Delphi Consensus on Attention Deficit Hyperactivity Disorder (ADHD): evaluation by a panel of experts

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Introduction. Attention Deficit Hyperactivity Disorder (ADHD) is one of the most prevalent neurodevelopmental disorders in childhood, which is frequently maintained in adolescent and adult age. It presents great clinical heterogeneity, significantly affecting the functioning of those who suffer it. Although drug treatments obtain results by themselves, the approach should be multidisciplinary and be adapted to the specific needs of each patient and his/her family. Given the variety of drugs currently available to treat ADHD, there are diverse opinions on the most effective way to approach this disorder. The objective of this work is to study the opinion of an expert clinical panel and to know the professional criteria used to define key concepts and therapeutic guidelines of ADHD in Spain.

Methodology. The project was carried out in four phases: 1) Constitution of a Scientific Committee, responsible for the preliminary biographic review and the formulation of the questionnaire; 2) selection of an expert panel of specialists with special interest and/or experience in the treatment of ADHD; 3) Likert type structured survey (online platform) in two rounds with interim processing of opinions; and 4) collection and final analysis of results.

Results. The experts' panel achieved a consensus in 55 of the 58 items making up the questionnaire, finding 3 items in which sufficient unanimity of criteria was not achieved because of the high number of experts were found in positions of non-certainty.

Conclusions. Overall, the experts of this study reached a high level of agreement in the criteria proposed in the survey, which could be generalized as indications for the clinical practice in the management of ADHD. Similarly, and given the dispersion of the results in some of the items and the lack of consensus in others, some points remain as object of discussion.

Keywords: Consensus, Delphi, Clinical practice, Attention deficit hyperactivity disorder, Treatment

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Consenso Delphi sobre el Trastorno por Déficit de Atención e Hiperactividad (TDAH): valoración por un panel de expertos

Introducción. El Trastorno por Déficit de Atención e Hiperactividad (TDAH) es uno de los trastornos del neurodesarrollo más prevalentes en la infancia, que frecuentemente se mantiene en la adolescencia y edad adulta. Presenta una gran heterogeneidad clínica, afectando notablemente al funcionamiento de quien lo padece. Si bien los tratamientos farmacológicos obtienen resultados por sí mismos, el abordaje debe ser multidisciplinar y adaptado a las necesidades específicas de cada paciente y su familia. Dada la variedad de fármacos disponibles actualmente para tratar el TDAH, existen opiniones diversas sobre cuál es la manera más efectiva de abordar este trastorno. El objetivo de este trabajo es explorar la opinión de un panel clínico experto y conocer el criterio profesional utilizado para definir conceptos clave y las pautas terapéuticas del TDAH en España.

Metodología. El proyecto se efectuó en cuatro fases: 1) constitución de un Comité Científico, responsable de la revisión bibliográfica preliminar y de la formulación del cuestionario; 2) selección de un panel experto de especialistas con especial interés y/o experiencia en el tratamiento del TDAH; 3) encuesta estructurada tipo Likert (plataforma online) en dos rondas con procesamiento intermedio de opiniones; y 4) recopilación y análisis final de resultados.

Resultados. El panel de expertos logró un consenso en 55 de los 58 ítems que conformaron el cuestionario, encontrando 3 ítems en los que no se consiguió suficiente unanimidad de criterio, debido a que gran cantidad de expertos se situaron en posiciones de indeterminación.

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Conclusiones. De manera global, los expertos de este estudio alcanzaron un elevado grado de acuerdo en los criterios propuestos en la encuesta, que podrían generalizarse como indicaciones para la práctica clínica en el manejo del TDAH. Del mismo modo, y dada la dispersión de los resultados en algunos de los ítems y el no consenso en otros, quedan algunos puntos objeto de discusión.

