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Review article

Parkinson's disease and pregnancy: An updated review

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ABSTRACT

Pregnancy does not often occur in the setting of Parkinson's disease (PD) as the most common age of onset is beyond the childbearing years, yet management of these two conditions is crucial for the health of both mother and child. Here we review treatment data of PD during pregnancy, primarily from case reports and drug registries, and focus on available evidence regarding the pregnancy risks for patient and fetus. Historically, it was reported that many women had worsening of symptoms during pregnancy but this may be because anti-parkinsonian medications were not recommended or were under dosed. Levodopa has the best safety data for use in pregnancy and amantadine should be avoided in women who are pregnant or trying to become pregnant. The data for other pharmacological and surgical treatments is less clear. There is no evidence that women with PD have higher rates of birth or fetal complications.

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1. Introduction

Pregnancy arising in the setting of a chronic neurodegenerative disorder, such as Parkinson's disease (PD), is rare. Yet, as the average maternal age is increasing, it may become a more common occurrence [1]. The typical age of onset of PD is in the early 60's and various epidemiologic studies have shown that men are one-and-a-half to two times as likely to develop PD than women. In addition, women tend to develop the disease on average about two years later [2]. PD presents before the age of 40 in approximately only 5% of cases, and it is estimated that around 400 women less than 50 years old are diagnosed with PD each year in the United States [3]. For these reasons, even neurologists have a misperception that PD and pregnancy do not occur together. The incidence of pregnancy in PD is unknown and our knowledge on the topic is limited to the cases reported in the literature. This review will examine these cases to gain a better understanding of how pregnancy in women with PD is approached. We will discuss how pregnancy can impact PD symptoms and how PD and its related treatments can affect a pregnancy. It is important for neurologists and movement disorder experts to be aware of how to counsel women with childbearing potential, who also have PD, to ensure optimal treatment for mother and child.

2. Impact of pregnancy on Parkinson's disease symptoms

2.1. Historical review

The literature on how PD symptoms are effected during pregnancy varies [4]. Some reports indicate clinical worsening of PD symptoms during or shortly after pregnancy, but there are also reports of stability and even improvement of PD symptoms throughout pregnancy [5–8]. In 1987, Golbe, published the first major examination in the English literature on idiopathic PD and pregnancy [9]. 18 women with PD who had a total of 24 pregnancies were surveyed about their experience during pregnancy. Seventeen of those pregnancies went to full term (four electively aborted and three spontaneously aborted), and 11 women or 65% reported worsening of their PD symptoms during pregnancy. Ten of those 11 women reported that they did not return to their baseline function after pregnancy. Five women were not on any medication to treat their PD and of those, four reported worsening of function. The topic of pregnancy in PD was not comprehensively reviewed for nearly another decade, until 1998, when Hagell published a review of 26 women with PD with a total of 35 pregnancies. In that series, 46% of women had worsening of PD symptoms during their pregnancy [5]. Nearly a quarter of the women did not receive any anti-parkinsonian treatment in this series. This suggests that there could be detrimental effects on a woman's PD symptoms from

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withholding treatment during pregnancy. Since 1998, there has not been another comprehensive review in the literature regarding women who have experienced pregnancy in the setting of PD.

2.2. Updated outcomes

2.2.1. Parkinson's disease symptoms during pregnancy

A literature search, restricted to English language publications, using the terms, "pregnancy" and "Parkinson's disease" was performed in December 2016 using PubMed and Ovid research databases, resulting in 591 and 361 publications, respectively. Articles were reviewed for relevance to the topic by authors and reference lists were also searched for additional pertinent publications. We complied 28 papers from the English literature or at least with English abstracts, ranging from 1985 to 2016, in which reports of pregnancy and PD were discussed (Table 1) [3–30]. These papers yielded a total of 74 live births, and 64 of these cases included descriptions or objective measurements on PD symptoms during pregnancy. Thirty-one pregnancies or 48% resulted in worsening symptoms and 33 pregnancies or 52% resulted in improved or no change in PD symptoms. This is in keeping with what has been previously reported in pregnancy and PD symptom outcomes from 1998 [5] but an improvement from the older literature [9]. These reports are limited by the variable methods used to ascertain changes in PD symptoms, some used patient or clinician subjective evaluation, while others reported changes in the Unified Parkinson's Disease Rating Scale (UPDRS) or in Hoehn and Yahr stage. Women were also at different stages and disease duration at the time of pregnancy. Age at time of pregnancy spanned from 23 to 46 years old. Additionally, and perhaps most importantly, these women were on different medications and treatments for their PD. Making definite conclusions from this heterogeneous data is limited, yet given the scarcity of information on this topic, we felt it important to include all relevant cases in the discussion.

