



Understanding the role of the Parkinson's disease nurse specialist in the delivery of apomorphine therapy



Roongroj Bhidayasiri ^{a, b, *}, Kamolwan Boonpang ^a, Onanong Jitkriksadukul ^a, Susan M. Calne ^c, Tove Henriksen ^d, Sally Trump ^e, Suchapit Chaiwong ^a, Phenprapa Susang ^a, Nonglak Boonrod ^a, Jirada Sringean ^a, Teus van Laar ^f, Martje Drent ^f, K. Ray Chaudhuri ^e

^a Chulalongkorn Center of Excellence for Parkinson's Disease & Related Disorders, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, 10330, Thailand

^b Department of Rehabilitation Medicine, Juntendo University, Tokyo, Japan

^c Pacific Parkinson's Research Center, University of British Columbia, Vancouver, (1982–2007), Canada

^d Movement Disorder Clinic, University Hospital of Bispebjerg, Copenhagen, Denmark

^e National Parkinson Foundation Centre of Excellence, King's College Hospital, London, United Kingdom

^f Department of Neurology, University of Groningen, Groningen, The Netherlands

ARTICLE INFO

Article history:

Received 29 October 2016

Received in revised form

20 November 2016

Accepted 22 November 2016

Keywords:

Parkinson's disease

Parkinson's disease specialist nurse

Apomorphine

Multidisciplinary team

ABSTRACT

Optimal care of Parkinson's disease (PD) patients should involve a multidisciplinary team (MDT) of which a PD nurse specialist (PDNS) is a key member. The role of a PDNS is particularly prominent in the care of advanced PD patients suitable for apomorphine because, in addition to nursing skills, apomorphine treatment requires liaison, training, interaction and coordination with patients, caregivers and other members of the MDT as well as the interface with primary care physicians. The therapeutic success of apomorphine therapy depends not only upon the pharmacologic drug response, but also on how well the patient understands his/her disease and how to handle the therapy. In this respect, a PDNS is a vital member of the MDT who provides education and training, support, and is available for consultation when problems arise. In this article, we review the literature on the contribution of PDNSs in both continuous subcutaneous apomorphine infusion and intermittent subcutaneous apomorphine injection and highlight the various beneficial aspects of PDNS care, supported by scientific evidence when available. Despite a low level of published evidence, there is strong clinical evidence that the impact of PDNSs on the management of apomorphine therapy is vital and indispensable for the success of this treatment.

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1. Introduction

Recent evidence suggests the efficacy of a multidisciplinary care team in the management of Parkinson's disease (PD) [1,2]. This is particularly true in the care of advanced PD patients, where the PD nurse specialist (PDNS) plays an important role in enabling patients to adjust to the different types of therapy offered, extending from oral medications to infusion therapies (both apomorphine and levodopa carbidopa intestinal gel) and deep brain stimulation.

A holistic healthcare model in PD focuses on patient-centered outcomes supported by multidisciplinary professionals, but the PDNS is involved in all aspects of PD care starting right from diagnosis, assisting patients through the various types of treatment, addressing non-motor symptoms (NMS), initiating palliative care, and finally, following death, supporting caregivers and bereaved families. PDNSs not only provide the nursing skills required for the management of PD, but act as the pivotal liaison for the PD patient and the MDT, collaborating, interacting and coordinating with other care providers to ensure the holistic model of care is provided. The inclusion of PDNS support delivers a more comprehensive care by providing professional competence, nursing support, continuity of contact, and emotional support [3]. The networks of PDNS are now well established, providing

* Corresponding author. Chulalongkorn Center of Excellence for Parkinson's Disease & Related Disorders, Chulalongkorn University Hospital 1873 Rama 4 Road, Bangkok 10330, Thailand.

E-mail address: rbh@chulapd.org (R. Bhidayasiri).

considerable cross-cutting knowledge based initiatives that result in the development of pathways of advanced therapies. However, the nurses' involvement should be tailored to individual patients. In this article, we describe the role of the PDNS in the apomorphine treatment of advanced PD patients by reviewing relevant literature, together with expert inputs from international tertiary PD centers that have extensive experience in apomorphine treatment.

