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Review

Management of the hospitalized patient with Parkinson's disease: Current state of the field and need for guidelines☆

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ABSTRACT

Objective: To review the literature and to identify practice gaps in the management of the hospitalized Parkinson's disease (PD) patient.
Background: Patients with PD are admitted to hospitals at higher rates, and frequently have longer hospital stays than the general population. Little is known about outpatient interventions that might reduce the need for hospitalization and also reduce hospital-related complications.
Methods: A literature review was performed on PubMed about hospitalization and PD between 1970 and 2010. In addition, *in press* peer-reviewed papers or published abstracts known to the authors were included. Information was reviewed by a National Parkinson Foundation workgroup and a narrative review article was generated.
Results: Motor disturbances in PD are believed to be a causal factor in the higher rates of admissions and complications. However, other conditions are commonly recorded as the primary reason for hospitalization including motor complications, reduced mobility, lack of compliance, inappropriate use of neuroleptics, falls, fractures, pneumonia, and other important medical problems. There are many relevant issues related to hospitalization in PD. Medications, dosages and specific dosage schedules are critical. Staff training regarding medications and medication management may help to avoid complications, particularly those related to reduced mobility, and aspiration pneumonia. Treatment of infections and a return to early mobility is also critical to management.
Conclusions: Educational programs, recommendations, and guidelines are needed to better train interdisciplinary teams in the management of the PD patient. These initiatives have the potential for both cost savings and improved outcomes from a preventative and a hospital management standpoint.

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Contents

1. Introduction

Much research has been devoted to the treatment of the patient with Parkinson's disease (PD). Although numerous reports have revealed that PD patients are admitted to hospitals at higher rates, and frequently have longer hospital stays than the general population [1–3], little is known about interventions that might reduce the need for hospitalization or reduce the complications related to hospitalization. Over the years, a number of movement-disorder specialists have independently developed informal recommendations for management of PD patients during hospitalization. Most of these informal recommendations/guidelines have been focused on facilitating communication between patients and hospital staff. One such guideline was published and widely distributed in a non-peer reviewed format [4]. This guideline highlights common complications experienced by PD patients including mental status change and worsened mobility. It also provides hospital staff with information regarding contraindicated medications (e.g. dopamine receptor-blocking medications), preferred treatments for nausea and psychosis, and managing patients with deep brain stimulation (DBS). It is unknown if recommendations/guidelines such as these have been widely utilized by patients, or whether they address the most important aspects of the hospitalized PD patient. It is also unknown whether these recommendations/guidelines improve patient care. In this article we review the current literature and identify practice gaps in the management of the hospitalized PD patient.

2. Methods

A complete literature review was performed on all international papers found on PubMed that included the terms hospitalization, hospital, and Parkinson's disease between 1970 and 2010. In addition, *in press* peer-reviewed papers or published abstracts known to the authors were included. Information was reviewed by a National Parkinson Foundation workgroup on PD hospitalization, and a review article was generated from the available information as well as discussion among PD experts.

3. Admissions and length of hospitalization for the PD patient

Reasons for admissions and the impact of PD complications on hospital stay have been sparsely characterized in the literature. Studies indicate that PD admissions are more often due to aspiration pneumonia, psychosis, trauma (e.g. hip fractures), and sepsis when compared to controls [5–7]. As a group, PD patients accumulate more inpatient days over their lifetime, (following the diagnosis of PD), when compared to the general population [8]. Length of stay appears to vary by study. A study of 367 PD patients and 246 emergency admissions in the United Kingdom found that the mean length of hospital stay was longer for PD patients than for controls (21.3 vs. 17.8 days) [7], while a recent longitudinal prospective study from the UK including PD and controls over 12 years, showed similar overnight durations (10 days for PD, 11.4 days for controls), but lower survival rates for PD. It should be kept in mind that these findings may be underestimated, as the

Table 1
Common reasons for hospital admission or discharge in the Parkinson's disease patient.

