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An Analysis of Psychoactive Medications Initiated in the ICU but Continued Beyond Discharge: A Pilot Study of Stewardship

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Abstract

Background: Psychoactive medications (PM) are frequently administered in the intensive care unit (ICU) to provide comfort. Interventions focused on preventing their continuation after the acute phase of illness are needed.

Objective: To determine the frequency that patients with ICU-initiated PM are continued upon ICU and hospital discharge.

Methods: This single-center, prospective, observational study assessed consecutive adult ICU patients who received scheduled PM. Frequency of PM continued at ICU and hospital discharge was recorded. The patient's primary treatment team was contacted by the pharmacist within 72 hours of ICU discharge to establish rationale for continued use or to suggest discontinuation.

Results: Of the 60 patients included, 72% were continued on PM at ICU discharge and 30% at hospital discharge. The pharmacist contacted 40% of treatment teams after ICU discharge and intervention resulted in PM discontinued in 50% of patients. Post ICU discharge, the indication of 41% of patients' PM was unknown by the non-ICU care team or incorrect. Medical ICU patients or those transferred to an outside facility were more likely remain on PM at hospital discharge.

Conclusion: PM are frequently continued during transitions of care and often without knowledge of the initial indication. Future studies should establish effective PM stewardship methods.

Keywords

psychoactive medications; atypical antipsychotics; medication reconciliation; medication safety; transitions of care

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Introduction

Psychoactive pharmacologic agents are commonly administered to intensive care unit (ICU) patients to alleviate agitation and delirium. Medications prescribed include, but are not limited to, antipsychotics, phenobarbital, valproate, clonidine, benzodiazepines, ketamine, propofol, and dexmedetomidine.[1-6] Despite the lack of definitive data to support the use of some of these agents for ICU agitation or delirium, they continue to be prescribed.[1,7-12] While this could be appropriate during the acute phase of illness, psychoactive medications (PM) may be continued upon ICU and hospital discharge, both purposefully and inadvertently.[3,13-24]

Multiple reports[3,4,13-24] have cited high rates of PM continued at hospital discharge and most of these reports are limited to descriptions of antipsychotics. Safety risks associated with short- and long-term use of antipsychotics make these data especially concerning, in addition to the unnecessary patient costs accrued.[25-32] Although some of these medications are continued appropriately (eg, ongoing management of agitation), many are continued without a clear indication.[4] Unfortunately, existing literature offers little insight regarding the rationale for PM continued at hospital discharge. Potential reasons include an incomplete understanding of the acute indication, concern for symptom reemergence, or lack of concern for potential adverse outcomes, but more data are needed.

Although the majority of data on continuation of PM involves antipsychotics, the problem extends beyond this drug class. Recent data suggest that approximately 25% of patients prescribed valproate or clonidine for ICU agitation continue therapy after hospital discharge.[3,4] The high rates of continuation of PM describes a trend that demands the attention of ICU caregivers with the focus on reasons for continuation and strategies to prevent it.

Methods

In order to address these issues, we developed a pharmacist-driven intervention that focused on prospectively evaluating the scope of the problem and the factors contributing to it. The primary objective of this study was to determine the frequency in which patients on select PM initiated in the ICU are continued on these medications at ICU and hospital discharge. The secondary objectives were to classify prescriber rationale for continuing these agents outside the ICU and to assess the role of a pharmacist as a psychoactive medication steward during transitions of care.

Study Design and Population

This single-center, prospective, observational study evaluated consecutive medical, neurological, and trauma/surgical ICU patients, aged 18 years or older, who were newly prescribed PM (clonidine, quetiapine, ziprasidone, risperidone, olanzapine, haloperidol, phenobarbital, and valproate) after admission to our 32-bed ICU in a tertiary care academic medical center from February 10, 2015, to June 10, 2015. Patients were excluded if PM were prescribed prior to hospital admission, the ICU length of stay was less than 24 hours, the medication was utilized for an indication other than behavioral control such as

hypertension or seizures, or if the PM were prescribed as a onetime or pro re nata (PRN) dose. This study was approved by our institutional review board as exempt and did not require patient consent.