Palabras clave: Consenso, Delphi, Práctica clínica, Trastorno por déficit de atención e hiperactividad, Tratamiento

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequent neurodevelopment disorders in childhood, with an estimated prevalence of 5.29%.[1] It is characterized by inappropriate levels of inattention, hyperactivity and/or impulsiveness in relationship with the evolutive age[2] that interfere in social, emotional and cognitive functioning,[3] an impact that is maintained in the adult age in up to 65%,[4-8] finding prevalence values close to 4% in the adult age.[9] As has been demonstrated in a recent epidemiological study in Europe,[10] these patients have a higher risk of accidents, behavior and learning problems in childhood, substance abuse, legal problems and comorbidity with other psychiatric disorders,[11-21] with important repercussions on quality of life and life expectancy.[22]

ADHD is a neurobiological heterogeneous disorders having multifactorial origin that implies genetic and environment interaction.[23,24]

The clinical manifestations and therefore the patients' needs, vary based on age,[23] so that the choice of treatment should be adjusted as much as possible to the characteristics of the patient since adequate treatment along with an early diagnosis is essential in the disease prognosis. The treatment should always include a complete program for the patient and his/her setting that approaches the psychological and educational/occupational difficulties.[25] Although the pharmacological treatments have demonstrated their efficacy,[26] and by themselves provide advantages reflected in an improvement of school performance, the relationship with the family and peers, and present and future psychosocial adaptation of the individual should not be administered as a single therapeutic intervention.[27] Thus, the low treatment adherence rates[28] and the frequent destructuration and management difficulties the family face must always be evaluated.[29,30] ADHD has traditionally been treated with stimulant drugs, mainly with methylphenidate, although other non-stimulant drugs have arisen in recent years[31] that are having good experimental and clinical results, such as atomoxetine. More recently, guanfacine has demonstrated its effectiveness in different short term studies in the European population with an active comparator arm[32,33] and the maintenance of said efficacy in the long term versus placebo.[34] The plurality of available pharmacological treatments open a possible diversity of opinions in the approach to ADHD.

The objective of this work is to examine the technical opinion of an expert clinical panel and know the majority professional criterion on the key concepts and therapeutic guidelines of ADHD in Spain, especially the therapeutic incorporations of recent years.

METHODOLOGY

The Delphi method, a non-on-site technique originally developed in the RAND Corporation (Santa Monica, California), used to develop this work[35,36] It is performed by means of a consultation, through questionnaires, whose objective is to examine the technical opinion of a panel of experts and to reach a consensus on a subject of interest subjected to variability of criteria or to professional controversy, in this case, ADHD treatment. To do so, the individual and anonymous opinion of each expert was requested through an online platform, in which the participants had access to both the complete questionnaire and the comments of the rest of the group. This online Delphi platform has several advantages regarding the traditional one, such as eliminating the leader effect of other experts' methods, since there is anonymity among those surveyed, favoring controlled interaction with the group opinions, offering a space for reflection and reconsideration of positions, eliminating times of management, sending and reception of responses, and statistically analyzing the degree of agreement in the responses to determine in which questions consensus of the panel of experts has been achieved, whether agreement or disagreement with the subjects proposed in the survey. The more extreme the average score of an item (closest to 1 or to 9), the more manifest consensus achieved will be considered, in the agreement or disagreement on the proposal expressed by each item.

The project was carried out in four phases: 1) constitution of a Scientific Committee, responsible for the preliminary bibliography and drafting of the questionnaire; 2) selection of a panel of experts of specialists with special interest and/or experience in the treatment of ADHD; 3) Likert type structured survey having 1-9 evaluation (online platform) in two rounds with interim processing of opinions; and 4) collecting and final analysis of results.

It is very important to make a good selection of the panelists and to adequately define the research field, using

precise questions, which are quantifiable and independent, in order to achieve a good result. For this, the Scientific Committee members (co-authors of the study), after performing a bibliographic review of the subject, analyzed and proposed the blocks and questions makings up the Delphi questionnaire. Each and every one of the questions were drafted in order to develop a questionnaire, which, with its responses, would contribute to the unification of the criteria to the professionals. The initial proposals of the Committee were revised and condensed until a unanimously satisfactory joint version was achieved.