2. The concept of Parkinson's disease nurse specialist

The concept of training nurses with a special interest in PD, or PDNSs, has been proposed for more than 20 years to allow the provision of specialized nursing services in all clinical, educational, and professional aspects of PD care [4–7]. Community nursing teams are usually responsible for the day-to-day management of PD in the community, supported by training from a PDNS [8]. However, the setup, organization, prescribing role, and availability of nurses involved in the management of PD varies across countries, subject to different policies and resources. Recently, the trend to include a PDNS as part of the multidisciplinary care team for PD has spread to many countries and regions and has highlighted the diverse roles provided by PD nurses in the various settings in which they practice, depending on the specific local needs and organizations.

3. Parkinson's disease nurse specialist as a recognized status

The PDNS status is officially recognized in the UK where training is formally provided with support from the UK Parkinson's Disease Society (www.parkinsons.org.uk) and Parkinson's Disease Nurse Specialist Association (www.pdnsa.org). According to the UK's national clinical guideline for diagnosis and management of PD (NICE guideline), the key roles and responsibilities of a PDNS are: 1) making and receiving referrals to create integrated and responsive service for PD; 2) admitting and discharging patients; 3) managing caseloads; 4) providing information, education, and support to patients in their homes, in clinics and in hospitals; 5) prescribing medicines and treatment and monitoring the effectiveness of changes; 6) using the latest information technology (IT) to triage PD patients; and 7) using IT to identify patients at risk [9]. In addition, PDNSs are also available in Thailand, Denmark and the Netherlands whose experts are represented in this review. Nurses with specialized PD knowledge also work in many other countries, such as the other Nordic countries, Germany, Australia, and the USA. The role of a PDNS also has been extended to support specific advanced therapies. Many centers in the UK, Denmark and Thailand have specific PDNS who specialize in DBS, apomorphine, or levodopa infusion therapy, and effectively run the coordination of such services [6,10]. Clinical experiences suggest that availability of a PDNS leads to greater adherence to advanced therapy as well as maintenance of therapy [11]. In North America, PDNSs are attached to specialty clinics, and are funded by research grants and specific funding from foundations (e.g. the National Parkinson Foundation) through their outreach and Center of Excellence programs [4]. In some cases, nurses are trained on the job and the amount of autonomy given will depend on the philosophy of the director. Some are exclusively associated with clinical trials and others have taken on the role of educator and counsellor for patients attending routine clinics.

4. Evidence-based on the role of Parkinson's disease nurse specialist

Despite the diverse and essential roles of the PDNS as described above, the evidence supporting the effectiveness of PDNSs still

remains inconclusive, largely due to limitations in study design, interventions and outcome measures used [12–15]. Another reason for a lack of efficacy may be because the studied outcomes are broad and not specific to certain types of intervention (e.g. apomorphine treatment). Nevertheless, patients, caregivers and physicians frequently have the clinical impression that PDNSs make a definition contribution to the care of patients with PD [13]. The clinical experience of the authors is that PD patients from centers with experienced PDNSs have a much better adherence to therapy. A good example is with apomorphine therapy, in which the PDNS plays a role in all therapeutic steps, beginning with the selection process and continuing on through initiation of treatment, maintenance of therapy, troubleshooting problems, and provision of regular education, consultation, and psychological support to both patients and caregivers [16]. Therefore, in this article, we review the literature on the contribution of PDNSs in both continuous subcutaneous apomorphine infusion (CSAI) and intermittent subcutaneous apomorphine injection (ISAI). However, before going into the details of the PDNS's role in apomorphine treatment, it is important to first understand the concept of multidisciplinary team (MDT) as the optimal care model in PD.