During the study period, our ICU's used the Sedation-Agitation Scale (SAS) and the Confusion Assessment Method for the ICU (CAM-ICU) to assess ICU agitation/sedation or delirium, an ICU order set for commonly prescribed sedative medications and daily assessment of patient behavior to guide treatment. Initiation, dosing, and continuation of therapy were determined by the interdisciplinary treatment team for each patient. Each ICU treatment team (medical, neurological, and trauma/surgery) has a dedicated rounding pharmacist, but the presence of a pharmacist on primary treatment teams after ICU stay was not consistent. ICU pharmacist recommendations regarding PM were not recorded due to inconsistencies between pharmacists, unreliable documentation, and inconsistent coverage. Patients were identified for inclusion using an electronic medical record alert when PM were prescribed in any adult ICU location except the cardiac and cardiothoracic ICU's. Readmissions to the ICU were assessed per patient. At the completion of the study, a total of 4 patients were read-mitted to the ICU once and each patient did not have pharmacist contact prior to readmission due to it occurring within 48 hours. Therefore, each patient's assessment and analysis of PM only included the hospital stay after the second ICU discharge.

Demographics and outcomes data.—Demographic data were collected for each patient including age, gender, admitting ICU service, Acute Physiology and Chronic Health Evaluation III score, mechanical ventilation status, any PM prescribed prior to admission, ICU and hospital length of stay, tracheostomy placement, documentation of self-extubation, days of mechanical ventilation, and discharge disposition.

Drug therapy data.—ICU patients meeting inclusion criteria were evaluated for documentation of behavioral issues and/or indication(s) for PM, the dosing and type of prescribed PM, adverse events possibly associated with the PM, and whether a psychiatric consult was requested throughout their ICU stay. SAS scores or CAM-ICU data were not collected due to our institution's previous demonstration[4] of unreliable documentation of these assessments. The intervening pharmacist reviewed the electronic medical record for the above information every 2 to 5 days during the ICU stay until the patient was discharged from the ICU. After ICU discharge, electronic medical records were reviewed daily and the above data were collected in addition to adverse effects that led to discontinuation of PM, day of discontinuation, and the nature of the pharmacist interaction with the non-ICU treatment team.

Pharmacist-Driven Intervention

Each consecutive ICU patient with active orders for newly prescribed, scheduled PM was identified and followed by the pharmacist throughout the ICU and hospital stay. The primary treatment team was contacted by this investigator within 72 hours of ICU discharge if the patient was continued on PM. The pharmacist contacted the primary treatment team once after ICU discharge to discuss continuation of PM. If unavailable, the pharmacist would

make 2 additional attempts to contact the team before documenting a failure to communicate with the non-ICU treatment team. A predetermined script helped to consistently establish the rationale for continued use and intervene if it was concluded that there was no longer an indication for the PM.

1. What is the current indication for the PM?
2. Is the patient still agitated or having behavioral disturbances?
3. Do you/the primary team have a plan for discontinuation/tapering off the PM?
4. I recommend discontinuing the PM due to a lack of indication.

   or

5. I would recommend the following tapering schedule to discontinue the PM prior to discharge.

If there was no indication for continuing the PM, the pharmacist recommended a discontinuation strategy such as a dosing taper,[3] when appropriate. If the PM were discontinued or the taper started within 24 hours of the pharmacist's intervention, the recommendation was considered "accepted."

Statistical Analysis

Descriptive statistics and exploratory data analysis were used to summarize the data. Categorical data were described using contingency tables. Continuously scaled measures were summarized with descriptive statistical measures (ie, mean [standard deviation)] and median [interquartile range]). A linear regression model and *t* test were used to assess the association between PM and the continuation post-ICU discharge as a continuous variable, while Fisher's exact test was used in data analysis for the categorical variables or dichotomized variables such as types of PM on discharge (yes/no). All statistical tests were 2-sided; $P < .05$ was considered statistically significant. Data analysis was performed using the statistical software R (version 3.31, R Foundation, Vienna, Austria).

Results

Study Population

Sixty-five patients were newly prescribed 1 or more scheduled PM and met inclusion criteria. Five patients were excluded as a result of incomplete data collection due to their ongoing hospital admission at the time of study completion. As a result, a total of 60 patients were included in final analysis. Demographic characteristics are listed in Table 1. The majority of patients were male (70%) with a median age of 59 years. Seventy-seven percent were admitted to either the medical or trauma/surgical critical care services and 68% required mechanical ventilation. The median ICU and hospital lengths of stay were 10.5 and 19.5 days, respectively. A total of 86 PM were newly prescribed to the 60 study patients during their ICU stay.

Study Outcomes

Of the 60 patients who were newly started on PM during their ICU admission, 43 (72%) were continued on PM at ICU discharge (Table 2). Of these 43 patients, 18 (42%) were discharged from the hospital with a prescription for newly initiated PM (Table 3).

Within 72 hours of ICU discharge, the pharmacist contacted the primary treatment team of 17 of the 43 (40%) patients who were continued on PM. The pharmacist did not contact the primary treatment team for the other 26 patients, largely because the target medication was discontinued within that time frame (Table 2).

