NECA National Evidence-based Healthcare Collaborating Agency

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RAPID program utilized for Coverage of Health Insurance

As the situation that requires rapid political judgment becomes more frequent caused by the change of diseases pattern, the social issues and the urgency of topic, the demand for the timely best evidence is increasing. Accordingly, National Evidence-based Healthcare Collaborating Agency(NECA) has introduced Rapid Assessment & Production of High Quality Information Demanded(RAPID) Program, and if there is the urgent need for an evidence, NECA provides the best available evidence that help in the health care decision-making by quickly and systematically providing existing evidence. In this leaflet, the projects conducted by the request of National Health Insurance Corporation that provide the evidence of decision-making for health insurance coverage are introduced.

1. Diagnostic Accuracy of Anti-CCP antibody testing for Rheumatoid Arthritis : Systematic Review

Introduction

Rheumatoid arthritis is the most common whole body inflammatory autoimmune diseases, and is characterized the chronic polyarthritis and the destruction of joint tissue, and early diagnosis and treatment are very important to improve the disease prognosis

Objective

This study aimed to provide the evidence of decision-making by examining rapidly the clinical usefulness for the diagnosis accuracy of anti-CCP antibody testing from Korean patients with the rheumatoid arthritis.

Methods

The prevalence and quality of life(QoL) of Korean rheumatoid arthritis patients was checked using the fourth Korea National Health and Nutrition Examination Survey(2007 – 2009) (KNHNES IV), and identified the preceding evidences by reviewing foreign health technology assessment reports and guidelines. Then, we reviewed the existing systematic review published by using the framework that AHRQ of the U.S. has proposed, and provided the up-to-date evidence by combining further evidence to existing systematic review for the literature targeting Korean.

Results

□ **The prevalence and QoL of Korean rheumatoid arthritis patients**

As the results the KNHNES IV, the prevalence rate of Korean patients with the rheumatoid arthritis was 2.2% based on the lifetime prevalence, and 1.9% based on the physician diag-

This leaflet has been produced to promote the research results performed by NECA. The whole texts of the research report may be downloaded from the website of NECA(www.neca.re.kr).

nosis. In addition, the average QoL index of the patient with rheumatoid arthritis was 0.803 based on the physician diagnosis. It was lower value than 0.933 that is the index of the average quality of life index of Korean people, and was lower than hypertension(0.865), diabetes(0.852), asthma(0.842) and angina(0.811) in comparison with other diseases.

□ **HTA Reports and Guidelines**

Many international clinical guideline and reports have been presented for the diagnosis of rheumatoid arthritis, and each countries and organizations are slight difference but it consistently says that anti-CCP antibody testing is required in the diagnosis of rheumatoid arthritis. The 2010 ACR/EULAR classification criteria that has recently announced yet did not identified for validity, but the most different points when compared to the 1987 ACR classification criteria, was that anti-CCP antibody tests were added to the classification criteria, and it has been mentioned that the anti-CCP test would contribute to raise the diagnostic specificity of the with early rheumatoid arthritis patients

□ **Overview of Systematic Review**

As a result of the analysis of nine existing systematic reviews for the existing anti-CCP antibody test, it was the difference such as the search DB or search term and research object, and even it was the difference in the quality assessment of the literature by AMSTAR. However, there was no disagreement about that the anti-CCP antibody test was similar to rheumatoid factors or showing the sensitivity of higher level in the diagnosis of rheumatoid arthritis and the specificity was much higher. In addition, higher sensitivity and specificity in the second generation than the first generation were identified in the case of the anti-CCP antibody test. It was concluded that the diagnosis of early rheumatoid arthritis was significant and was the factor to help the prediction of the possibility to develop to the rheumatoid arthritis.

□ **Using Systematic Review for Korean rheumatoid arthritis patients**

As a result of the assessment of the quality of the primary study for the anti-CCP antibody test targeting Korean of nine studies finally selected, the area of the patient selection of QUADAS 2 had higher risk of bias or uncertainty because the study type was a patient control group study or a cross-section study, and the case of items except for them was evaluated that the quality of most studies was high. As the results of a meta-analysis of the entire control group, the calculated integrated sensitivity was 0.76(95% CI: 0.73-0.79), and the integrated specificity was 0.96(95% CI: 0.93-0.97). The positive likelihood ratio that was calculated with the integrated sensitivity and specificity, was 18.04(95% CI: 11.80-27.57), and the negative likelihood ratio was 0.25(95% CI: 0.23-0.28). In the case of the disease control group, the integrated sensitivity was 0.79(95% CI: 0.73-0.83), the integrated specificity was 0.92(95% CI: 0.88-0.94). The positive likelihood ratio that was calculated with the integrated sensitivity and specificity, was 9.43(95% CI: 7.00-12.71), and the negative likelihood ratio was 0.23(95% CI: 0.19-0.29).