5. Multidisciplinary team as the optimal care model in PD: an emphasis on nurse's role

Optimal care in PD no longer is viewed as a one-to-one physician-patient relationship. With the current understanding of the complexity and heterogeneity of motor and non-motor symptoms, comorbidities and polypharmacy in PD, it is now clear that one treating physician alone cannot deliver a comprehensive management of this disorder. A number of recent studies also support the concept of integrating all the participating disciplines into a streamlined care team with the PD patients at the center, supported by a single or group of dedicated coordinators [1,17,18]. However, the nature of multidisciplinary treatment may vary across countries and even between centers within a given country [19]. In this respect, the PDNS's role can be viewed as a multidisciplinary one as he/she acts as a professional as well as the person who is close to the PD patient and is able to work in an interdisciplinary environment consisting of experts from different health professions, either in a community or hospital-based setting (Fig. 1) [5,12,20]. Many PDNSs run their own clinics, make home visits, refer to other experts and coordinate care packages according to a patient's needs (Fig. 2). In some centers in Denmark, PDNS even have a restricted

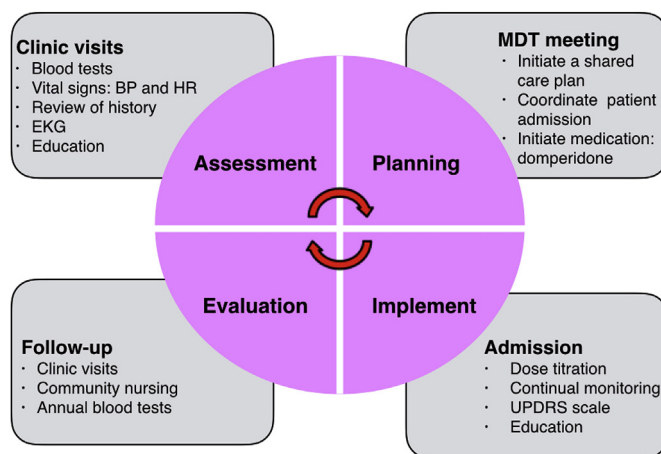


Fig. 1. The diagram illustrating the role of Parkinson's disease nurse specialist list. MDT: Multidisciplinary team.

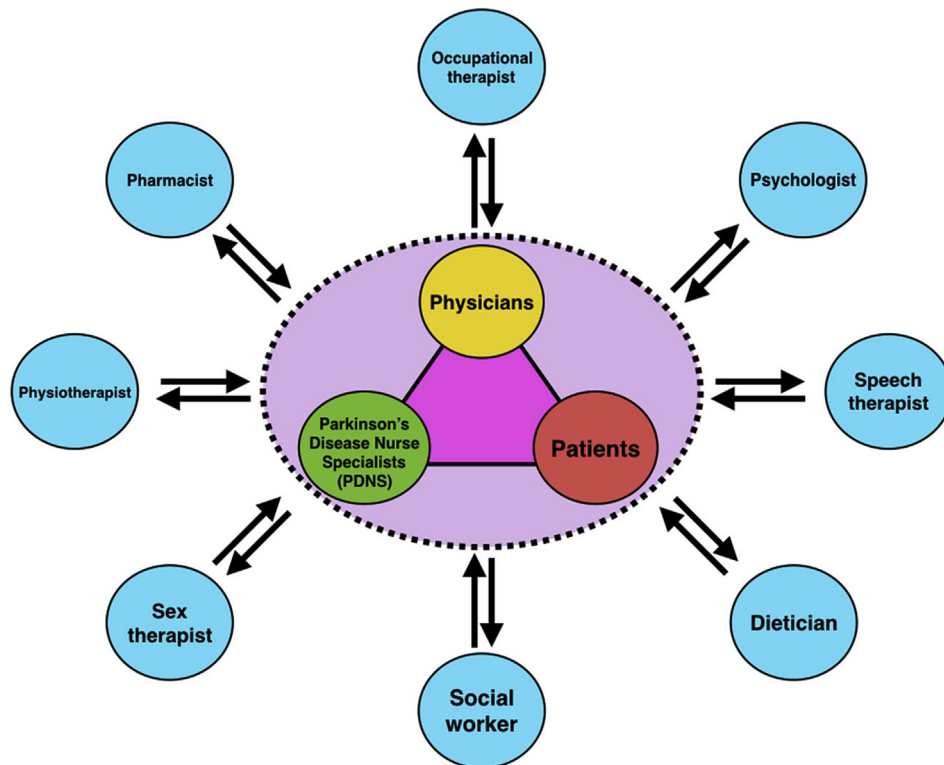


Fig. 2. Members of the multidisciplinary care team with patients at the center along with physicians and Parkinson's disease nurse specialists who are involved in the care of each patient on a regular basis.

