring tasks daily per protocol.

Objective: To evaluate the impact of pharmacist-led DOAC management service on patient care.

Methods: Single center, retrospective, observational study was performed by reviewing electronic medical health records at MHH for the months of March and June 2021 for pre and post pharmacist-led DOAC management service respectively. A total of 134 patients were included in this study with the age of 18 years old or greater who received at least 24 hours of DOAC treatment. The primary outcome was the percentage of the patients with appropriate DOAC selection and dosing in both groups. DOACs selection and dose was evaluated based on indications and patient factors such as renal function, liver function and age. Secondary outcomes included percentage of pharmacist interventions including dose recommendations, medication management, untreated indication and medication selection.

Results: A total of 77 patients for pre pharmacist - led DOAC service and 57 patients for post pharmacist-led DOAC services were included in this study. A pre pharmacist-led DOAC group included 85.7% of patients on apixaban, 7.79% on rivaroxaban and 6.49 of patients on dabigatran while a post pharmacist-led DOAC group included 75.43% of patients on apixaban, 22.80% on rivaroxaban and 1.75% on dabigatran. The percentage of the patients with appropriate DOAC selection and dosing was 90% in pre pharmacist-led DOAC service group compared to 100% in post pharmacist-led DOAC management service with p value of 0.01. After pharmacist intervention, percentages of appropriate agent and dose was increased to 95% in pre pharmacist-led DOAC group. Pharmacists intervention for DOAC dosing was required in 14% in pre pharmacist-led DOAC service compared to 1.75 % in post pharmacist-led DOAC service.

Conclusion: There was a significant improvement in appropriate DOAC dosing at initiation with pharmacist-led DOAC service.

Evaluating the safety and efficacy of intravenous antihypertensives prior to the administration of intravenous alteplase for acute ischemic stroke in a community hospital setting

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Purpose: Approximately 750,000 people in the United States experience a stroke every year, 87% of which are ischemic¹. The 2019 American Heart Association/American Stroke Association guidelines recommend IV alteplase 0.9 mg/kg for treatment of acute ischemic stroke (AIS)². Blood pressure of $\geq 185/110$ mmHg excludes a patient from receiving alteplase; however, if this is the only exclusion criteria the patient meets, then it is appropriate to lower the blood pressure to $< 185/110$ mmHg before administering alteplase. As a certified stroke center, Suburban Hospital/Johns Hopkins Medicine treats approximately 400 stroke patients annually. Given this population of stroke patients, we evaluated the safety and efficacy of antihypertensive use prior to alteplase administration.

Methods: This retrospective chart review included patients admitted to Suburban Hospital/Johns Hopkins Medicine from January 1, 2019 - December 31, 2020 whom were at least 18 years old and received alteplase for AIS within 0 to 4.5 hours of symptom onset. Patients who received any blood pressure lowering medication other than intravenous (IV) nicardipine, IV labetalol, or IV hydralazine were excluded. The primary outcome measured the efficacy of antihypertensive use prior to alteplase administration by evaluating the National Institutes of Health Stroke Scale (NIHSS) score, the frequency of thrombectomy, and the incidence of death after alteplase administration. The secondary outcome measured the safety of antihypertensive use prior to alteplase administration by evaluating the following: incidence of intracranial hemorrhage, major and minor bleeding, the incidence of guideline directed alteplase dosing, the incidence of hypersensitivity reactions, the presence of cerebral edema, cerebral herniation, seizure, new ischemic stroke, or embolism following the administration of alteplase, the length of ICU and hospital stay, and the incidence of mechanical ventilation. Statistical analysis included a paired t-test to evaluate continuous data.