Reasons for admission	Temlett 2006[9] 761 patients	Woodford 2005[7] 367 patients	Klein 2009[1] 143 patients	Vossius 2010[6]* 108 patients
Motor complications/ reduced mobility		8%	37%	
Falls/fractures	13%	18%	24%	
Pneumonia	12%	11%		6%
Other pulmonary				6%
Cardiac issues/syncope	16%	18%		1%
Genitourinary infections	11%	9%		4%
Gastrointestinal issues	11%	3%		
Encephalopathy/ drug-induced psychosis	7%		29%	
Cancer	10%			7%
Stroke	4%	2%		2%
Dementia with or without psychosis	3%	8%		
Elective surgery/DBS		4%		
General medical problems			14%	
Motor and psychiatric combined			25%	
Other				20%

This table details four large hospitalization PD studies. Temlett, Woodford, and Klein are studies of admission diagnoses, and Vossius* utilized discharge diagnoses (different than the other three studies). Data included are a compilation of what was included in the published papers and may be collapsed into categories. Please also note that due to differing methodologies data do not always add up to 100%.

hospitalization of a patient with PD may be shortened by a discharge to a long-term care facility and this remains unaccounted for.

Although motor disturbances in PD are believed to be a causal factor in the higher rates of admissions and complications, other conditions are in fact commonly recorded as the primary reason for hospitalization (Table 1). For example, in a recent report from Australia, the primary reason for hospitalization among 761 admissions of parkinsonian patients was found to be related to PD related symptoms in only 116 instances (15%) [9]. The remaining reasons for admission were: falls (12.6%), pneumonia (12%), cardiac disorders (11.6%), genitourinary infections (11%), gastrointestinal disorders (11%), neoplasia (9.9%), encephalopathy (7%), syncope (4%), stroke (3.6%), and dementia (3%) [9].

The reasons for admission, and findings regarding length of hospitalization in young-onset PD (YOPD defined as onset before age 40) bear some similarities to those observed in older patients. In a nationwide inpatient sample (1000 hospitals) 714 patients and 2007 controls from the United States between 1998 and 2003, the duration of hospitalization, and the number of discharge diagnoses were higher in YOPD patients than in age-matched controls [10]. Moreover, YOPD patients were more likely to be discharged to a rehabilitation or to a skilled nursing facility. Twenty percent of them required extended care. Admission for psychosis made up 25% of the YOPD patient cohort, and this was elevated compared to controls (it is unknown why the increase, but it could have been related to higher doses, self-dosing, impulse control disorders, or dopamine dysregulation). The hospitalization rates for pneumonia and fractures in this study were surprisingly not elevated, and this was possibly due to less susceptibility of the younger age group [10]. The YOPD definition could have biased this study, as patients may have been older at the time of admission.

In a small study PD patients admitted to non-DBS surgical services had a more complex hospital course than non-PD patients. A review of hospital records from 1993 to 2006 (16 patients and 16 controls) revealed that post-operative falls occurred more frequently in PD patients than in controls, and that discharge to inpatient rehabilitation was necessary in more PD patients than in controls [11].

3.1. Hospitalization-related issues

3.1.1. General principles

When PD patients are hospitalized, there are a number of important areas that may affect outcome (Table 2). It is important for the hospital staff to carefully review and confirm patients' PD medications, dosages, and specific dose schedules. Also, if the patient desires to take their own medications while in the hospital, many facilities will only allow prescription of regimens from the bottle, and these may not reflect the actual in practice effective dosages. If medical records are available, this is a starting point, but dosages and schedules should be confirmed with patients and/or care partners. All other medications should be recorded and confirmed to rule out potential drug-induced side effects or interactions. PD medications should be administered as closely to the specific home schedule as possible. Often, PD medication schedules are changed in the hospital (author observations) to match that of other required medications (such as antibiotics) or to better accommodate a nursing schedule. This change may result in greater risk for disability and consequently an increased risk of accidents and other complications. The acute discontinuation of PD medications may place the patient at risk for a neuroleptic malignant-like syndrome (NMS), which although rare can be life threatening [12–14]. Abrupt discontinuation of PD medications should be avoided if at all possible, as NMS may manifest with symptoms of extreme rigidity, high fever, and delirium, and sometimes with profound muscle damage. Treatment is usually via restitution of the discontinued medications. If the patient cannot absorb his/her medications due to GI problems, then, if available, transdermal (rotigotine), subcutaneous (apomorphine), intravenous dantrolene,

Table 2
Management considerations for a hospitalized Parkinson's disease patient.