license to prescribe antiparkinsonian medications, and in some centers in the UK, PDNSs serve as consultants with full prescribing authority, running their own clinics for specialized treatment. Community nurses also have an important role in monitoring and administering on-going drug therapy, such as monitoring skin health and apomorphine therapy at home. In addition, they help reduce the workload of neurologists and geriatricians who are in short supply not only in developing countries like Thailand, but also in many developed countries, such as England [21,22].

Evidence is growing to support the effectiveness of various allied health disciplines in PD. While the case already is strong for specific physiotherapy techniques, and the evidence supporting the important role of the PDNS in disease management is starting to emerge. At a randomized controlled trial level, PD patients attended by a PDNS had significantly better scores on the Global Health Questionnaire at a 2-year follow up, better communication scores on the 39-item Parkinson's Disease Questionnaire, an improved sense of wellbeing with no increase in healthcare costs, and better access to information and referrals to other healthcare agencies [13,14,23,24]. In addition, the results from an independent assessment of patient satisfaction demonstrated the usefulness of nursing intervention and the high preference for home visits [23]. A recent, albeit, weaker, study involving qualitative interviews also reported the beneficial impact of PDNSs in providing individually tailored and competent care that focused on alleviating the impact of the disease on daily life [3]. Compared to neurologists, PDNSs were found to provide longer consultations and pay more attention to patients' concerns [13]. In the evaluation of a nurse-led multidisciplinary inpatient rehabilitation program, significant improvement was observed in health-related quality of life of patients following a short intervention of 5–10 days [25]. A longer study documented high patient and stakeholder satisfaction with nurse-led Parkinson's services, which helped patients understand their

care plans and achieve patient self-management, when measured at a 2-year follow-up [26]. However, the high workload of PDNSs has been highlighted as a major constraint on the implementation of outreach services and national guidelines, at least in England and Australia [21,26].

Although the effectiveness of nursing care for PD has not been widely studied, what little evidence is available supports the value of PDNSs. In clinical terms, it is clear that the PDNS is an essential member of the MDT, with a vital role in providing clinical monitoring and medication adjustment and acting as a continuing point of contact for support and education for PD patients and their caregivers at all stages of the disease. The value of PDNS involvement should not be based on the direct cost effectiveness, but also on the indirect savings due to the reduction of costly hospital admission and extended hospital stays [27].

6. Continuous subcutaneous apomorphine infusion: a nurse's role

CSAI therapy is indicated in PD patients with unpredictable 'off' periods that can no longer be adequately controlled by oral treatment, or when rescue doses of apomorphine injections are effective but either are needed too frequently or are associated with unacceptable dyskinesia [16,28]. With the support of PDNS, several steps as detailed below are needed to ensure the successful implementation of CSAI.

6.1. Selecting candidates for continuous subcutaneous apomorphine infusion

Although the decision regarding the suitability of suitable candidates for CSAI therapy is the responsibility of treating neurologists who have experience in the management of PD, PDNSs can assist

physicians in the process by screening patients with motor complications for those with frequent and prolonged 'off' periods associated with swallowing difficulties or gastrointestinal problems [16]. This information can be retrieved easily by reviewing patient's diaries and obtaining confirmation from direct communication with district nurses or caregivers (Fig. 3). The PDNS also can assist treating neurologists by ensuring the use of validated screening tools (e.g. the Non-Motor Questionnaire, NMSQuest) in the review of profiles of potential candidates for possible exclusions, such as severe dementia and psychiatric and behavioral disorders [16].