Of the 17 primary treatment teams contacted by the pharmacist, 7 (41%) did not know the indication of the PM or held misinformation about the initial indication of the PM. Incorrect rationale was defined by the pharmacist based on dosing, ICU documentation of indication, and conversation with providers. Ten patients had documented adverse effects possibly associated with the PM that led to discontinuation in 6 patients; 3 patients experienced the adverse effect prior to ICU discharge. Corrected Q-T interval prolongation was noted for 5 patients, over-sedation was noted for 3 patients, and hemodynamic changes were noted for 2 patients. Of the 27 patients using clonidine for behavioral control, 9 (33%) did not have a plan for dose tapering[3] (Table 2). Overall, patients were treated with PM for a mean of 13 days for the entire hospitalization and 5.6 days post-ICU discharge.

The pharmacist recommendation to discontinue or taper PM was accepted for 8 patients within 24 hours, a success rate of approximately 50% (Table 2). An additional 2 patients had their PM discontinued greater than 24 hours after intervention but prior to hospital discharge, and the effect of the pharmacist interaction could not be assessed for these patients. Eighteen of the 43 patients with PM continued after ICU discharge were prescribed these medications upon hospital discharge. Documented rationale for continued use included maintenance of the sleep/wake cycle, management of sustained agitation or delirium, completion of dosing taper, continuation per psychiatry recommendation, and blood pressure management. No therapeutic rationale was available for 4 of the 18 patients (Table 3). It is relevant to note that most of the information regarding the rationale for continuation of therapy was based on pharmacist conversations with the primary treatment team since there was very little documentation in the medical record. One patient was unintentionally discharged on clonidine with 6 months of refills despite a stated plan for a 3-day taper.

The types of PM that were started and continued at the transitions of care were identified (Table 4), and although not found to be statistically significant ($P = .513$), we found atypical antipsychotics were continued more often at ICU and hospital discharge than other PM. An analysis of patients discharged on PM at ICU and hospital discharge was performed to determine risk factors for continuation of PM. As described in Table 5, patients discharged from the hospital on PM were more likely to be admitted to the medical ICU service ($P = .009$) or transferred to an outside facility ($P = .002$).

Detailed information was collected for all patients continued on PM after ICU and hospital discharge with and without pharmacist intervention. While pharmacist interventions were successful in drug discontinuation for about half of patients, multiple patients were

discharged from the hospital with extended prescriptions for PM without strong, documented rationale. For medications with a documented indication for continuation, we found most involved off-label uses without strong supportive clinical data (eg, quetiapine used for sleep). Interestingly, these data demonstrate the lack of consensus between documented behaviors, documented indications, and discussion between the team and the pharmacist.

Discussion

Our study confirms and extends the findings that PM initiated in the ICU are commonly continued following ICU and hospital discharge. It is the first to prospectively examine the reasons for continuing antipsychotics as well as other PM when patients are recovering from critical illness. Understanding the rationale for this practice is essential to create strategies to avoid inadvertent or inappropriate psychoactive therapeutics. The use of an electronic handoff tool, pharmacist-driven medication protocol, as well as an antipsychotic discontinuation bundle have not demonstrated any effect on medication continuation upon hospital discharge.[15,21,22] Within our institution, 70% of patients with PM initiated in the ICU continue on these medications when transitioning to non-ICU nursing units, and of these patients, about half continue taking them as outpatients. Our data, based on discussions with prescribers, suggest there is confusion about the intended indication and therapeutic goals for PM, especially for agents such as clonidine and valproate. Our data also suggest that a thorough evaluation of the need for these medications is often lacking, that prescribers are hesitant to change or stop medications for fear of resurgence of patient behaviors, and lastly, advice from psychiatry plays an important role by giving legitimacy to the continuation of these medications. Other potential contributors to the continued use of PM include an unfamiliarity of their potentially serious acute and long-term adverse effects and methods for safely discontinuing or tapering. This was demonstrated by our collection of discharge data, identifying multiple patients prescribed PM for up to 6 months postdischarge. However, per recently updated recommendations,[1] PM prescribed for distressing symptoms should be discontinued at resolution of symptoms and additionally, exposure leads to an increase in morbidity and financial cost.

