The incidence of worsening impulse control disorders in the initiation of apomorphine therapy

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Abstract

Apomorphine therapy was first discovered in the 19th century and became clinically available for use in 1980's. Apomorphine therapy has been described as an underutilised therapy for Parkinson's disease (The aim of this study was to determine the incidence of Impulse Control Disorders (ICD) using a clinician administered rating scale the 'Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease Rating Scale' (QUIP-RS). The results of this study were consistent with the current literature that was reviewed. We found that apomorphine therapy were unlikely to worsen ICD and the use of apomorphine infusion may even improve ICD. In addition, concomitant use of dopamine agonists was not likely to worsen ICD.

Introduction

In the treatment of Parkinson's, currently there are three advanced treatments including apomorphine therapy, levodopa-carbidopa intestinal gel (LCIG) and Deep Brain Stimulation (DBS). These therapies use the concept of continuous stimulation to provide stability in preventing motor fluctuations (Tsui, 2014)

Apomorphine therapy was first trialled in Parkinson's disease in 1884 and became more widely used clinically in 1984 (Auffret et al. 2018). It is a clinically established therapy for participants with Parkinson's disease with motor fluctuations. Randomised control trials and open label studies have shown its effectiveness in reducing 'off' times and dyskinesias (Katzenschlager et al., 2018; Prakash & Simuni 2020). However, dopamine agonists have always been closely associated with the impulse control disorders (ICD) (Weintraub & Classen, 2017). Impulse control disorders are defined by a failure to resist an impulse, drive, or temptation to perform an act that is harmful to the person or to others (Evans et al., 2019). Despite evidence to support apomorphine as a highly tolerable and effective treatment with minimal psychiatric complications, apomorphine is still described as an underutilised therapy (Powe & Wenning, 2000).

Literature Review

We performed a literature search on the database PubMed using the key terms of 'apomorphine AND impulse control disorder' which resulted in 22 articles. No other filters were applied. The year of publication was not filtered due to the limited amount of publications available. An abstract review of all 22 articles was performed and 9 articles were selected were for more detailed review . The number of results and the year of publications of this search suggests the limited amount of literature and research around this topic.

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Impulse Control Disorders (ICD) occurs in 25% among the Parkinson's population . The risk factors for ICD include being male, younger age, drug abuse, Parkin gene mutation and a family history of ICD. Manifestations such as hypersexuality and gambling were more common in males and compulsive shopping was more prominent in females . Suggested treatment of ICD include considering a prolonged release version of a dopamine agonist or cessation of dopamine agonist (Bhattacharjee, 2008). However, not all patients can tolerate cessation of dopamine agonists due to severe worsening of Parkinsonism and/or dopamine agonist withdrawal symptoms (DAWS) (Weintraub & Nirenberg, 2013).

From the articles analysed in this literature review, two studies similarly examined the incidence of ICD in the use of apomorphine. The first study included 41 patients using apomorphine with only 7 (17%) developing new onset of ICD with one discontinuation of therapy (Todorova et al. 2015). In another open label, prospective, multicentre observational study, this study had 43 patients on apomorphine with only 4 (9.3%) of new cases of ICD occurring and no cases of discontinuation of therapy (Martinez-Martin et al. 2015). Besides the low incidence of ICD in using apomorphine therapy, there is evidence to suggest that ICD rates may even reduce or even improve with the use of apomorphine therapy despite being a dopamine agonist (Todorova et al. 2015).

Aim of Study

The aim of the study was to determine if apomorphine therapy worsens Impulse Control Disorders (ICD) as measured by the 'Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease Rating Scale' (QUIP-RS).

Method

The study was conducted in a Movement Disorders clinic in a single tertiary Australian teaching hospital over a 3-year period between 2014 to 2017. We reviewed (n=25) participants who was started on apomorphine therapy and prospectively collected their QUIP-RS score at baseline prior to treatment initiation and at the 6-month mark post-treatment. Inclusion criteria included patients who had a clinical diagnosis of Parkinson's disease, diagnosed by a Movement Disorders neurologist, and referred for initiation of apomorphine therapy. The participants were naïve to apomorphine, and we included participants using both intermittent injections (n=19) and infusions (n=6). Participants were sequentially recruited in an unbiased fashion, and we recruited (n=13) males and (n=12) females. During the apomorphine initiation visit, a QUIP-RS was conducted. At the 6-month follow-up appointment, we repeated the QUIP-RS as a way of clinically monitoring side effects including ICDs.

Results

The average age of participants was 59 (range 30-70 years) with an average disease duration of 9.8 years (range 2-21 years). Of the 25 participants recruited, there was worsening of the QUIP-RS in 32% (n=8), no change in score for 8% (n=2) and there was an improvement in QUIP-RS score in 60% (n=15).

Of the 13 male participants, 46% (n=6) worsened in QUIP-RS scores whereas the 12 female participants, only 25% (n=3) worsened in QUIP-RS score.

It was noted that 17% (n=2) had no change in their score.

When comparing participants using only apomorphine intermittent injections (n=19) (excluding infusion participants), there was worsening QUIP-RS scores in 31.5% (n=6), no change in score for 10.5% (n=2) and an improvement in QUIP-RS score in 57% (n=11). Participants using infusion therapy of apomorphine (n=6) experienced worsening in QUIP-RS score in 17% (n=1) and improvement in 83% (n=5).

Of the 25 participants recruited, 3 participants were using concomitant dopamine agonists and none of them had worsening in QUIP-RS scores at the 6-month mark post-treatment.

Limitations of the study

The limitations of the study include small number size for both groups in comparison to other published studies. Another limitation is we omitted to capture the breakdown of the ICD manifestations such as gambling, hypersexuality, compulsive shopping, compulsive eating, punding or dopamine dysregulation syndrome and which type was most likely to occur. In addition, the degree of improvement or worsening was not measured at depth.

Discussion

The results from this study seem to correlate consistently with the current literature that was reviewed. Firstly, the incidence of worsening impulse control disorders occurred in only 32% of participants which is slightly higher compared to the 25% of general Parkinson's population. Notably, the initiation of apomorphine therapy improved QUIP-RS scores in 60% of the participants at the 6-month post-treatment mark compared to the 9% new onset of ICD in the literature (Martinez-Martin et al. 2015).

Secondly, it appears the infusion delivery method of apomorphine were less likely to worsen ICD but more likely improve it even in comparison to apomorphine intermittent injections . This could be due to the reduction in other dopaminergic agents when initiating an infusion therapy.

Furthermore, although our sample size of participants using more than one dopamine agonists concurrently was small (n=3), the use of concomitant dopamine agonists did not seem to increase the risk of worsening ICD in our cohort. However, the small number of participants prevents us from generalising this result.

Other relevant results we also found consistent with current literature is that males were more likely than females to have a worsening in ICD when using apomorphine therapy.

Conclusion

Apomorphine is a safe and tolerable but still an underutilized therapy in the treatment of Parkinson's disease. This study supports the notion that apomorphine therapy is not likely to induce a worsening of ICD and even possibly improve it. In addition, concomitant use of other dopamine agonists should not deter us from using this therapy.

Relevance to Clinical Practice

With appropriate side effect monitoring, this treatment can be safely initiated and tolerated in the treatment of Parkinson's disease and should be encouraged to be used more widely.

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