Once potential candidates for CSAI therapy are identified, it is usually the PDNS who leads a group discussion involving the patient, caregiver, and the treating neurologist to ensure that the patient understands the treatment goals, what to expect, possible adverse events and what support that is available to them. Whenever possible, information from a peer in a local Parkinson's Association is often very helpful. Basic education is usually provided at this stage so that a patient can recognize their 'on' and 'off' periods as well as dyskinesias and other dose-related adverse effects. Before starting on CSAI therapy, it is important that patients understand how apomorphine therapy works and the rationale for its use and that they are able to keep reliable 'on/off' diaries [29]. Questionnaires such as Questionnaire 10 (AQ10) and information booklets on apomorphine may be administered or given at this stage [30]. Once patients pass the evaluations that include ECG (to exclude prolonged QT interval, arrhythmias) and blood tests confirming no signs of hemolytic anemia, the consent for CSAI therapy can be obtained, followed by a schedule for apomorphine titration.

6.2. Starting patients on continuous subcutaneous apomorphine infusion and setting up educational training

The setup of the initiation phase of CSAI therapy may differ across PD centers depending on local guidelines, resources, and the philosophy of the MDT. However, all centers share the same goal of establishing a good therapeutic response to apomorphine and teaching the patient and caregiver how to manage the infusion. Although most guidelines recommend hospitalization during the initiation, a recent consensus statement offers the possibility of starting CSAI therapy as an out-patient or day-care patient if the team is equipped and experienced in such settings [28]. The PD centers at King's College in London and Chulalongkorn University in Bangkok have adopted the day-care approach for the titration based on experience from many years of apomorphine therapy [6,16]. Some centers initiate the treatment with an apomorphine challenge test performed by the PDNS who gradually increases the doses of apomorphine given during a period of 5 h. The effects of the injections are registered by the PDNS, along with the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS-III), and video documentation in some cases.

Supplementary video related to this article can be found at <http://dx.doi.org/10.1016/j.parkreldis.2016.11.014>.

In most places, PDNSs usually take a lead in the arrangements, including activating local pathways (in the UK, known as shared care), pre-appraising the primary care physician regarding the plan to start apomorphine, and ensuring that all home support is in place. Pre-treatment with domperidone for at least 3 days is

Name: Mr. XXX XXX		Date. 23/3/16				Day	1					
Dose												
Test time	8:45		10:00	11:00	12:00	13:00	14:00	15:00	16:00	17:00		
Injection time		9:00										
Bolus dose												
Continuous dose		0.5 mg	1 mg	1 mg	1.2 mg	1.4 mg	1.6 mg	1.8 mg	1.8 mg	1.8 mg		
Additional dose												
Blood Pressure	132/68		129/68	118/62	110/53	135/62	161/70	135/66	144/66	138/72		
Pulse	66		58	76	70	63	70	57	67	64		
Tapscore Right (times in second)	96		88	90	92	100	132	84	88	86		
Tapscore Left (times in second)	76		76	78	76	80	120	64	80	76		
Walking test (steps in seconds)	23				55	16	19	23	12	14		
Walking test (Steps in seconds)	26				37	22	15	20	16	18		
UPDRS III	off:52/on:31											
Side effect			dizziness					dizziness				
+3 Very dyskinesia												
+2 Moderate dyskinesia												
+1 Mild dyskinesia					x	x		x	x			
0 Normal	x	x					x			x		
-1 Light rigid			x	x								
-2 Moderate rigid												
-3 Very rigid												
Medications / Time	5	8		11			14			17	20	hs
Levodopa/ benserazide (200/50)	3/4	1/2		3/4			1/2			1/2	1/2	0
Levodopa/ benserazide HBS (100/25)	1	0		1			0			1	0	1
Rivastigmine patch	1											
Rotigotine patch (4)											0	
Quetiapine (25)											1/2-1	
Clonazepam (0.5)											1/2-1	
Domperidone (10)		1		2						1		

Fig. 3. An example of electronic medical record for apomorphine titration.