Similar Studies

Multiple authors have documented high continuation rates of psychoactive agents at ICU and/or hospital discharge.[3,4,13-24] The literature is not uniform regarding risk factors for continuation of antipsychotics after hospital discharge, but most available data cite admission to a medical ICU service, longer hospitalization, and disposition to a place other than home. Knowledge of risk factors may help focus efforts to limit prescribing of PM after hospital discharge, but clearly other issues are important. Our study shows that the rationale for continuing these medications is weak, inconsistent, unfounded, or even completely unknown. This is also supported by Rowe et al[23] who performed a single-center retrospective study in trauma, surgical, and neuroscience ICU patients prescribed atypical antipsychotics, thiothixene, or haloperidol. The authors reported a continuation rate of 24% for antipsychotics at hospital discharge and found that 67% of these patients did not have a documented indication for continuation in the medical record. Of note, the majority (82%)

of these prescriptions were for quetiapine and risk factors for continuation included ICU and hospital length of stay, duration of mechanical ventilation, and morphine and benzodiazepine administration. In a retrospective, single-center sample, Flurie et al[18] also reported that 64% of atypical antipsychotics and haloperidol continued at hospital discharge were inappropriate. This was determined by negative CAM-ICU scores within 24 hours of transfer out of the medical ICU.

The significant risks, including death, associated with PM emphasize the importance of avoiding their unnecessary use in this vulnerable population.[25-32] However, to date, we have yet to determine the most appropriate system to avoid these agents and therefore the adverse effects associated with them. In a single-center, retrospective study, D'Angelo and colleagues[15] studied the effectiveness of an antipsychotic discontinuation bundle at the time of transfer out of the medical ICU in 141 patients. The bundle led to a significant decrease in antipsychotic prescribing at ICU discharge but not hospital discharge. Although this study was the first of its kind to evaluate the effectiveness of education and intervention, its limitations include the retrospective nature of the study, confounding variables for pre- and post-bundle groups, and focus on patients from 1 unit predominantly prescribed haloperidol. In a study[21] evaluating the efficacy of a pharmacist-initiated electronic handoff tool to reduce the number of patients on ICU-initiated antipsychotics at hospital discharge, a 22.2% relative risk reduction was observed in the postintervention group. Unfortunately, this tool was not associated with a reduction in hospital discharge prescribing rates or the number of patients receiving atypical antipsychotics during the admission. Our study further adds to the number of flawed methods to reduce PM prescribed on hospital discharge while highlighting the lack of indication for these continuations.

Limitations

There are many limitations to our study, including the small sample size and single-center design. Because we only spoke to a single non-ICU treatment team representative, it is possible that others within that treatment team had greater insight about the need for PM. We recognized this possibility and encouraged the contacted prescriber to discuss the issue with the team and readdress at a later time. We relied heavily on the documentation of behavioral changes and possible adverse effects instead of systematic, subjective scales such as SAS, CAM-ICU, or Naranjo and as a result may have missed undocumented behaviors or adverse events associated with PM. It is likely that our service-based pharmacists made discontinue or taper recommendations for PM during transitions of care and this may have led to a lower incidence of PM continued. However, pharmacist interventions are inconsistently documented and may have further confounded our results. While chart review[33-36] has been a valid method to collect information on patient behavior, future endeavors should include both documentation in the electronic medical record and direct assessments. One distinguishing feature of our study was the use of a single pharmacist who contacted patient care teams and intervened in a systematic manner to encourage the discontinuation of PM after ICU stay. Although this consistency allowed for standardization, it may have affected hospital continuation rates and limits generalizability to other institutions where this type of pharmacist intervention is not feasible. In addition, our pharmacist did not complete medication histories to confirm prior home medications including PM, and therefore, some

patients may have been excluded or included based on inaccurate documentation. We chose to exclude other potential PM such as benzodiazepines, opioids, trazodone, and even PRN doses of PM to allow us to focus on prespecified types of PM, but we recognize that more information is needed regarding the continuation patterns of those agents as well. In addition, we did not assess patient adherence to the medication regimen upon hospital discharge and could not evaluate for adverse effects, behavior changes, or additional costs resulting from extended use of these medications. Finally, we did not record the number of patients prescribed PM within the ICU who did not meet inclusion criteria within the study period. These data should be collected and analyzed in future studies in an effort to inform on PRN dosing, short ICU durations, or inaccurate medication reconciliation.