The final questionnaire was made up of 58 items grouped into seven blocks: General ADHD (6 items); Diagnosis of ADHD/ comorbidity (6 items); ADHD Treatment 10 items); Efficacy and response to pharmacological treatment (12 items); Action mechanisms of pharmacological treatment (7 items); Pharmacological treatment and comorbidity in ADHD (11 items) and Adverse events to pharmacological treatment (6 items). Each item was formulated as an assertion (affirmative or negative) that collected a professional criterion or a clinical recommendation on some aspect of interest or controversy in the approached to ADHD.

An ordinal evaluation Likert type scale with nine response categories described through linguistic qualifiers and numerical scores was used: 1-3: In disagreement with the assertion (the lower the score, the greater degree of disagreement); 4-6: Neither agree nor disagree with the assertion; there is no totally defined criterion on the question (4 or 6 is chosen if one is either close to disagreement or to agreement, respectively); 7-9: Agreement with the assertion (the higher the score, the greater degree of agreement). If one desires (optatively), the responses can be accompanied by some free comments that qualify or clarify the choice.

The panel of experts was formed by selection of a multicentric group of specialists in psychiatry, neurology and neuropediatrics with clinical experience and specific professional recognitions in the approach to ADHD. It was performed using a strategy initiated through the professional network (contacts) of the Scientific Committee, who in turn proposed new experts. The process was completed with the active search of national authors of the original articles related with the study subject in the Pub-Med - NCB data base. The 58 experts, psychiatrists, neurologists and neuropediatricians of state environment invited by the Committee (Annex 2) accepted to participate in the project and completed the two consecutive rounds of distribution and collection of questionnaires.

The field work of the project was developed during 9 weeks, from 8 November 2015 to 11 January 2016, in two rounds of structured survey. The second round, regarding items that were not consensuated in the first attempt, made it possible to reconsider opinions and bring divergent positions closer, achieving the greatest consensus possible in the group.

To analyze the results of the Delphi survey, a double statistical validation was used. The RAND/UCLA method[37,38] proposes the use of the median scores and the "concordance level" of the opinions of the panel of experts. It states that consensus exists when there is concordance in agreement or disagreement and it states that there is no consensus when there is discordance or uncertainty. There is concordance in agreement with an item when at least 66% of the panelists score between the score range of 7-9, while there is concordance in disagreement when the same amount of experts score between 1-3. Discordance is determined when the scores of one third or more of the panelists are in region 1-3, and another third or more in region 7-9. The items in which no concordance or discordance were observed are considered as having an uncertainty consensus level, which is defined to exist when at least 66% of those surveyed score between 4-6. On the other hand, and in order to have greater mathematical accuracy, a second statistical proof, the dispersion of the results, measured through the interquartile range (scores between the p25 and p75 values of the distribution) were used. When this mediator of dispersion is ≥4 points, even when the first point is fulfilled, it is considered that sufficient mathematical support does not exist (disperse opinions) to perform the assertion.

RESULTS

The 58 experts making up the panel achieved a consensus in the first round on 48 of the 58 questions analyzed, according to the pre-established evaluation criteria (45 of them in terms of group agreement and 3 in terms of group disagreement). Of the ten remaining items proposed to the reconsideration of the experts in the second round, it was possible to achieve a consensus in 7 more (all of them in the group agreement with the item posed).

Table 1 details the agreed on and not agreed on contents by the panel, organized in thematic blocks. The statistics defining these results are specified in Annex 1, indicating the mean and median scores of the group, as well as the proportion of experts who scored outside the group median.

