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Review article

Considerations for general anaesthesia in Parkinson's disease

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ABSTRACT

Parkinson's disease is a common neurodegenerative disorder in the elderly which when present has a significant influence on surgical management. These patients necessitate additional perioperative and anaesthetic considerations across disease specific domains as well as in relation to the respiratory and cardiovascular systems. This brief review focuses on the factors which contribute to perioperative morbidity, including the use of medications that may exacerbate symptoms or adversely interact with treatments for Parkinson's disease. Recommended dosing practices to reduce complications during hospitalisation are covered. In addition, recent concerns regarding anaesthetic exposure in early childhood as a risk factor for the development of Parkinson's disease are discussed in light of data from animal models of anaesthetic neurotoxicity and epidemiological studies.

1. Introduction

Parkinson's disease (PD) is a disorder of the central nervous system with clinical features arising predominantly from degeneration of the dopaminergic neurons in the substantia nigra pars compacta [1,2]. This progressive cell death manifests with the classical motor features of bradykinesia, rigidity and tremor [3]. More recently, the importance of non-motor symptoms including autonomic dysfunction, sleep disturbances, depression, psychosis and cognitive changes has also been recognised [4]. The disease is most commonly idiopathic [5] and more common in the elderly, with 80% of cases diagnosed in those aged 65 years and above [6]. While there is a paucity of prevalence data in Australia [7] a recent report estimated that 69,000 individuals suffer from PD [6], which is similar to estimates in developed countries worldwide [8]. It should also be noted that an increased prevalence of PD is to be expected in our ageing populations internationally [5].

There is good evidence that PD influences the risk profile for surgery and contributes to perioperative morbidity and mortality [9]. For example, Eventov et al. [10] found that PD patients undergoing hip fracture surgery had a 3-month mortality rate more than double the rate for non-PD patients. Higher rates of in-hospital mortality have also been observed in PD patients undergoing elective bowel resection, cholecystectomy and radical prostatectomy when compared to a control group [11]. Complications commonly arise from the impact of disease on the respiratory, cardiovascular and neurological systems [3,12,13], with rates of postoperative aspiration pneumonia, bacterial infections, urinary tract infections and falls significantly increased in this population [9,11,14]. Adverse effects of anaesthetic drugs may also contribute to morbidity [15,16,17], while there is a risk of interaction between PD medications and drugs used during surgery and the postoperative period [18]. Additionally, inappropriate medicating practices by non-specialist staff have been associated with complications during hospitalisation [19].

Anecdotally, anaesthetic management has been perceived as inadequate by some patients with PD [20]. This has been attributed mainly to a lack of consideration of the specific requirements associated with the disease. With an increasingly ageing population in most societies (e.g. Australia [21]), surgical treatment of individuals with PD will become more frequent and awareness of these complications increasingly relevant in clinical practice. As an enriched patient population at risk of deteriorating with lengthier hospitalisation [22], the prevention and effective management of these complications is important for reducing morbidity and improving patient outcomes.

2. Complications in patients with PD

As discussed in Nicholson et al. [3], patients with PD may experience impaired functioning of several physiological systems, including respiratory, cardiovascular, gastrointestinal, urological, endocrine and musculoskeletal. This brief review focuses on

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respiratory and cardiovascular complications which may arise perioperatively and emerging evidence regarding management.

2.1. Respiratory

Obstructive respiratory dysfunction has previously been reported in patients with PD [23]. Reduced ventilatory function contributes to morbidity with impaired clearance of secretions predisposing individuals to developing respiratory infections [13]. Many patients with PD also experience difficulty swallowing and may have an impaired cough reflex [24]. Accordingly, the incidence of aspiration pneumonia postoperatively in patients with PD has been reported to be significantly higher when compared to controls [11] and is a leading cause of death in this population [25,26]. Intraoperatively, dysfunction of the laryngeal musculature may increase the risk of laryngospasm [27,28,29] and the airways may be at a greater risk of collapse due to a combination of decreased respiratory muscle strength [30] and fatigue [31].

Treatment of dysphagia and pulmonary dysfunction may reduce the incidence of aspiration and subsequent respiratory complications in hospitalised PD patients [32,33]. Previous studies investigating the effect of dopaminergic treatment on these abnormalities of function have returned mixed findings [33]. While it has been suggested that dysphagia is responsive to levodopa, as yet there is no consensus [34]. Similarly, Monteiro et al. [35] found that only particular measures of respiratory function (e.g. forced vital capacity) showed improvement with the use of levodopa while other measures (e.g. forced expiratory volume) did not. Non-pharmacological interventions for dysphagia such as Expiratory Muscle Strength Training (EMST) and Video-assisted Swallowing Therapy (VAST) have shown some efficacy in reducing the incidence of aspiration [36], however these are home-based programs and less suited to the acute environment. Currently, there is limited evidence on how to best manage dysphagia and prevent aspiration in hospitalised patients with PD [37,38] necessitating further research.