2.2.2. Medication use during pregnancy

Changes in PD motor symptoms and medication status were reported in 54 of the previously mentioned 74 pregnancies. In 83% of these pregnancies, women reported taking anti-parkinsonian medications. Of those on medications, 64% reported improvement or no change in PD symptoms. In the women not on medications for their PD, only 33% reported improvement or no change. Thus, it appears that use of anti-parkinsonian medication during pregnancy improves PD symptom control and should be strongly considered. This data suggests that women should be counseled that: while PD symptoms could worsen during pregnancy, there is a much better chance of sustained symptom control when anti-parkinsonian treatment is administered throughout the duration of pregnancy.

2.3. Other factors affecting PD during pregnancy

Despite use of medications during pregnancy, 36% of women still had worsening of PD symptoms. The etiology of this worsening is not yet determined, but several theories have been purposed. Natural progression of PD that occurs during a pregnancy needs to be considered, but many women in the above discussion reported a much more dramatic worsening than would be expected in a nine to ten-month period. In those cases where the UPDRS was

Table 1
Reports discussing pregnancy in the setting of Parkinson's disease.

Author	Pregnancies	Medication	Motor outcome	Fetal outcome
Allain 1989	1	B/L	Motor fluctuations in last week before delivery	Normal
Asha 2010	1	C/L, ropinirole, bromocriptine, trihexyphenidyl	Stable symptoms	Normal
Ball 1995	1	C/L	Stable symptoms	Normal
Benbir 2014	1	pramipexole	Worsening by UPDRS	Normal
Benito-Leon 1999	1	bromocriptine	Stable symptoms	Normal at 12 years
Campos-Sousa 2008	8	levodopa	Stable symptoms	Not reported
Cook 1985	4	3 C/L and 1 none	Stable symptoms	Normal at 1.5, 5 and 7 years
De Mari 2002	1	C/L, pergolide	Wearing off better	Normal at 13 months
Gershanik 1986	2	C/L	Stable symptoms	1 miscarriage and 1 normal
Golbe 1987	20	12 on medications, 5 none	11 worse, 1 better, 1 worse dyskinesia, 4 stable	3 miscarriages, 17 normal an average of 7 years
Ha 2007	1	levodopa, bromocriptine	Stable symptoms	Not reported
Hagell 1998	5	B/L plus other medications	4 without mention of symptoms, 1 stable UPDRS	1 with osteomalacia, 1 with hypotonia, 3 normal
Jacquemard 1990	1	levodopa	Worsening	Not reported
Kranick 2010	10	no mention of medications	Worsening, self reported	Not reported
Kupsch 1998	1	B/L, selegiline	Improvement and less levodopa needed	Normal at 10 years
Lamichhane 2014	2	1 on pramipexole and 1 on ropinirole	1 increase dose at 6 months post-partum and 1 stable	1 normal at 3 years and 1 normal at 14 months
Lindh 2007	2	1 on B/L and 1 on C/L, entacapone, bromocriptine	No reported worsening	1 normal and 1 seizure but normal after
Mucchiut 1004	1	pramipexole	Worsening on motor UPDRS 12→25→35	Normal at 6 months
Robottom 2008	1	not on medications	Worsening motor UPDRS 12→24→32	Not reported
Routiot 2000	1	B/L	Moderate worsening	Normal
Scelzo 2016	3	1 none, 1 levodopa, 1 rasagiline and ropinirole	Stable UPDRS on patient not on medication	Normal
Scott 2005	2	C/L, cabergoline	1 stable symptoms and 1 Slight worsening post-partum	Normal
Serikawa 2011	1	C/L, entacapone, selegiline	Worsening, H&Y 2→4	Normal twins at 2 years, except 1 had VSD
Shulman 2000	1	C/L	Worsening, UPDRS: 8 to 27	Normal
Thulin 1998	1	C/L	No outcomes reported	Normal at 4.5 months
Tobiassen 1991	2	not on medications	No outcomes reported	Normal
Von Graeventiz 1996	1	B/L	No outcomes reported	Normal
Zlotnik 2014	2	1 none and 1 C/L intestinal gel	No worsening, increase in dyskinesia	Normal

C/L = carbidopa/levodopa, B/L = benserazide/levodopa.