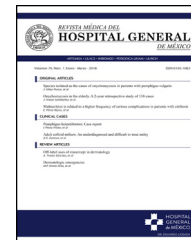




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REVIEW ARTICLE

Current treatments in Parkinson's including the proposal of an innovative dopamine microimplant



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Abstract Parkinson's disease is a chronic, debilitating, progressive neurological disorder of multifactorial origin. It affects between 0.3% and 2% of the over-65 population worldwide, with a predilection for men, and is characterised by bradykinesia, muscular rigidity, resting tremor and postural instability. Parkinson's is caused by decreased dopamine levels due to the loss of dopaminergic neurons in the substantia nigra. Because dopamine is a highly oxidisable molecule, precursors such as levodopa, together with catechol-O-methyltransferase and monoamine oxidase inhibitors to prevent degradation, are used in the treatment of this disease. These therapies, however, are not without their adverse effects. Surgical treatments for Parkinson's include pallidotomy, therapy deep brain stimulation, and stem cells. A more recent development involves a titanium dioxide micro-implant containing nanopores that stabilise the dopamine for continuous release. When inserted into the caudate nucleus, this micro-implant was found to counteract 85% of symptoms in hemiparkinsonian rats, and is a promising therapy for patients with Parkinson's disease.

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PALABRAS CLAVE

Enfermedad de Parkinson;
Microimplante dopaminérgico;
Núcleo caudado;
Fármacos;
Efectos secundarios;
Sustancia nigra

El Parkinson y los tratamientos actuales que incluyen la propuesta de un innovador microimplante dopaminérgico

Resumen La enfermedad de Parkinson es un trastorno neurológico con una prevalencia del 0.3 a 2% de la población mundial mayor de 65 años de edad, es crónica, debilitante y progresiva, de origen multifactorial. Afecta mayormente a los hombres que las mujeres en una proporción de 2:1. Se caracteriza por la bradicinesia, la rigidez muscular, temblor de reposo e inestabilidad postural. Esta enfermedad es causada por una pérdida de neuronas dopaminérgicas en la sustancia nigra y la consecuente disminución de la dopamina en el cuerpo estriado. La dopamina es una molécula altamente oxidable, es por ello que se utiliza en los tratamientos precursores de la misma, como la levodopa, también se emplean inhibidores de la catecol-O-metiltransferasa y de la monoamino oxidasa, para evitar su degradación. El uso de estos tratamientos farmacológicos tienen efectos colaterales. Entre los tratamientos quirúrgicos utilizados se encuentran la palidotomía, la terapia de estimulación profunda del cerebro, la aplicación de células madre y recientemente se ha desarrollado un microimplante de dióxido de titanio con nanoporos que contienen a la dopamina estable y misma que se libera de forma continua. Este microimplante insertado en núcleo caudado de ratas hemiparkinsonianas, contrarresta los síntomas en un 85%. Este microimplante es una terapia muy prometedora para los pacientes con Parkinson.

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History of Parkinson's disease

Parkinson's disease has been known for over 4000 years. Descriptions of people afflicted with trembling of the head and hands, who have difficulty eating, swallowing saliva, and who lose their power of concentration have been found in documents dating from the time of the Hindu Vedas, Ancient Egypt and China (2000–800 BC).^{1,2}

The Renaissance genius Leonardo da Vinci (1452–1519) was one of the first to directly characterise Parkinson's, describing it as "the movements of paralytics whose head and members move without control of the soul; the soul, with all its force, cannot stop these extremities from trembling".²

In 1810, British sailors exposed to mercury showed signs of "trembling, paralysis and sialorrhoea, followed later by more changes", an example of Parkinson's due to mercury poisoning.² Modern research has shown that certain pesticides, herbicides and chemical can also cause Parkinson's.³ Despite these descriptions, it was not until 1817 that British doctor James Parkinson described the disease in his "Essay on Shaking Palsy". Based on his observation of 6 patients, Parkinson described "shaking palsy" as "Involuntary tremulous motion with lessened muscular power in parts not in action and even when supported; with a propensity to bend the trunk forward and to pass from a walking to a running pace. These patients at times become immobilised, as if frozen, although their hands show a slight tremor".⁴

Parkinson's disease around the world

Parkinson's disease (PD) is a progressive, degenerative disorder of the nervous system. It is usually brought on by a combination of genetic and environmental factors associated, in some cases, with ageing, although the disease has

also been described in young patients. Parkinson's is a progressive disease with a mean duration of between 10 and 13 years, affecting more men than women.⁵

Worldwide, the disease is estimated to affect between 4.1 and 4.6 million individuals over the age of 50 years, with a prevalence of between 0.3% and 2% in the over-60 age group.⁶

The disease is found in all regions of the world, and among all ethnic groups. It is most prevalent among Caucasians aged between 60 and 84 years, with 260 cases per 100,000 inhabitants, and less so among black, Hispanic and Asian people. Studies from China, Taiwan, Japan and Singapore have reported a higher prevalence in individuals aged between 69 and 79 years.⁵

A study of 588 patients with PD diagnosed between 1994 and 1995 by members of the Kaiser Permanente Medical Care Programme of Northern California reported an increased incidence in individuals over the age of 60 years, with only 4% of cases being under the age of 50 years. The age- and gender-adjusted rate per 100,000 inhabitants was highest among Hispanics (16.6, 95% CI: 12.0, 21.3), followed by non-Hispanic whites (13.6, 95% CI: 11.5, 15.7), Asians (11.3, 95% CI: 7.2, 15.3), and blacks (10.2, 95% CI: 6.4, 14.0). These data suggest that incidence of Parkinson's disease varies by race and ethnicity (Table 1).⁷

Parkinson's disease in Mexico

No official epidemiological reports on the prevalence and incidence of PD in Mexico have yet been published, and too few studies have been conducted to draw up a reliable demographic and clinical profile of PD patients. The only data available are estimates of the number of individuals diagnosed with PH nationwide, which suggest a prevalence of between 40 and 50 cases per 100,000 inhabitants/year.

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