2.2. Cardiovascular

The cardiovascular system is commonly affected in patients with PD and requires thorough assessment prior to surgery. Orthostatic hypotension (OH) is the predominant cardiovascular symptom related to autonomic dysfunction in these patients [39] and is associated with an increased incidence of hypotension postoperatively [40]. The effect of OH may be exacerbated in patients taking dopaminergic medications as these drugs dilate the vasculature through inhibition of the sympathetic nervous system [41]. Tricyclic antidepressant (TCA) use in patients with comorbid depression can also cause OH through blockade of α-adrenergic activity [3,42].

Additional cardiac risks in these patients include arrhythmia, hypertension and hypovolaemia [3]. Drugs known to prolong the QT interval are commonly prescribed to patients in PD such as domperidone for nausea, quetiapine for psychosis [43] and the selective serotonin reuptake inhibitor (SSRI) antidepressants like citalopram [44]. Prolongation of the QT interval has been associated with cardiovascular mortality and may increase stroke risk [45,46]. Also, as chronic use of ergot-derived dopamine agonists such as pergolide and cabergoline has been associated with a significantly increased risk of valvular heart disease [47] tests of cardiac function (e.g. ECG, echocardiogram) are particularly important in these patients to screen for underlying cardiac pathology preoperatively even if the medication has been discontinued in favour of non-ergot preparations.

In patients undergoing stereotactic neurosurgery as part of Deep Brain Stimulation (DBS) treatment for advanced PD, chronic hypertension has been associated with an increased incidence of intracranial haemorrhage (ICH) [40]. There is also strong evidence for an association between patients over 60 years and ICH [48], putting a large number of individuals with PD in a higher risk category. A review of the literature on haemorrhagic complications in functional neurosurgery by Zrinzo et al. [48] found that the risk of ICH could be significantly reduced with an image-guided and image-verified method. In the authors' own unit, an image-guided approach to DBS of the subthalamic nucleus (STN) in 79 patients with PD compared favourably to results from a meta-analysis of non-image-guided surgical techniques, with mean overall improvement in off-medication motor score equal at 52% with the use of both methods. The image-guided approach, however, reduced the incidence of haemorrhage from 3.9% to 0% avoiding the debilitating neurological outcomes and mortality associated with ICH.

3. Perioperative considerations

Common surgical presentations are for orthopaedic, urological, ophthalmological and incidental general procedures associated with the geriatric population [13]. Additionally, patients may undergo surgery to ameliorate parkinsonian symptoms such as DBS therapy and much less commonly pallidotomy or thalamotomy. Medicating practices perioperatively contribute to patient morbidity in this population [49,50] necessitating particular consideration with the use of certain drugs.

3.1. Antiemetics

It is well known that for the control of nausea and vomiting, dopamine antagonists derived from phenothiazine, thioxanthene and butyrophenone compounds (e.g. haloperidol) are contraindicated as they exacerbate symptoms of PD [20]. Domperidone has been recommended due to its peripheral mode of action [51] and compares favourably to metoclopramide as an antiemetic [52]. However, it has also been associated with an increased risk of ventricular arrhythmia [53] and sudden cardiac death [54]. This risk may be even higher in elderly patients [53] and must be considered when treating patients with PD, the majority of whom are over 65 years of age. Alternatively, ondansetron and the antihistamine cyclizine may be used safely without exacerbating parkinsonism [51].

3.2. Analgesia

Opioids are often prescribed for patients who require analgesia following a surgery. Care must be taken with the use of fentanyl as severe bradykinesia unresponsive to PD medication has been observed previously in a single patient. Symptoms resolved only several hours after discontinuation of fentanyl [17]. Similarly, acute dystonia after administration of the synthetic opioid alfentanil has also been reported [55]. Interestingly, in a patient without PD, the use of an opioid antagonist (naloxone) has been reported to alleviate opioid-induced rigidity [15].

It has been suggested that opioids may induce a hypokinetic response by altering the expression of dopamine receptors in the basal ganglia, a mechanism which may have implications for patients with PD [56]. Increased expression of opioid precursors in the striatum and enhanced opioid signalling in the basal ganglia have also been associated with the development of levodopa-induced dyskinesia [57]. Animal studies have shown that the nature of this association is unclear, with opioid antagonists reported to both increase the dyskinetic response to dopaminergic agents [58] and decrease the response [57]. Clinically, Berg et al. [59]

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