Implications for Clinical Practice

Several types of medications are initiated and intended only for ICU administration, yet are continued beyond hospital discharge,[37,38] but PM may have the most serious consequences. Adverse effects associated with atypical antipsychotics include acute respiratory failure,[32] neuroleptic malignant syndrome,[39] acute kidney injury, serious falls,[25,26] and even sudden cardiac death.[40] Adverse effects associated with valproate and phenobarbital are no less severe and include hyperammonemia, thrombocytopenia, hepatotoxicity, pancreatitis, and Stevens-Johnson syndrome and sedation, hypotension, and respiratory depression, respectively.[6,41] The main safety concern surrounding clonidine is the potential for withdrawal with hemodynamic repercussions upon abrupt discontinuation.[2,3,5] Despite these safety issues, data consistently suggest that these medications are continued in approximately 25% of patients after hospital discharge.[3,4,13-24]

The development of mitigating strategies requires insight about the rationale for continuation of these potentially harmful therapies. Published interventions, including electronic handoffs and process improvement efforts, have only been partially effective; they limit post-ICU, but not hospital discharge medication use. Our intervention was time-intensive, but allowed an exploration and discussion about the indications and need for continuing PM. It is important to note that even after pharmacist contact, 6 patients were prescribed PM 6 months postdischarge.

In our study, 30% of patients started on PM in the ICU were continued at hospital discharge despite pharmacist intervention, indicating that hospital discharge continuation rates could have been higher without this intervention. Considering previous institutional data and similar studies,[3,4,13-24] it more likely indicates that our intervention was only partially successful. We believe that our results demonstrate that pharmacist intervention as a method of stewardship to prevent continuation of PM could be successful, but there were some potential flaws in our design that prevented discontinuation in some patients. There are opportunities for improvement in future study. The addition of an indication, predetermined duration, or action plan for discontinuation in psychoactive medication orders may establish a discontinuation plan early on in therapy, meet current recommendations,[1] and reduce confusion for teams caring for the patient after ICU discharge. If PM are continued after ICU discharge outside the initial plan, an intervening pharmacist can establish rationale for continuation by discussing with post-ICU caregivers. If a recommendation by the

intervening pharmacist is not accepted, follow-up should take place daily to establish rationale for continuation, in particular, at hospital discharge. Establishing the cause for successful discontinuation prior to hospital discharge can give us insight as to what providers need to feel comfortable with the discontinuation of ICU-initiated PM. Education is needed for providers inside and outside the ICU regarding importance of PM discontinuation or taper and stewardship. Lastly, the addition of a control group without pharmacist intervention will allow for comparison and establish a success rate of pharmacist intervention as a form of stewardship to prevent the use of unnecessary PM and possible adverse effects.

While our data exemplify an additional strategy to limit inappropriate use of PM, additional strategies include, but are not limited to, identification of the indication within the medication order, adding stop dates or taper orders prior to ICU discharge, using the electronic medical record to alert clinicians if ICU-initiated PM are continued after ICU discharge, ensuring that transitions of care focus on all aspects of psychoactive medication use, and utilizing post-intensive care clinics[42] as follow-up opportunities to confirm proper discontinuation or tapering. As important as these mitigating strategies are, there should be an emphasis placed on not initiating these therapeutic options in the first place since most do not have strong supportive data for treating ICU behavioral issues and the risks of therapy have not been well defined.[1]

Conclusion

At our university teaching hospital, the majority of patients started on PM in the ICU for agitation and delirium were continued on them at ICU discharge and approximately one-third of those that were continued at ICU discharge were prescribed PM at hospital discharge. Pharmacologic treatment or prevention strategies for ICU mood/behavioral disturbances should be implemented only after nonpharmacologic efforts have failed. Clinicians need to better define patient-specific goals of therapy with consideration of the short- and long-term risks of inadvertent or inappropriate use of PM. Institutions should develop protocols or methods to evaluate the need for PM both at ICU discharge and hospital discharge. Further studies are warranted to evaluate the utility and success rates of such protocols.

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References

1. Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46(9):e825–e873. [PubMed: 30113379]
2. Gagnon DJ, Kovacic N, Fraser GL. Agitation and comfort in the intensive care unit In: Critical Care Pharmacotherapy. Lenexa: American College of Clinical Pharmacy; 2016 161–185.