provided to patients in most, although not all centers. PDNSs also can determine the infusion dosage by evaluating a patient's motor response at hourly intervals under the supervision of the treating neurologist (Fig. 3). One option is to run both patients' and PDNSs' diaries in parallel, which are continually reviewed for concordance during this period. Another option is to use an ambulatory objective monitoring device to evaluate motor responsiveness, reported as the severity of bradykinesia and dyskinesia. Apomorphine is usually initiated at a low rate (1–2 mg/h). The dosage is slowly titrated over 5–7 days until the optimum dose is reached or unacceptable side effects develop [16,28]. Experience suggests that a slower increase in the hourly flow rates may be appropriate for the out-of-hospital settings [28]. However, a recent case series of PDNS lead titrations of CSAI in a wide variety of settings including day hospitals and patients' own homes, reported good tolerability to a rapid titration schedule with most patients successfully titrated within 2 h [31]. In the published literature, several protocols are available for commencing CSAI therapy, details of which are beyond the scope of this review [32–36]. During the titration, PDNSs should look for potential adverse events, including nausea, vomiting, and hypotension, which commonly occur at both initiation and dose escalation. Reviewing injection sites for any problem also is important.

In the titration period, the PDNS should set aside time on a daily basis to provide the patient and caregiver with information and education, to encourage discussion, and to answer any questions. Hands-on training for both patient and caregiver can be provided at this stage to review injection and needle-insertion techniques and how to handle and operate the device. Training should be given in a structured manner and not left to chance. An objective worksheet signed by both PDNS and patient/caregiver is one way that the PDNS can ensure that various aspects of training are covered and understood by both patient and caregiver [34]. This worksheet also provides good evidence that training was given and that the nominated person is proficient in performing the needle insertion and administering the pump. In most cases, apomorphine is currently administered via the Crono Apo-Go III portable infusion pump (Genus Pharmaceuticals Ltd., Berkshire,

UK) for ambulatory use connected to a subcutaneously inserted cannula. This pump is specifically designed for the purpose of delivering apomorphine. It is portable and can be carried in a pocket, placed under a shirt, attached to a belt, or worn around the neck (Fig. 4). The pump is only licensed for the use with apomorphine, so it is possible that many healthcare professionals will be unfamiliar with it. The PDNS usually is responsible for teaching patients, caregivers, district nurses, or local nurses on how to use the pump. Our center in Thailand provides a useful video and step-by-step guide to give practical information about the Apo-Go pump (Supplementary data 1). The level and the quality of the education given to patients on CSAI can influence the compliance with and the success of this treatment. Patients with inadequate education and support often discontinue apomorphine therapy within weeks [8].

Close interaction between patient and PDNS (preferably with caregiver as well) is crucial to ensure that patients are able to handle the device correctly, that they know how, where, and when to administer apomorphine and how to take the best possible advantage of the treatment (Fig. 4). The length of the initial setup depends on when a reasonably balanced clinical state can be reached and when the patient is able to handle the pump safely. According to most published literature as well as our own experience, this process usually takes at least a week [16,28,29]. The first follow-up visit after discharge usually takes place within a week and can be at the patient's home or in the medical center, depending on local availability.

6.3. Maintenance of continuous subcutaneous apomorphine infusion

The focus during the maintenance of CSAI therapy is to ensure that patients are able to manage treatment independently or with the help of their caregiver, or if necessary with outside assistance from a PDNS or community nurse. Independent management of CSAI therapy by the patient is associated with a higher success rate [33]. Although the patient is encouraged to be independent with the administration of infusion, it is vital for patients to have access