Considered globally, the panel achieved consensus in 94.8% of the proposed contents. In 3 items, representing 5.2% of the total questionnaire, sufficient unanimity of criterion was not achieved, either due to disparity of professional opinion or due to lack of professional criterion established in a majority of the experts. In item 31 ("Within the non-stimulant treatments, guanfacine presented greater

Table 1 **Agreed on and non-agreed on contents by the panel of experts (Annex 1 details the express definition of each item of the survey and the statistical criteria for the interpretation of the level of consensus)**

BLOCK 1. GENERAL ADHD

CONSENSUS

It is considered confirmed that ADHD:
- Is one of the most frequent neurobiological disorders in childhood, characterized by inappropriate levels or lack of attention and/or hyperactivity/impulsivity.
- It can affect all areas of the life of the individual, academic performance, social relations, work world, etc.
- Lack of diagnosis generally entails a negative evolution for the individual.
- Its associated costs are high: education, work productivity, legal problems, substance abuse, etc.
- Its correct management and treatment decrease its consequences and therefore its associated costs.
- Due to the complexity it has, an individualized plan in each patient is essential.

BLOCK 2. DIAGNOSIS OF ADHD / COMORBIDITY

CONSENSUS

There is agreement in that the early diagnosis:
- Improves the patient's evolution.
- Determines a lower risk of mortality.

Regarding the clinical presentation of the symptoms and comorbidity, it is validated that:
- The symptoms vary over the lifetime.
- More than two thirds of patients with ADHD present some type of comorbidity over their lifetime.
- Comorbidity increases the severity and impact of ADHD, decrease quality of life of the patient and his/her setting.
- It is essential to establish a differential diagnosis of the comorbidities related with the ADHD.

BLOCK 3. TREATMENT OF ADHD

CONSENSUS

- The treatment recommended by the clinical practice guidelines is the multimodal one.
- Cognitive-behavioral therapy is recommended as initial treatment.
- A psychoeducational program for parents is recommended.
- Children with ADHD require an individualized intervention program in the school that includes academic, social and behavior aspects.
- Teachers need to receive training that enables them to detect and manage these children in the school.
- Drug treatments approved in Spain include stimulant and non-stimulant drugs.
- Children under 6 years of age can be treated with drugs.
- Rest periods should be performed to reevaluate the utility/need of pharmacological treatment.
- Pharmacological treatment rest periods ("therapeutic holidays") are not systematically recommended during treatment of ADHD.

WITHOUT CONSENSUS

- No unanimous opinion exists on whether non-stimulant treatment can be an alternative to psychotherapy in some mild cases.

BLOCK 4. EFFICACY AND RESPONSE OF PHARMACOLOGICAL TREATMENT

CONSENSUS

Unanimous agreement exists that the pharmacological treatment:
- Is the most effective treatment for ADHD.
- It should be considered as first choice considering the age of the patients, severity of the symptoms, functional repercussion and characteristics and preferences of the family.
- The time interval up to initiation of the response is an added value to any medication.

Regarding treatment with stimulants:
- This is the one, in general lines, that has a greater efficacy in the control of the symptoms of ADHD, compared with all the pharmacological treatments.
- Due to its efficacy, normally it is generally chosen as the first choice of pharmacological treatment.
- It has a greater effect size.

Table 1 Continuation

BLOCK 4. EFFICACY AND RESPONSE OF PHARMACOLOGICAL TREATMENT

CONSENSUS

Regarding the treatment with non-stimulants:
- It is of first choice in some patients, even though it is generally considered less effective than the stimulant.
- Guanfacine has less response initiation time compared with atomoxetine.
- Guanfacine has a faster action initiation than atomexetine.
- Guanfacine can improve the response compared with the continued isolated use of a stimulant, when there is a suboptimal response to said long duration treatment.
- In the studies, guanfacine has been shown to be effective both in the control of attention and in hyperactivity/impulsivity in comparison with the control group.

WITHOUT CONSENSUS

- Within the non-stimulant treatments, guanfacine has greater efficacy in the control of core symptoms of ADHD in comparison with other non-stimulant treatments approved in Spain with indication of ADHD.