Conclusions

It is considered that as the results of HTA reports and guidelines, overview of systematic review, or using systematic review targeting Korean, because it showed the consistent the conclusion that anti-CCP antibody test is necessary and useful in the diagnosis of rheumatoid arthritis, the anti-CCP antibody test will contribute to early treatment of the patients with rheumatoid arthritis by increasing the diagnostic specificity of rheumatoid arthritis - especially, early rheumatoid arthritis diagnosis.

2. Polysomnography in Diagnosis for Sleep Related Breathing Disorder

Introduction

Sleep related breathing disorder(SRBD) is has been well known to be a common syndrome, and to be associated with various medical problems that have impact on morbidity and mortality, causing an additional burden of the public health service. The prevalence of SRBD was 27.1% and 16.8% in men and women, respectively in Korea. Therefore it is needed to accurately diagnose in early stage. Although the standard method for diagnosing SRBD is Polysomnography(PSG) presented in American Academy of Sleep Medicine and several clinical practice guidelines, the assessment of clinical effectiveness for PSG have never made in Korea. Accordingly, the need of the study evaluating the clinical evidence of the PSG for the diagnosis of SRBD is required.

Objective

The objective of this study is to verify clinical evidence of PSG in the diagnosis of SRBD.

Methods

In this study systematic review was performed to investigate scientific evidence about the diagnostic accuracy of PSG for the SRBD. The clinical textbooks and guidelines were also determined for the medical standard.

Results

The primary article could not be found in systematic review performed for examining evidence of the diagnostic accuracy of the PSG in the SRBD diagnosis. The PSG, instead, was being applied as medical standard at evaluating abbreviated polysomnographic techniques such as division nocturnal PSG, portable PSG for SRBD diagnosis. From the clinical textbooks and guidelines recommended by clinical experts, the PSG performed in a sleep laboratory was considered as the medical standard for SRBD diagnosis and severity assessment.

Even in the laboratory test, various influential factors have been emphasized, which is the environment of sleep laboratory, standardization of PSG, the continuous supervision of professional sleep inspector, the night-to-night variability, the test-retest reliability, and the intra-rater, inter-rater event recognition errors.

Conclusions

The PSG that is performed in the sleep laboratory under the supervision of a polysomnographic technician was suggested as the most standard test method at the time of the SRBD diagnosis and severity assessment. As more and more the SRBD prevalence and its impact on morbidity and mortality have been emphasized, this study has the great significance in the terms of providing of the evidence for the policy decision.

3. Systematic Review of Diagnostic Accuracy of FDG PET/PET-CT for Fever of Unknown Origin

Introduction

Fever of unknown origin(FUO) is defined as temperature > 38.3°c(101°F) on several occasions duration of fever of more than 3 weeks and failure to reach to diagnosis despite one week of inpatient investigations. There is no diagnostic gold standard in FUO. Although the clinical validity of FDG PET/PET-CT scan is not yet established, recent studies on the diagnostic accuracy of the test have been progressed actively

Objective

This study aimed to perform a systematic review to examine the overall diagnostic performance of FDG-PET/PET CT in identifying the causal source of FUO, and provide objective evidence to decision-making for clinical experts and patients.

Methods

This study was carried out in prompt systematic literature review method through RAPID program, which is a prompt-based evaluation program of NECA. We searched the literature using several electronic databases(Ovid-Medline, Ovid-EMBASE, Cochrane library, KoreaMed, and Kmbase) from their inception to May, 2012. The selection criteria were as follows: the patients examined in the studies had to have met the criteria for the definition of FUO; all the reference standards used in the individual studies were accepted; the reported primary data must have been sufficient to discriminate between the true positive(TP), false positive(FP), false negative(FN), and true negative(TN) results of FUO and to allow us to determine the sensitivity and specificity. All articles were read by more than 2 independent reviewers, who extracted data from the articles according to predefined criteria. Disagreements were resolved by discussion between the reviewers, with the opinion of a third reviewer being sought if necessary. The quality of the eligible studies was assessed using Quality Assessment of Diagnostic Accuracy Studies-2(QUADAS-2). Meta-analyses of included studies were performed to evaluate the diagnostic accuracy of FDG-PET and FDG-PET/CT. Subgroup analyses were performed if results of individual studies were heterogeneous.