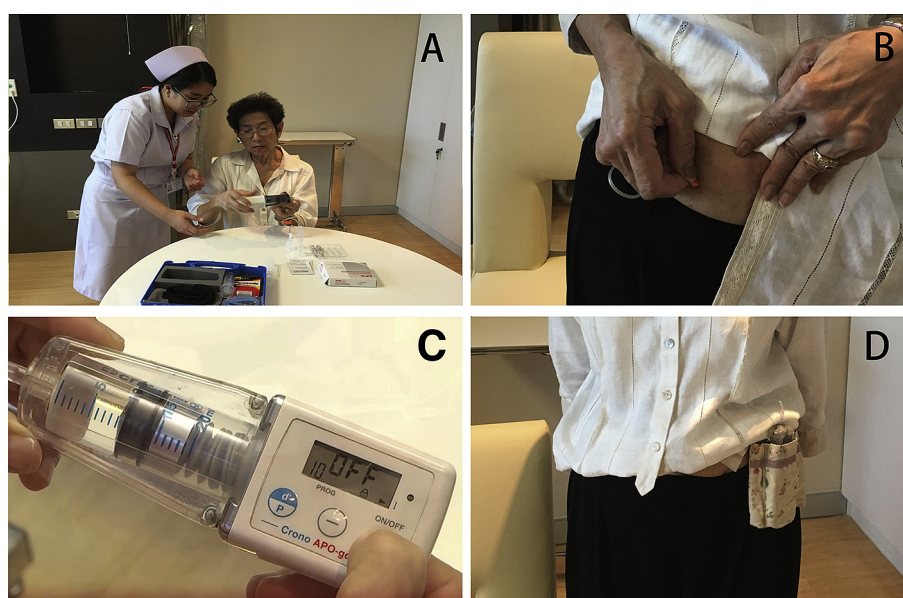


Fig. 4. The set of photographs illustrating a role of Parkinson's disease nurse specialist (PDNS) during the titration of a patient for continuous subcutaneous apomorphine infusion. A: A PDNS taught a patient on how to operate the pump; B: A patient performed self-placement of the injection needle; C: A patient operated the pump by herself; D: This patient made her own pouch for carrying apomorphine pump, attached to a belt.

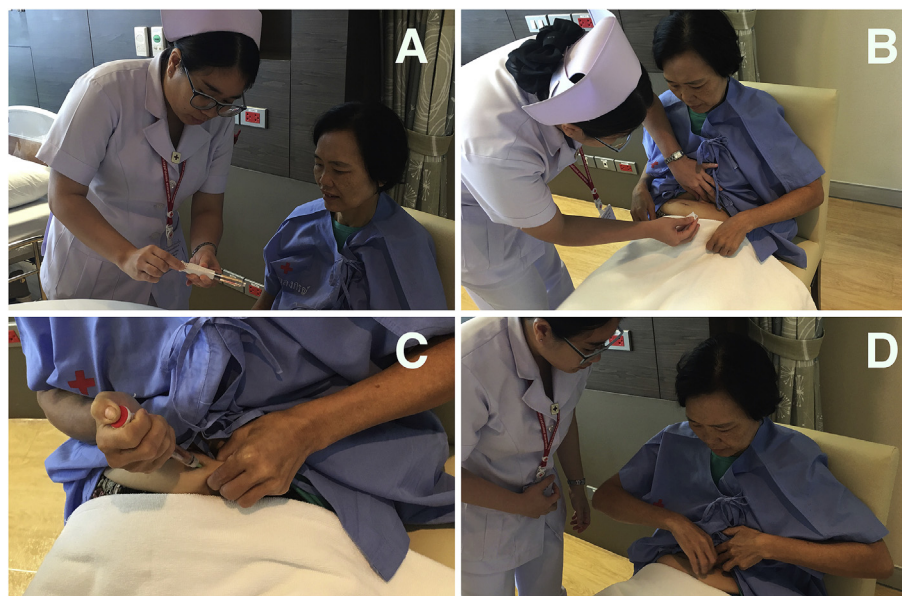


Fig. 5. The set of photographs illustrating a role of Parkinson's disease nurse specialist (PDNS) in teaching patient on how to perform a subcutaneous apomorphine injection. A: A PDNS taught a patient on how to operate a penject; B: A PDNS cleaned patient's skin at the injection site; C–D: A patient performed self-injection under a supervision of PDNS.

to, and support from, PDNSs, even after they have completed the initiation period [8]. A step-by-step guide, Shared Care guidelines, and contact details for the patient's PDNS should be made readily available to the patients and caregivers [34]. In our experience, many problems can be solved with a direct telephone consultation with a PDNS. In certain circumstances, a district nurse or PDNS should be available to provide home visits to relieve the stress or burden that may be put on the patient's family [8]. The availability of such support may be different across PD centers depending on local guidelines and resources.