3. Gagnon DJ, Riker R, Glisic EK, et al. Transition from dexmedetomidine to enteral clonidine for ICU sedation: a pilot study. Pharmacotherapy. 2015;35(3):251–259. [PubMed: 25809176]
4. Gagnon DJ, Fontaine GV, Smith KE, et al. Valproate for agitation in critically ill patients: a retrospective study. J Crit Care. 2017;37:119–125. [PubMed: 27693975]
5. Gagnon DJ, Fontaine GV, Riker RR, et al. Repurposing valproate, enteral clonidine, and phenobarbital for comfort in adult ICU patients: a literature review with practical considerations. Pharmacotherapy. 2017;37(10):1309–1321. [PubMed: 28833346]
6. Fraser GL, Riker RR. Phenobarbital provides effective sedation for a select cohort of adult ICU patients intolerant of standard treatment: a brief report. Hosp Pharm. 2006;41(1):17–23.
7. Patel RP, Gambrell BA, Speroff T, et al. Delirium and sedation in the intensive care unit (ICU): survey of behaviors and attitudes of 1,384 healthcare professionals. Crit Care Med. 2009;37(3):825–832. [PubMed: 19237884]
8. Yassin SM, Terblanche M, Yassin J, et al. A web-based survey of United Kingdom sedation practice in the intensive care unit. J Crit Care. 2014;30:436. e1-e6.
9. Mehta S, McCullagh I, Burry L. Current sedation practices: lessons learned from international surveys. Crit Care Clin. 2009;25(3):471–488. [PubMed: 19576525]
10. Egerod I, Christensen BV, Johansen L. Trends in sedation practices in Danish intensive care units in 2003: a national survey. Intensive Care Med. 2006;32(1):60–66. [PubMed: 16283160]
11. Devlin JW, Bhat S, Roberts RJ, et al. Current perceptions and practices surrounding the recognition and treatment of delirium in the intensive care unit: a survey of 250 critical care pharmacists from eight states. Ann Pharmacother. 2011;45(10):1217–1229. [PubMed: 21934036]
12. Girard TD, Exline MC, Carson SS, et al. Haloperidol and ziprasidone for treatment of delirium in critical illness. N Engl J Med. 2018;379(26):2506–2516. [PubMed: 30346242]
13. Jasiak KD, Middleton EA, Camamo JM, et al. Evaluation of discontinuation of atypical antipsychotics prescribed for ICU delirium. J Pharm Pract. 2013;26(3):253–256. [PubMed: 23184410]
14. Kram BL, Kram SJ, Brooks KR. Implications of atypical antipsychotic prescribing in the intensive care unit. J Crit Care. 2015;30(4):814–818. [PubMed: 25887805]
15. D'Angelo RG, Rincavage M, Tata AL, et al. Impact of an antipsychotic discontinuation bundle during transitions of care in critically ill patients. J Intensive Care Med. 2016;doi:10.1177/0885066616686741.
16. Tomichek JE, Stollings JL, Pandharipande PP, et al. Antipsychotic prescribing patterns during and after critical illness: a prospective cohort study. Crit Care. 2016;20(1):378. [PubMed: 27881149]
17. Scales DC, Fischer HD, Bierman AS, et al. Unintentional continuation of medications intended for acute illness after hospital discharge: a population-based cohort study. J Gen Intern Med. 2016;31(2):196–202. [PubMed: 26369941]
18. Flurie RW, Gonzales JP, Tata AL, et al. Hospital delirium treatment: continuation of antipsychotic therapy from the intensive care unit to discharge. Am J Health Syst Pharm. 2015;72(23 suppl 3):S133–S139. [PubMed: 26582298]
19. Farrokh S, Castle AC, Heavner M, et al. Continuation rate of atypical antipsychotics after discharge when initiated in the intensive care unit. J Pharm Pract. 2017;30(3):342–346. [PubMed: 27129913]
20. Marshall J, Herzig S, Howell MD, et al. Antipsychotic utilization in the intensive care unit and in transitions of care. J Crit Care. 2016;33:119–124. [PubMed: 26818629]
21. Kram BL, Schultheis JM, Kram SJ, et al. A pharmacy-based electronic handoff tool to reduce discharge prescribing of atypical antipsychotics initiated in the intensive care unit: a quality improvement initiative. J Pharm Pract. 2018. doi:10.1177/0897190018761412.
22. Martz C, Peters M, Swiderek J, et al. Evaluation of a pharmacist-driven medication discontinuation protocol in an intensive care unit. Crit Care Med. 2017:46(suppl 1). abstract 962.
23. Rowe AS, Hamilton LA, Curtis RA, et al. Risk factors for discharge on a new antipsychotic medication after admission to an intensive care unit. J Crit Care. 2015;30(6):1283–1286. [PubMed: 26383104]
24. Gilbert B, Morales JR, Searcy RJ, et al. Evaluation of neuroleptic utilization in the intensive care unit during transitions of care. J Intensive Care Med. 2017;32(2):158–162. [PubMed: 28103769]