Hospitalization issue/prevention	Management consideration
PD patient admitted to the hospital	Obtain early neurological consultation
Early ascertainment of a medicine list	Obtain early information on prescription medications as well as the length of time taking over-the-counter medication which could impact cognition and motor symptoms (e.g. diphenhydramine).
Rehabilitation and aspiration prevention	Mobilize the patient as much as possible
Understand dosing intervals	Pay as much attention to the dosing interval as to actual doses of both prescription and over-the-counter medications
Determine if patients can self-medicate	If the hospital allows patients to take their own medications, it may be required that the medication doses and times match the medicine bottle (this may not be the case for many PD cases)
Mental status change	Consider temporarily simplifying the medication regimen if a mental status change is present (e.g. carbidopa/levodopa only)
Prevention of aspiration	Minimize aspiration risk (consider swallow therapy chin-down swallow, EMST, education)
Patients who cannot take meds P.O.	Consider nasogastric tubes, apomorphine, and dopamine patches when patients can't take medicines by mouth
Nutrition and swallowing assessment	Consider PEG tubes earlier, especially if there is a potential for improvement in quality of life
Confusion and encephalopathy	Aggressively screen for and treat genitourinary and other infections
Skin changes	Treat decubital sores aggressively
Drugs that may worsen PD	Avoid dopamine-blocking drugs (including metoclopramide and many common anti-nausea drugs such as prochlorperazine) with the exceptions of quetiapine and clozapine which are useful for psychosis
Fall prevention	Use fall prevention, bisphosphonates, Vitamin D, physical therapy and assistive devices in those at risk
Assess bone strength	Have a low threshold for bone density scans for those at risk of falling
Orders that caution abrupt drug holiday	Do not stop dopamine drugs abruptly (stopping may result in neuroleptic malignant syndrome (NMS))
Dizziness, faintness, syncope	For orthostatic hypotension consider a cardiac workup, a tilt table test, reducing/discontinuing anti-hypertensives that raise blood pressure, reducing dopaminergics, hydration, stockings, and in some cases medications
Avoid pulmonary emboli	Use prophylactic subcutaneous heparin to avoid deep venous thrombosis
Screen for non-motor features	Treat anxiety, depression and non-motor features including cognitive issues (medically and behaviorally), make sure medications are taken on time; and if wearing off non-motor effects are seen, consider moving dosage intervals closer
Patient/family pre-education	Educate patients and families prior to elective procedures and hospitalization
Encourage patient advocacy	Encourage family members to request neurological and other interdisciplinary consultations when in the hospital setting

or intravenous (amantadine) therapy may be helpful [12]. This syndrome is preventable with proper education of staff and physicians.

An early return to mobility is also important. Most experts agree that mobilizing patients as soon as possible is the best approach. A formal physical therapy evaluation should be considered. Finally, the risk of aspiration is often underappreciated in PD patients [15], and if necessary a formal swallowing evaluation should be considered. It should be kept in mind that in stroke units, patients are kept NPO until seen by speech/swallow therapy and this may be important for consideration for future PD guidelines.

3.1.2. Infections

When PD patients aspirate it increases their risk of pneumonia. Pneumonia is the most commonly reported cause of death in PD [16–19]. Aspiration risk may be reduced by the use of mechanical swallowing techniques, including changing the consistency of food, or alternatively teaching chin-down swallowing [16]. Another recently used approach has been expiratory muscle strength training [20–25]. The use of feeding tubes may be considered for PD patients at higher aspiration risk. There are few data to suggest these tubes actually prevent aspiration, since in most cases patients must swallow their saliva, and can thus still aspirate. PEG tubes have been studied in cognitively impaired patients, and found to produce no benefits in aspiration, survival or suffering [26]. It should be kept in mind that the feeding tubes can facilitate medication intake and gastric motility, but they do not improve swallowing. Whether the available data on feeding tubes applies to PD is unclear. One prospective study reported that PEG tubes in non-demented neurological patients prevented aspiration for as long as three months, but this was small (three PD patients) [27] and there was no comparator group.