BLOCK 5. ACTION MECHANISMS OF PHARMACOLOGICAL TREATMENT

CONSENSUS

The panel shows consensus in that the drug action mechanism:
- Is unique for each one of the drugs.
- Affects the safety of each treatment.
- Influences the efficacy of each treatment.
- The most accepted one within the stimulant treatments is that of inhibition - competitive inhibition of the synaptic catecholamine reuptake.

Agreement exists regarding the fact that:
- Atomexetine is a selective inhibitor of the pre-synaptic transporter of norepinephrine.
- Guanfacine, although it is non-stimulant as atomexetine, has a different action mechanism consisting in the stimulation of the alpha-2 adrenergic receptors.
- Guanfacine and clonidine has a high affinity for the alpha-2 adrenergic receptors.

BLOCK 6. PHARMACOLOGICAL TREATMENT AND COMORBIDITY OF ADHD

CONSENSUS

Consensus exists that the comorbid disorders that often accompany ADHD are fundamental when choosing the type of treatment for the patient.

There is an unanimous opinion regards the fact that the non-stimulant treatments:
- Should be considered as first choice in patients:
  - With substance abuse, tic or anxiety disorders.
  - Who have had adverse events to treatment with stimulants.
  - Whose family has a preference for this type of treatment.
- They can be a therapeutic alternative in those patients who:
  - Have previous experiences of lack of efficacy with stimulant treatment.
  - Need a more constant and continued control over time (greater duration).
  - Who have elevated irritability or episodes of emotional lability.

WITHOUT CONSENSUS

- There is no consensus regarding whether non-stimulant treatments are the best therapeutic option in patients who have seizures / epilepsy.

Table 1 Continuation

BLOCK 7. ADVERSE EVENTS TO PHARMACOLOGICAL TREATMENT
CONSENSUS
The experts show agreement that: · Before initiating the medication, it is recommendable to perform a physical examination that includes: blood pressure, heart rate, weight and height. · In general, drugs for ADHD are safe and well tolerated. · The side effects profile should be a criterion of choice of the drug. · The most frequent adverse events within the treatment with stimulant medications are: lack of appetite, headache and insomnia. · The most frequent adverse events of atomoxetine are: drowsiness, digestive problems and dizziness. · The most frequent adverse events of guanfacine are: drowsiness, headache and tiredness.

efficacy in the control of the core symptoms of ADHD compared with other non-stimulant treatments approved in Spain with indication for ADHD") an adequate agreement in the panel is observed, but there is a large proportion of experts (36.21%) located in uncertainty position ("neither agreement or disagreement"), none of them shows disagreement. In item 50 ("The non-stimulant treatments are the best therapeutic option in patients who have seizures / epilepsy"), however most of the panel stated a similar opinion, but jointly they do not have an unanimous criterion since many of them state an uncertain or contrary opinion. In item 21 ("In some mild cases, a non-stimulant can be an alterative to psychotherapy"), in spite of the fact that the proportion of experts who scored outside the median is ≤33%, it cannot be stated that there is consensus since a great dispersion of the results is observed (the interquartile range has a vale of 4). In this way, as the double validation proposed is not fulfilled, it is considered that there is no consensus in said item.

CONCLUSIONS

Overall, the evaluation of the panel of experts in ADHD (of multicentric origin and state environment and with very different professional profiles) who participated in this study makes it possible to confirm an elevated level of agreement (close to 95%) with the affirmations proposed by the Scientific Committee. Most of these proposals were agreed on in the first Delphi round, reflecting a considerably uniform professional criterion.

A more detailed analysis reflects that the experts show points of view close to full agreement in the general questions of ADHD, since practically all the panel agreed in the first round with the questions posed. An elevated unanimity of criterion was also observed in the first round regarding the diagnosis and comorbidity of ADHD, except for one item ("A late diagnosis determines greater risk of mortality") in which the consensus was reached in the second Delphi round. In this regards, it should be stressed that the experts who initially did not show agreement state that the late diagnosis implies greater risk of morbidity and associated comorbidity, which indirectly could suppose greater mortality.