6.4. Prevention and troubleshooting of potential side effects

One of the key success factors of CSAI therapy is to prevent or minimize potential side effects with apomorphine therapy. Secondary adverse effects are one of the main reasons for discontinuation of CSAI [37]. Although most patients (over 80%) in a long-term efficacy study of CSAI therapy reported at least one adverse event, there were usually manageable and no serious adverse effects were documented in this study [37]. The three most common adverse events in this study were skin reactions (87%), followed by confusion and hallucinations (35%), and sedation/drowsiness (29%) [37]. District nurses and general practitioners have a vital role in identifying and reporting these adverse effects to the PDNS or medical team before they become problematic [8].

Local skin reactions can range from temporary flushing or itching of the abdominal wall to formation of skin nodules, infection and development of abscesses, or in the worst cases, necrotic ulcers [38]. Of these, skin nodules are the most common and are frequently associated with discoloration and scarring. The duration of the reaction and the size, severity and appearance of nodules can vary considerably between individuals and is linked to the dose of apomorphine, skin type, body mass index, needle type, and insertion techniques [39]. A minority of patients discontinue CSAI therapy because of skin reactions [33]. Therefore, proper instructions on needle insertion techniques and a record chart, completed by patients, caregivers, or nurses, are crucial to prevent or minimize the severity of nodule formation. Several methods, mostly based on expert opinions, have been described for effective

management of skin nodules but details are beyond the scope of this review [16,28,38,39].

7. Intermittent subcutaneous apomorphine injection (penject): a nurse's role

Due to its rapid onset of action and its reliable effect, ISAI is suitable as a rescue therapy for PD patients with motor and non-motor fluctuations who experience unpredictable 'off', symptomatic early morning akinesia with dystonia, delayed 'on' due to poor levodopa absorption, or require reliable and fast relief when anticipating an 'off' [16,28]. In the most commonly used form, ISAI comes in a pre-filled penject device so it does not require much preparation by the patient or caregiver. However, the patient needs to learn when to administer the injections; therefore, the patient must be able to recognize the 'off' and 'on' stages of his/her symptomatology. Since ISAI usually is administered on an 'as needed' basis, on most occasions, the injection is performed by the patient. Caregivers also may be trained as a backup for situations in which the patient is unable to perform the injection. Training can be delivered on as an outpatient basis and should focus on teaching the patient how to operate the penject and perform the injection with confidence, particularly during the 'off' state when some patients may find it difficult to handle the device leading to stress and anxiety (Fig. 5) [34]. For best results, injections should be given at the very beginning or, ideally, in anticipation of an 'off' state [40]. Patients should be instructed to recognize and respond promptly to the earliest, and often extremely brief, premonitory signs of impending immobility [40]. It is the responsibility of the PDNS or physician to ensure sufficient training for patients so that they are able to handle the injection device and administer the injection in a safe and correct manner.

8. Conclusion

The therapeutic success of apomorphine therapy is related not only to the pharmacologic drug response, but also to how well the patient understands his/her disease and how to handle the delivery of their therapy. In this respect, the PDNS, as a vital member of MDT,

makes an especially important contribution by ensuring adherence to therapy, providing education and training and ongoing support, and being available as a backup for consultation when problems arise. The PDNS can ease caregivers' burden and relieve physicians' workload pressures by providing ongoing management of PD patients on a daily basis. In this respect, the contribution of a PDNS can be appreciated throughout the apomorphine therapy process, from candidate selections to dose titration and maintenance of treatment and reduction of adverse events. Despite a low level of published reports, there is strong clinical evidence that the high level of competence, continuity and availability of PDNSs in the management of apomorphine is vital and indispensable for the success of this treatment.

Conflict of interest

The authors have no conflict of interest.

Acknowledgments

This study was supported by the grant from the National Research Council of Thailand (GRB-APS_05_59_30_04), the International Research Network grant from the Thailand Research Fund (IRN59W0005), Chula Research Scholar of the Ratchadapiseksomphot Endowment Fund (GCRS_58_05_30_02) and Chulalongkorn Academic Advancement Fund into Its 2nd Century Project of Chulalongkorn University, Bangkok, Thailand.

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