25. Fraser LA, Liu K, Naylor K, et al. Falls and fractures with atypical antipsychotic medication use: a population-based cohort study. JAMA Intern Med. 2015;175(3):450–452. [PubMed: 25581312]
26. Pratt N, Roughead EE, Ramsay E, et al. Risk of hospitalization for hip fracture and pneumonia associated with antipsychotic prescribing in the elderly. Drug Saf. 2011;34(7):567–575. [PubMed: 21663332]
27. Zemrak WR, Kenna GA. Association of antipsychotic and antidepressant drugs with Q-T interval prolongation. Am J Health Syst Pharm. 2008;65(11):1029–1038. [PubMed: 18499875]
28. Meulendijks D, Mannesse CK, Jansen PAF, et al. Antipsychotic-induced hyponatraemia: a systematic review of the published evidence. Drug Saf. 2010;33(2):101–114. [PubMed: 20082537]
29. Hwang YJ, Dixon SN, Reiss JP, et al. Atypical antipsychotic drugs and the risk for acute kidney injury and other adverse outcomes in older adults. Ann Intern Med. 2014;161(4):242–248. [PubMed: 25133360]
30. Loh KP, Ramdass S, Garb JL, et al. Long-term outcomes of elders discharged on antipsychotics. J Hosp Med. 2016;11(8): 550–555. [PubMed: 27062675]
31. Park Y, Bateman BT, Kim DH, et al. Use of haloperidol versus atypical antipsychotics and risk of in-hospital death in patients with acute myocardial infarction: cohort study. BMJ. 2018;360:k1218. [PubMed: 29592958]
32. Wang MT, Tsai CL, Lin CW, et al. Association between antipsychotic agents and risk of acute respiratory failure in patients with chronic obstructive pulmonary disease. JAMA Psychiatry. 2017;74(3):252–260. [PubMed: 28055066]
33. Pisani MA, Araujo KL, Van Ness PH, et al. A research algorithm to improve detection of delirium in the intensive care unit. Crit Care. 2006;10(4):R121. [PubMed: 16919169]
34. Burk RS, Grap MJ, Munro CL, et al. Agitation onset, frequency, and associated temporal factors in critically ill adults. Am J Crit Care. 2014;23(4):296–304. [PubMed: 24986170]
35. Burk RS, Grap MJ, Munro CL, et al. Predictors of agitation in critically ill adults. Am J Crit Care. 2014;23(5):414–423. [PubMed: 25179037]
36. O'Connor H, Al-Qadheeb NS, White AC, et al. Agitation during prolonged mechanical ventilation at a long-term acute care hospital: risk factors, treatments, and outcomes. J Intensive Care Med. 2014;29(4):218–224. [PubMed: 23753245]
37. Pavlov A, Muravyev R, Amoateng-Adjepong Y, et al. Inappropriate discharge on bronchodilators and acid-blocking medications after ICU admission: importance of medication reconciliation. Respir Care. 2014;59(10):1524–1529. [PubMed: 24847095]
38. Scales DC, Fischer HD, Li P, et al. Unintentional continuation of medications intended for acute illness after hospital discharge: a population-based cohort study. J Gen Intern Med. 2015;31(2):196–202.
39. Caroff SN, Mann SC, Campbell EC. Atypical antipsychotics and neuroleptic malignant syndrome. Psychiatr Ann. 2000;30(5):314–321.
40. Ray WA, Chung CP, Murray KT, et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med. 2009;360(3):225–235. [PubMed: 19144938]
41. Brodie MJ, Dichter MA. Antiepileptic drugs. N Engl J Med. 1996;334(3):168–175. [PubMed: 8531974]
42. Stollings JL, Bloom SL, Wang L, et al. Critical care pharmacists and medication management in an ICU recovery center. Ann Pharmacother. 2018;52(8):713–723. [PubMed: 29457491]

Table 1.

Demographics and Patient Characteristics.

Data Points for Demographic and Patient Information	n = 60
Years of age, median (Q1, Q3)	59 (47, 68)
Male, n (%)	42 (70)
Admitting service, n (%)	
Medical critical care	25 (42)
Trauma/surgical critical care	21 (35)
Neuroscience critical care	11 (18)
Internal medicine	3(5)
APACHE III score, mean (SD)	58 (23.9)

Abbreviations: APACHE III, Acute Physiology and Chronic Health Evaluation III; Q1, first quartile; Q3, third quartile; SD, standard deviation.

Table 2.

ICU Discharge Outcomes Data.

