DIAGNOSTIC ACCURACY AND CLINICAL UTILITY OF PET/CT AMYLOID IN MILD COGNITIVE IMPAIRMENT

Enlace al texto completo

Introduction: according to the World Alzheimer's Report, the prevalence of dementia stood at 46.8 million cases in 2015 (10.5 million in Europe). Due to the progressive ageing of the population, an increase in the number of cases is expected, reaching 74.7 million in 2030 and 131.5 million by 2050. In Spain, the prevalence of Mild Cognitive Impartment (MCI) in people over 65 years of age has reached a rate of 18.5% (IC95% 17.3-19.7) (February 2014-March 2015). The diagnosis of dementia begins with a neuropsychological assessment of the patient using various clinical criteria with the aim of establishing the underlying aetiology and complementary tests, such as the determination of biomarkers in urine, blood or cerebrospinal fluid (T-tau protein, Aβ-42 and P-tau) and structural or functional imaging tests (positron emission tomography-PET) in order to rule out reversible causes of dementia and to support clinical diagnosis. PET can be used with neurogeneration markers (18-fluorodeoxyglucose-FDG) or amyloid deposits. The latter have been proposed as a tool that could be useful for the early and in vivo diagnosis of Alzheimer's disease (AD) or other dementias characterized by an increase in amyloid plaques in the early stages of the disease. The first amyloid radiopharmaceutical developed was the Pittsburgh B compound (PiB). Other amyloid radiopharmaceuticals have now become available: 18F-Florbetapir (Amyvid®), 18F-Florbetaben (Neuraceq®) and 18F-Flutemetamol (Vizamyl®), which have a longer half-life than PiB.

Aims: the main objectives of this report are to evaluate the effectiveness and safety of amyloid cerebral PET in the diagnosis of cognitive impairment, Alzheimer's disease or other dementias, as well as its impact on the diagnostic and therapeutic management of these patients.

Methods: specific search strategies were designed to identify studies that assess the safety and/or effectiveness of amyloid PET in the diagnosis of MCI, AD or other dementias, its economic and organizational impact, patient acceptability and satisfaction, and ethical, social and legal aspects derived from its use. These strategies were performed in March 2018 in the main medical literature databases.

A qualitative synthesis of the evidence was performed using the GRADE system, for which 12 outcomes were selected, classified by clinicians as important or critical, except for two, which were considered of low importance and therefore eliminated from the analysis (complications derived from the use of radiopharmaceuticals and mortality). In order to evaluate the risk of bias of the studies, specific tools were used according to the type of study. The quality of evidence was evaluated using the GRADE system for quantitative studies and the GRADE-CERQual version was used for qualitative studies. Both the extraction of data from the studies and the synthesis and evaluation of the evidence were carried out by two researchers independently and blindly.

Results: based on the selection criteria of previously established studies, three systematic Cochrane reviews were included that evaluated the effectiveness of each of the amyloid radiopharmaceuticals (florbetaben, florbetapir and flutemetamol) in the diagnosis of the progression of MCI to AD or other dementias, and two systematic reviews with meta-analysis that evaluated in both cases the diagnostic validity of the three radiopharmaceuticals in the detection of AD. By updating one of the meta-analyses, 12 primary studies, 8 diagnostic test studies and 4 on the influence of amyloid PET on the clinical management of patients with dementia were identified. In addition, by carrying out complementary searches, we located two cost-effectiveness studies, 4 qualitative studies on the perspectives of patients, relatives/caregivers or clinicians and 4 consensus papers on ethical issues. The percentage of false positives and false negatives was highly variable (11-34.3% and 8-58% respectively). Two studies in which flutemetamol and florbetapir were used did not report any cases of false positives or negatives. The sensitivity (S) and specificity (E) of amyloid PET in the progression from MCI to AD or other dementias was around 50-100% and 50-88% respectively, while poor results were described for the progression from MCI to other non-AD dementias (S=0% and E=38-40%) (florbetapir only). As regards the diagnostic validity of amyloid PET in AD, highly variable results were also described (S=60-100% and E=52-100%). The percentage of patients who experienced modification in diagnosis and medical/therapeutic management after performing amyloid PET was very variable (11-92%), with differences between the group of patients who obtained a positive or negative PET result. The economic and organisational impact of amyloid PET does not seem to be relevant; on the one hand, it is a cost-effective technique and, on the other, its implementation in clinical practice should not imply a high impact, especially in centres with the necessary equipment for PET imaging. The literature states that most patients wish to know the outcome of PET in order to plan their future before the progression of cognitive impairment prevents them from making decisions.

From an ethical point of view, adequate informed consent should be given prior to testing, and the communication of results should be ruled out by the bioethical principles of autonomy, nonmaleficence and benefit.

Conclussions: according to the literature reviewed, there is great variability in the diagnostic accuracy and clinical usefulness of amyloid PET. Therefore, following the recommendations described in the main expert consensus, this technique should be used in a small group of patients with clinically confirmed MCI with the aim of increasing diagnostic certainty or modifying the clinical management of the patient.

In addition, special attention should be paid to the indication process of the test to be performed by appropriate informed consent, as well as the communication of PET results.