Pneumonias in PD are likely due to the same bacterial organisms found in community and age-matched control populations. One caveat in the treatment of pneumonia is that patients permanently dwelling within institutions likely have different bacterial organisms than community dwellers. Therefore antibiotic choices should be dictated by culture, as well as by the clinical setting. PD patients with impaired coughing and restrictive lung disease, usually due to muscle rigidity, PD progression, comorbidity, or a combination thereof, should follow an aggressive pulmonary toilet regime [15,28,29].

Bladder infections and decubital sores should be treated aggressively as would be done for any hospitalized or ambulatory patient with or without PD. Delirium may frequently accompany infection, and should be identified early, and treated aggressively. When anticholinergic agents are utilized for bladder overactivity, it should be noted that these may contribute to delirium and/or psychotic symptoms [7,17,30–32].

Some patients have reported that antibiotics have worsened their mobility, but this observation has been largely anecdotal, and may simply reflect the effects of the infection. Alterations of gut motility or drug absorption are also hypothetical mechanisms for this phenomenon. No specific antibiotics have been implicated by any data-driven studies.

3.1.3. Delirium/encephalopathy

Many factors may result in delirium/encephalopathy in the PD patient, including hospitalization itself (being in an unfamiliar place), infection, changes in medications, changes in the environment, lingering effects of anesthesia or pre-existing dementia. Patients with pre-existing dementia may have lingering effects of anesthesia for a few days and this may be accompanied by psychosis. When delirium occurs, infections should first be excluded (surgical, pneumonia, bladder). Medications with central nervous system (CNS) effects should then be discontinued, if possible. These medications include pain or sleeping pills such as narcotics, anxiolytics, hypnotics, and antidepressants. Clinicians should also be aware that other commonly prescribed medications, including anti-emetics, antispasmodics for the bladder, H_2 receptor antagonists, antiarrhythmic agents, antihypertensive agents, nonsteroidal anti-inflammatory agents, etc. may also contribute to the delirium. The family/staff will need reassurance if the presumed etiology is simply pain medication or alternatively anesthesia effects. Encouraging a family member to spend as much time as possible in the hospital room, and encouraging physicians to utilize only lightly sedating medications may help in controlling delirium and behavioral issues. Although not formally studied, the use of atypical antipsychotics/neuroleptics (and avoiding typical neuroleptics) with low sedating potential may be an option but there must be monitoring for exacerbation of motor dysfunction [1,6,11,33,34]. Finally actylecholinesterase drugs may have a role in treatment of select cases [35,36].

3.1.4. Falls and fractures

Hip fractures commonly occur in PD [37], and are usually addressed similar to the management of an age-matched cohort. The main difficulties facing hip fracture patients in the hospital setting include pneumonia and delirium. There are no specific studies to guide the management of PD patients who suffer from hip fractures. Fall prevention and use of biphosphonates/vitamin D may be indicated for prophylaxis against future fractures [38,39]. Also potentially important for fall prevention is the assessment of PD patients for appropriateness of ambulatory aids including canes, walkers and wheelchairs.

Other injuries may also occur in the hospital setting, or alternatively precipitate hospitalization. Patients may spend many hours on the floor after a fall before being discovered, and breakdown of muscles with elevated levels of CPK leading to muscle damage-induced acute tubular necrosis and renal failure should be evaluated in this setting.

Practitioners must separate fall and fractures leading to admission from those occurring after admission. Patients at risk to fall should be placed under observation and measures to avoid wandering and walking without assistance should be employed.

3.1.5. Hypotension

Hypotension and fainting, when not clearly associated with orthostatic hypotension, should precipitate a relatively standardized evaluation, including real-time in-hospital cardiac monitoring, Holter monitoring, and possibly a thirty-day event monitor. Diagnostic bedside evaluations should include measures of seated and standing blood pressure, and a tilt table test are very useful [40]. Since orthostatic hypotension is very common in PD and may vary significantly throughout the day, frequent measurements, with recordings of clinical symptoms such as lightheadedness can prove useful. Orthostatic hypotension can be treated with reductions of anti-hypertensives, increases in circulating blood volume via intravenous fluids, oral intake, increases in salt intake (e.g. salt tablets, diet changes), or fludrocortisone, or increases in arterial pro-contraction drugs such as midodrine, or possibly pyridostigmine [41–44]. Night time head elevation and tight thigh high stockings should also be considered.