Patients discharged from ICU on PM, n = 60 (%)	43 (72)
Number of PM prescribed at discharge	22
Number of PM prescribed at ICU discharge	1.22 (0.8)
Pharmacist contacted team, n = 43 (%)	17 (40)
Reasons team not contacted, n = 26	
Clear discontinuation plan in medical record	11
Medication discontinued within 72 hours of ICU transfer	7
Psychiatry consult recommended to continue medication	5
Clear, current indication for medication in medical record	2
Attempt to contact team × 3, no return contact	1
Number of PM prescribed to patients not contacted by pharmacist due to appropriate discontinuation by the provider	
Quetiapine	8
Olanzapine	0
Risperidone	3
Haloperidol	1
Clonidine	15
Valproate	7
Phenobarbital	2
Pharmacist recommendation accepted, n = 17 (%)	8 (47)
Recommendation accepted or PM discontinued prior to discharge, n = 17 (%)	10 (59)
Patients with unknown/incorrect indication when team was contacted by pharmacist, n = 17 (%)	7 (41)
Safety	
Number of patients with documented AE leading to discontinuation of PM, n = 43 (%)	6(14)
Number of patients with clonidine taper outside of established recommendations[3], n = 27 (%)	9 (33)
Total days of ordered PM per patient during hospitalization, mean (SD)	13 (4.2)
Total days of ordered PM per patient post-ICU discharge, mean (SD)	5.6 (3.5)

Abbreviations: AE, adverse effect; ICU, intensive care unit; PM, psychoactive medications; SD, standard deviation.

Table 3.

Hospital Discharge Data and Outcomes Data.

Patients discharged from hospital on PM, n = 60 (%)	18 (30)
Documented indication for PM continued at hospital discharge, n =18 (%)	
Sleep–wake cycle/agitation/delirium (2 as PRN)	6 (33)
Completing taper	5 (28)
Undocumented rationale	4 (22)
Psychiatry recommendation	2 (11)
Blood pressure management	1 (6)
Patients without an “accepted” pharmacist intervention continued on PM at hospital discharge	8 (44)
Length of stay, median (SD)	
ICU	10.5 (14.1)
Hospital	19.5 (38.9)
Required mechanical ventilation (MV), n (%)	41 (68)
Days of MV, median (IQR)	10 (18)
Tracheostomy, n (%)	6 (10)
Self-extubated, n (%)	2 (3)[a]
Discharge disposition, n (%)	
Home	21 (35)
Death	8 (13)
Transfer to an outside facility	25 (42)
Rehabilitation facility	3 (5)
Transfer to outside institution	3 (5)
Skilled nursing facility (SNF)	

Abbreviations: ICU, intensive care unit; IQR, interquartile range; PM, psychoactive medication; PRN, pro re nata; SD, standard deviation.

[a]One patient required reintubation.

Table 4.

Number of Patients Started and Continued on Each PM

Different Types of PM	Started in ICU	Continued at ICU Transfer	Continued at Hospital Discharge	Days continued Posthospital Discharge
Haloperidol	4	1	0	/
Olanzapine	1	1	0	/
Quetiapine	25	20	12	2-180[a]
Risperidone	3	3	1[b]	30
Clonidine	33	26	6	4-180[c]
Phenobarbital	8	4	1	40
Valproate	12	10	2	1-2
Any AP at hospital discharge	34	24	13	
No AP at hospital discharge	26	18	5 (P = .513)	

Abbreviations: AP, atypical or typical antipsychotic; ICU, intensive care unit; PRN, pro re nata.

[a]Five were undocumented durations.

[b]Risperidone prescription was PRN.

[c]One was an undocumented duration.

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Table 5.

Comparison of Patients Continued on PM at ICU/hospital Discharge Versus Not Continued.

Data Points for Outcomes Data and Patient Characteristics	No PM at ICU Discharge Group, n = 17	PM at ICU Discharge Group, n = 43	*P* Value	No PM at Hospital Discharge Group, n = 41	PM at Hospital Discharge Group, n = 18	*P* Value
Age	62.5	55.7	.16	58.1	57.1	.84
Male gender	13	29	.99	26	16	.18
Admitting service						
Medical ICU	10	15	.049	18	7	.009
APACHE III score	60.6	56.9	.58	57.9	58.3	.95
Days of MV	12.6	12.	.91	10.4	16.	.3
Tracheostomy	1	5	.78	4	2	.99
ICU length of stay, days	19.6	15.3	.32	15.2	19.6	.3
Hospital length of stay, days	24.7	28.8	.59	24.1	35.1	.15
Discharge disposition						
Outside facility	8 (44%)	23 (55%)	.13	15 (37%)	16 (84%)	.002
Home	5 (28%)	16 (38%)		18 (44%)	3 (16%)	
No documented indication for PM during ICU stay	6 (33%)	14 (33%)	.99	13 (32%)	7 (37%)	.77

Abbreviations: APACHE III, Acute Physiology and Chronic Health Evaluation III; ICU, intensive care unit; MV, mechanical ventilation; PM, psychoactive medication; SD, standard deviation.