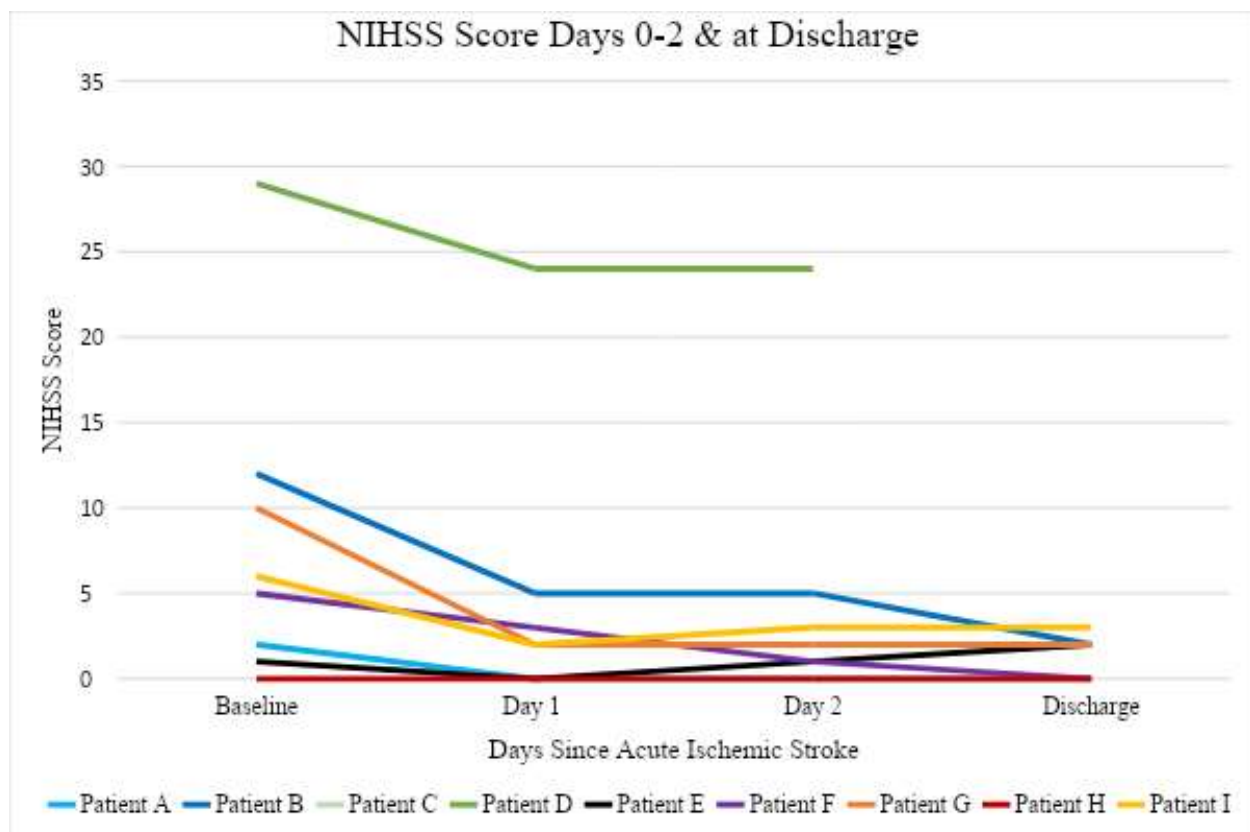
Results: Of the 97 screened patients, 9 were included [mean age 70 years; 7 female]. A statistically significant difference was found in NIHSS score from baseline to day 1 ($p=0.012$) and baseline to day 2 ($p=0.014$), however, significance of the NIHSS score from baseline to discharge could not be determined due to lack of all endpoint values being available. One patient underwent thrombectomy and subsequently died following the administration of IV alteplase.

Conclusion: Patients with a blood pressure of $< 185/110$ mmHg qualify for IV alteplase in the treatment of AIS. Patients with mild or moderate strokes experienced an improvement in NIHSS score after IV alteplase administration. A trend towards quicker blood pressure control was observed in patients who received IV labetalol 10 mg as compared to other IV antihypertensive agents/strengths.

Table 1: Effect of antihypertensive medications

| IV Antihypertensive | Mean length of time between IV antihypertensive and IV alteplase administration – minutes (range) | Average Blood Pressure - mmHg |
|----------------------|---|-------------------------------|
| IV Labetalol 10 mg | 7.6 (2-18) | 201/87 |
| IV Labetalol 20 mg | 52 (50-54) | 220/119 |
| IV Hydralazine 20 mg | 54 (N/A) | 260/115 |
| IV Nicardipine | N/A (N/A) | N/A |

Figure 1: Primary endpoint NIHSS score



1. American Heart Association/American Stroke Association. About stroke. <https://www.stroke.org/en/about-stroke>. (Accessed 2021 Nov 1).
2. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019; 50: 344-418.

Use of anticoagulants and antiplatelet agents in living donor liver transplant (LDLT) recipients

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Purpose: LDLT was first attempted in the 1980s in children to shorten the waiting period for a liver transplant (LT).¹ According to the Organ Procurement and Transplantation Network (OPTN), 569 LDLTs were performed in 2021.² Despite the advancements in LT, there remain a significant number of complications. One of the most significant complications is vascular thrombosis of the reconstructed hepatic artery and portal vein, which potentially results in hepatic failure and graft loss.³ In addition to thrombotic risks, LT is associated with a high bleeding risk, as it is performed in a setting of already unstable hemostasis. For this reason, routine peri- and post-operative prophylactic anticoagulation is usually not the standard of care. The purpose of this study is to evaluate the use of anticoagulants and antiplatelet agents in living donor liver transplant recipients and to assess safety and efficacy outcomes associated with these therapies.

Methods: Our study is a single center retrospective study of all adult and pediatric patients who received a living donor liver graft between July 1, 2016 to December 31, 2020. Patients were excluded from the study if any of the following criteria were met: received a deceased donor graft, recipients with a history of concomitant hypercoagulability disorders such as antiphospholipid syndrome, Factor V Leiden, hyperhomocysteinemia, active malignancies, hormone replacement, contraceptives (estrogen), and COVID-19 infection. Data was collected on recipient demographics, anticoagulant and antiplatelet regimens, pertinent clinical labs values and recipient outcomes.