3.1.6. Venous thrombosis

Venous thrombosis is an important complication that may occur in the setting of PD, and even in the deep brain stimulation (DBS) patient on a short hospital stay [45]. Venous thrombosis is a preventable and potentially overlooked problem [46]. In a 1994 report, pulmonary embolism was second only to pneumonia as

a cause of death in 60 autopsied patients with parkinsonian-like symptoms [46]. Pulmonary embolism/venous thrombosis has been well studied, and is best avoided with anticoagulants, subcutaneous heparin, with intermittent pressure devices (utilized either as supplementary aides or when anticoagulation has been deemed clinically unsafe) [47].

3.1.7. Psychiatric problems

While most psychiatric problems in PD are managed at home, hospitalization may be both necessary and appropriate. Psychotic syndromes, depression, or anxiety may each require hospitalization. It is important to note that patients with primary psychiatric disorders may also develop idiopathic PD or secondary parkinsonism from exposure to dopamine-blocking medications.

When encountering a psychotic PD patient it is critical that the treating healthcare providers be aware that only two medications have been shown in double-blind placebo-controlled trials to not worsen motor dysfunction in PD; quetiapine and clozapine [48–60]. The American Academy of Neurology (AAN) task force on PD has endorsed quetiapine as the drug of choice for treating psychosis, as it was proven safe and did not seem to compromise motor dysfunction, although it did not reduce psychosis in all placebo-controlled studies [34,61]. There are smaller studies that have supported quetiapine as a good choice for psychosis [62]. Of note, quetiapine has been associated with treatment of post-operative delirium although the effectiveness has not been confirmed by controlled studies [63]. Clozapine, on the other hand, has been shown safe and effective in two placebo-controlled multicenter trials [48,52,64].

There few existing reports on the treatment of anxiety in PD and no placebo-controlled trials. PD patients are thought to respond similarly to the general population, however data are needed to clarify this issue. Psychiatric consultation may be indicated to determine whether the anxiety is a generalized anxiety disorder, wearing off non-motor anxiety, or another anxiety-related DSM diagnosis. It is interesting to note that PD patients with anxiety may experience anxiety as a "wearing off" phenomenon, and therefore changes in dosing interval may prove useful in management [65]. Benzodiazepines, can be effective treatments for anxiety, but may carry the potential for confusion, increased fall risk, and sleepiness. Finally, selective serotonin reuptake inhibitors (SSRI) or tricyclic antidepressants may be useful, but data in PD are lacking. Severe anxiety in PD may result in emergency room visits or hospitalization often with the chief complaint of shortness of breath. Practitioners should always consider anxiety as a potential diagnosis in PD patients with shortness of breath [66–69].

Depression in PD has been shown in double-blind placebo-controlled studies to benefit from tricyclics as well as SSRIs. Tricyclics in low dose were better tolerated than expected in the PD population, and this should be kept in mind by clinicians [67]. Electroconvulsive therapy (ECT) can be effective for treating medication-resistant depression in PD [70]. ECT may also significantly improve motor function, although the latter benefit usually wears off days to weeks following treatment [67,69,71–73].

3.1.8. Elective hospitalization and PD

There are few studies in the literature specifically examining the frequency and reasons for elective PD hospitalization. There is also great variation among different countries as to the numbers and circumstances of such admissions. In a recent report from Israel, all neurology ward admissions of PD patients in a community hospital were through the emergency room [1], while in a recent study of health care resource utilization in Italy, as many as 20% of hospitalizations and visits were pre-planned [74].

Presumed reasons for elective hospitalization of the PD patient would include elective surgery [75], rehabilitation [76], or medication management, including "drug holidays [77]". However, elective hospitalizations for "medication management" are difficult to justify for insurance purposes in the U.S., unless they have resulted from intolerable treatment complications, in which case they are not likely to be elective.

The majority of the available information on elective hospitalizations among PD patients comes from studies of elective surgery, including general surgical and orthopedic procedures [78–80]. Patients with PD who underwent elective bowel resection, radical prostatectomy, or cholecystectomy had longer hospital stays, higher in-hospital mortality, and increased post-operative complications, particularly bacterial infections, when compared to patients without PD. In a mixed surgical cohort (including elective and emergency procedures), PD patients also suffered more perioperative falls, especially among trauma related admissions [2,75].

