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Title Surgical Treatment of Parkinson's disease

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This is a systematic review of the literature on the safety and effectiveness of three surgical treatments for Parkinson's disease: pallidotomy, deep brain stimulation (DBS), and transplantation.

The MEDLINE, EMBASE, INAHTA, and Cochrane databases were searched using a specific strategy for each surgical procedure (English, Spanish, French, and German languages, from 1990 to 1999). Three HTA reports on pallidotomy were found (Wessex, Alberta, and VATAP), and 23 articles were selected from 147 identified after applying inclusion criteria. Six articles were related to pallidotomy, eight to DBS (4 thalamus, 2 globus pallidum, 2 subthalamic nuclei), eight to transplantation, and one was a comparative study.

The report includes a synthesis of efficacy and safety studies, current physiopathologic knowledge, and descriptions of each procedure. Diffusion in Spain and other countries and social and ethical issues are also considered. Most studies are case series, with only one well-designed trial recently published, but followup is too short. Although most researchers draw similar conclusions, the quality of evidence is poor, and many methodological problems remain unsolved, particularly outcome assessment.

Surgical procedures are mainly applied to advanced Parkinson's disease stages after failure of medical treatment. <u>Pallidotomy</u> shows some reduction in symptoms, mainly in tremor, bradykinesia, and drug-related dyskinesias, generally maintained for at least 2 years. <u>DBS</u> of the globus pallidus shows similar results and better antiparkinsonian effects. DBS of the subthalamic nucleus involves a wider range of benefits on parkinsonian symptoms, including postural stability and gait, but its beneficial effect on dyskinesias is due, in part, to the reduction in medication.

Pallidotomy is followed by adverse effects that must be taken into account when the indication is considered (visual field defects, intracerebral hematomas) and some authors recommend exclusion of the bilateral procedure. Adverse effects of DBS are usually well tolerated and only occasionally are they serious and permanent. The high cost of the devices and the difficulty in setting the stimulation parameters may counterbalance the indication in some instances.

<u>Fetal mesencephalon transplantation</u> to the striatum is usually followed by amelioration of parkinsonian symptoms in the case series that have been published. The transplant is usually well tolerated, but adverse effects including confusion and small hemorrhages, and more often problems derived from immunosuppression can occur. Ethical issues and the difficulty in obtaining 4 to 8 human fetuses per patient are additional limitations associated with this technique. <u>Coimplants of adrenal medulla and peripheral nerves</u> are reported to have benefits similar to fetal mesencephalon transplantation, but the method seems to have been abandoned due to high mortality and morbidity rates. Recent experiences in animal models with <u>autotransplants of carotid body cells</u> showed promising results. The procedure could be safer and more available, and the first study in humans is currently underway in Andalusia.

Recommendations:

The procedures listed above should be performed only in carefully selected patients by neurosurgeons with a high level of expertise in stereotactic methods. A national registry for outcome evaluation should be established. Well-designed randomized controlled trials are needed to provide better evidence, particularly concerning long-term outcomes, functional ability, and quality of life measures.

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