Results

A total of 15 studies representing 592 patients were eligible for inclusion. Overall, the studies had 'poor' methodological quality. Concerns about applicability are rated as 'low'.

For the six FDG-PET studies that we evaluated, pooled sensitivity and specificity using the bivariate model was 0.859(95% CI: 0.729-0.932), and 0.664(95% CI: 0.416-0.845), respectively. The area under the curve(AUC) of SROC was 0.7955, and the pooled diagnostic odds ratio(DOR) was 9.38(95% CI: 1.44-60.91).

For the nine FDG-PET/CT studies, pooled sensitivity and specificity was 0.838(95% CI: 0.715-0.914), and 0.714(95% CI: 0.588-0.814), respectively. AUC of SROC based on nine literatures was 0.8071, and the pooled DOR was 10.93(95% CI: 4.67-25.57).

We evaluated additionally the overall diagnostic accuracy in

the 15 included studies. The pooled sensitivity and specificity was 0.844(95% CI: 0.760-0.902), and 0.681(95% CI: 0.553-0.787), respectively. The pooled DOR was 10.31(95% CI: 4.23-25.11), and AUC was 0.7978.

Conclusions

FDG PET/PET-CT test appeared to have a high sensitivity and a moderate specificity for the detection of the causes of FUO. FUO has the characteristics that the cause is not found as primary test method, it is important to find the cause of disease in the early. The results suggest that FDG PET/PET-CT are helpful in the diagnosis of the source of origin for patients with FUO and may play an important role in the assessment of patients with FUO.

4. Effects of Atomoxetine, Methylphenidate in Adult Attention-deficit Hyperactivity Disorder

Introduction

Attention deficit hyperactivity disorder(ADHD) of adults is the mental illness that have difficulties in sustained attention and impulse control. According to National institute of Mental Health in the United States, approximately 4.4% of the adults experience ADHD. The drug treatment in adult ADHD is applied as the primary treatment to adult ADHD patients with more than severity, and the typical pharmaceutical drugs are Methylphenidate and Atomoxetine.

Objective

This study tried to evaluate the effectiveness and safety of Methylphenidate and Atomoxetine in adult ADHD through the rapid review.

Methods

The existing systematic reviews as the subject of this study were examined through search and quality assessment. However, twenty of them did not score high enough grade in their quality, and the last one had high quality grade but was not acceptable because its research results may be out of date since it was published in 1999. Thus, instead using existing systematic reviews, de novo systematic review was studied according to the framework of this research. The risk of bias(RoB) for final selected literature was evaluated.

Results

Finally selected literatures were 39 literatures. Among them, the literature addressed both Atomoxetine and Methylphenidate was one, and a study on Atomoxetine was 13, and Methylphenidate was 26. Because one literature was a duplicate study among 13 literatures for Atomoxetine, the RoB for total 12 studies were assessed, and in one study, the RoB was assessed as ‘low risk’, and remainder studies were rated as ‘uncertain’. In the study evaluated as ‘low’, it was concluded that Atomoxetine has the clinical effect, and it was concluded that remainder studies was effective in the study with relatively low RoB. As three studies among 27 research literatures for Methylphenidate was duplicated, the RoB for total 24 studies were evaluated, which two studies were assessed as ‘low’, and it was concluded that in these two studies, Methylphenidate had the clinical effect. When six studies that relatively the RoB was low, among remainder studies, were examined, and it was concluded that two studies were no clinical effect, but one study was the study of different characteristics, and it was concluded that Methylphenidate was not particular relation for the executive function deficits of adult ADHD. Because it was concluded that other one study was no effect due to conservative capacity and a shorter duration of treatment at its conclusion, the study complementing it will be proposed in the future.
In the most studies on Atomoxetine, it was concluded that there is the effect to alleviate the symptoms of ADHD in adult, but because in most studies, the research was invested by the company that developed Atomoxetine, the attention considering it will need in accepting the conclusions.
It has been reported that in most studies, there were some adverse events such as nausea, headache and loss of appetite. But the symptoms were not severe, and if stops taking a dose, these symptoms disappear.

Conclusions

As the results using the method of rapid review to evaluate the effectiveness and safety of Atomoxetine and Methylphenidate in adult ADHD, it is considered that the use of both drugs in adult ADHD will be appropriate because it was concluded that there was the effect to alleviate the symptoms of adult ADHD in most of studies that both Atomoxetine and Methylphenidate were included, and severe adverse event was not shown. However, it should be considered that in the case of Atomoxetine, most of the studies were supported by the pharmaceutical company that has been developed Atomoxetine.