Among elective surgery interventions that were aimed at improving outcomes, early neurologic consultation was associated with better, sustained surgical outcomes, and shorter hospital stays in a cohort of PD patients undergoing total knee arthroplasties [79]. In a recent review of the orthopedic literature, the following interventions were advocated to optimize surgical outcomes among PD patients: medical optimization by a neurologist; early mobilization and physical therapy; careful monitoring for post-operative complications; and early discussion with the patient and family regarding long-term care and prolonged rehabilitation [78–81].

The most common elective hospitalization for PD patients at expert centers is usually DBS surgery. Patients undergoing DBS or battery change operations are subject to the same complications as any hospitalized patient, but in many cases the experience levels of the teams caring for the patients are much higher than a typical operation. In addition to mental status changes, worsening parkinsonism and medication-related issues, patients may also experience surgical and hardware-related complications [82].

Since there is limited information available from existing retrospective studies, further prospective assessments of the effectiveness of such interventions are necessary. Considering the intricacies of medication management, especially in the advanced PD patient – and the widespread use of antidopaminergic medications as part of perioperative management protocols (e.g. neuroleptics for post-operative delirium, or anti-emetics as part of standard post-operative orders), there is a need for education and anticipatory intervention. Such interventions to be studied should include: (1) pre-operative and post-operative consultation with the neurologist, (2) the interface between the neurologist and the surgeon, and (3) the efficacy of pre-planned early rehabilitation. Based on the few published retrospective studies, there is a high likelihood that such interventions may lead to improved medical and utilization outcomes [1,3,11].

3.1.9. Elective surgery

Prior to elective surgery, the patient and family should be prepared for the possibility of an emergent delirium. Pre-operative education can prevent panic and excessive test ordering on the part of the clinical team. The hospital interdisciplinary team must also understand the importance of restarting and maintaining medications in the PD patient. Mobilization as early and as frequently as tolerable, and maintenance of familiar visitors can be useful strategies. The trade off between pain control and delirium should be assessed daily, but in general reducing pain medications usually results in an improved mental status.

Many surgeries (especially those involving the GI system) may result in an ileus. Gastric stasis presents a particularly challenging problem for PD patients, because no conventional PD medication can be given parenterally, and the acute discontinuation of antiparkinsonian medications puts the patient at risk for an NMS-like

syndrome. Levodopa is not available as an intravenous preparation for commercial use. Similarly, simply missing PD medication dosages can result in patient discomfort. While L-Dopa exists as an intravenous preparation, this may only be utilized for research. Dopamine agonist patch formulations and apomorphine may be options when medicines cannot be taken by mouth. Passing a nasogatric tube for temporary use in administering medications may also become necessary.

3.1.10. Keeping PD patients out of the hospital

As outlined in this article, there is ample evidence of significant risks associated with hospitalization of PD patients. In many cases, hospitalization may potentially be avoided and a more appropriately tailored approach to care provided to the PD patient. Better access to an urgent care appointment at a neurology type clinic may also potentially reduce the need for hospitalization in select cases. A study of 143 hospitalized PD patients conducted over a 6-year period in Tel Aviv, Israel, found that 37% were admitted for motor complications, 24% for psychosis, 14% for general medical problems, and 25% for a combination of general medical and psychiatric disorders [1]. After initiating of an "open door policy" to their PD clinics (which allowed established patients to come to the clinic without appointment), the annual number of admissions was cut in half, and the duration of hospitalizations was reduced by four days within a period of two years [1]. While hospitalization is sometimes unavoidable, patients are often best served by facilitating urgent access to an outpatient clinic.

3.2. Conclusions

Educational programs are needed to better train hospital-based interdisciplinary teams in PD management. The threshold for consulting a neurologist, speech therapist, occupational therapist, physical therapist, neuropsychologist and/or a psychiatrist in care of the hospitalized PD patient should be low. Better educational programs will have the potential for cost savings and improved outcomes. Based on the available literature there appears to be an opportunity for improvement in PD related hospital-based healthcare management protocols. Guidelines are needed to address the best management approaches for the hospitalized PD patient. Subsequent studies should be directed at investigating whether guidelines will improve outcomes.

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