Study endpoints that were described include, anticoagulant/antiplatelet therapy, reversal agent use, thrombotic and bleeding events, graft loss and one-year patient survival.

Results: During the study period, 55 LDLT recipients were transplanted and 41 patients met inclusion criteria. Of those included, 11 (27%) experienced a hepatic thrombotic event (HTE), 34 (83%) received at least one anticoagulant post-transplant and 38 (93%) received an antiplatelet agent post-transplant. HTE occurred in 29% (n=10) of patients on an anticoagulant vs 14% (n=1) of patients who were not on an anticoagulant (p=0.651). Anticoagulant use did not reduce the incidence of HTE. Antiplatelet use resulted in fewer HTE [26% (n=10) vs 33% (n=1)] compared to patients who were not on an antiplatelet regimen. Overall, 91% of patients in the HTE group received at least one anticoagulant or antiplatelet agent. In the thrombosis-free group, 80% received an anticoagulant and 93% an antiplatelet agent.

No patients experienced graft loss. One death occurred in the thrombosis-free group unrelated to LT complications. Use of vitamin K for reversal occurred in 27% of patients in the HTE group vs 3% in the thrombosis-free group (p=0.052). A hemorrhagic event was identified in 27% of

patients with HTE vs 30% of patients in the thrombosis-free group during the 1-year post-transplant period ($p=1$).

Conclusion: Hepatic thrombosis had a lower incidence in patients who were receiving an antiplatelet regimen; however, this was not a statistically significant finding. Anticoagulant use post-transplant did not decrease the incidence of hepatic thrombosis. Graft loss and one-year patient survival did not significantly differ between the two groups.

1. Nadalin, S, et al., Living Donor Liver Transplantation. *HPB: The Official Journal of the International Hepato Pancreato Biliary Association*, U.S. National Library of Medicine. 2006
2. OPTN Metrics. OPTN Metrics, <https://insights.unos.org/OPTN-metrics/> (accessed Dec. 2021)
3. Onda, S, et al., "Renal Infarction during Anticoagulant Therapy after Living Donor Liver Transplantation." *Case Reports in Gastroenterology*. 2018

Evaluation of the clinical impact of decreasing the maximum osmolarity of neonatal peripheral parenteral nutrition

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Objective: The objective of this study is to describe the clinical impact of lowering the peripheral parenteral nutrition (PPN) maximum osmolarity limit from 1000 mOsm/L to 900 mOsm/L in neonatal patients in two neonatal intensive care units.

Methods: This is an institutional review board-approved retrospective cohort study conducted in two neonatal intensive care units (NICUs). Patients were included if they were inborn to the two NICUs and received PPN for at least 3 consecutive days within the first 14 days of life. Patients were excluded if they required fluid restriction defined as an initial combined intravenous lipid emulsion and PPN order volume of less than 60 ml/kg/day. Data pertaining to patient demographics and PPN order components were collected via electronic medical record reports between August 9th, 2020 and September 30th, 2020 for the pre-implementation cohort with a PPN osmolarity limit of 1000 mOsm/L, and data were collected between October 1st, 2020 to January 3rd, 2021 for the post-implementation cohort with a PPN osmolarity limit of 900 mOsm/L. Data were evaluated to compare the ability of PPN to provide daily recommended macronutrient doses, daily recommended goal calories, and incidence of peripheral IV infiltrates between cohorts.

Results: A total of 200 PPN orders representing 57 patients were included for analysis, with 100 PPN orders and 25 patients in the pre-implementation cohort and 100 PPN orders and 32 patients in the post-implementation cohort. The average gestational age of included patients was 33 weeks. Patients in the post-implementation cohort weighed significantly more with a median dosing weight of 2.1 kg compared to 1.8 kg in the pre-implementation cohort ($p=0.047$). The median osmolarity in the pre-implementation cohort was significantly higher than the post implementation cohort (990 mOsm/L vs 892 mOsm/L, $p<0.001$). Significantly more patients reached goal amino acid doses (45% vs 24%, $p=0.003$) and goal lipid doses (61% vs 37%, $p=0.001$) in the pre-implementation cohort compared to the post-implementation cohort. Ten patients achieved goal daily calories from their PN lipids and enteral formula combined with 6 in the pre-implementation cohort and 4 in the post-implementation cohort ($p=0.748$). A total of three patients received hyaluronidase for PN infiltration, two in the pre-implementation cohort and one in the post-implementation cohort ($p=0.576$).

Conclusion: The lower PPN osmolarity limit of 900 mOsm/L significantly limited the ability to provide goal amino acid doses to NICU patients compared to the previous osmolarity limit of 1000 mOsm/L without reducing the incidence of PIV infiltration or extravasation. This suggests a PPN osmolarity limit of 1000 mOsm/L may be more appropriate for neonatal patients to optimize clinical nutrition outcomes, although evaluation of this impact in larger patient populations is still needed.