Regarding the items related with ADHD treatment, its efficacy, action mechanisms and adverse effects, the panelists globally show nine unanimous opinions, although in said aspects, greater discrepancy is observed than in the previous blocks, which is reflected in the data through a greater proportion of experts who score outside of the median and the fact that consensus was reached in the second Delphi round. These circumstances are especially observed in the items related with the non-stimulant pharmacological treatments, finding among them the only three items not agreed on by the panel (items 21, 31 and 50).

Regarding item 21 ("In some mild cases, a non-stimulant can be an alternative to psychotherapy"), in which consensus is not reached due to the dispersion of the results, there is a majority agreement of the panelists, although their comments point to the importance of making a detailed analysis of each specific case and offering a combined treatment that approaches the multiple difficulties (scholastic, family, social) associated with ADHD in stead of considering both alternatives as mutually excluding.

In this sense, as indicated by the comments of the experts regarding item 31 ("Within the non-stimulant treatments, guanfacine presented greater efficacy in the control of the core symptoms of ADHD compared with other non-stimulant treatments approved in Spain with indication for ADHD"), the reason for the non-consensus is due to limited clinical experience with some of said drugs, given that they are novel treatments or treatments still not on the

market, and the absence of comparative studies, except for meta-analytic ones.[39-43]

In another of the non-agreed on questions by the experts, item 50 ("The non-stimulant treatments are the best therapeutic option in patients who have seizures / epilepsy"),the panelists highlight the generality of the statement in their commentaries, indicating that said indication depends on the clinical status of the epilepsy.

All in all, and in general lines, the experts who participated in the panel have shown a high degree of unanimity in most of the contents subjected to their consideration. The professional criteria that reached consensus in this project can be considered as indications for the clinical practice supported by the unanimous professional criterion of these Spanish experts and should be taken into account in the management of ADHD.

Annex 1 **Professional criteria and clinical recommendations of ADHD evaluated in the project. In each case, the principal descriptive statistics criteria used to determine the existence or not of consensus in the**

no.	Item	Mean	Median	% outside of range of 3 points of where the median is located	Inter-quartile range	Result
	Block 1. General ADHD					
1	ADHD is one of the most frequent neurobiological disorders in childhood, characterized by inappropriate levels or lack of attention and/or hyperactivity/impulsivity.	8.70	9	0%	0	Agreement
2	The disorder can affect all areas of the life of the individual, academic performance, social relations, work world, etc.	8.75	9	1.67%	0	Agreement
3	Lack of diagnosis generally entails a negative evolution for the individual.	8.37	9	0%	1	Agreement
4	The costs associated to ADHD are high: education, work productivity, legal problems, substance abuse, etc.	8.35	9	3.33%	1	Agreement
5	Correct management and treatment of ADHD decreases its consequences and therefore its associated costs.	8.58	9	1.69%	1	Agreement
6	Due to the complexity presented by this disorder, an individualized plan in each patient is essential.	8.78	9	0%	0	Agreement
	Block 2. Diagnosis of ADHD / comorbidity					
7	Early diagnosis improves the patient's evolution.	8.43	9	0%	3	Agreement
8	Late diagnosis determines greater risk of mortality.	7.52	8	15.52%	2	Agreement 2nd round
9	The clinical presentation of the symptoms varies over the lifetime.	8.51	9	5.08%	1	Agreement
10	More than two thirds of patients with ADHD present some type of comorbidity over their lifetime.	8.27	9	3.33%	1	Agreement
11	Comorbidity increases the severity and impact of ADHD, decrease quality of life of the patient and his/her setting.	8.63	9	0%	1	Agreement
12	It is essential to establish a differential diagnosis of the comorbidities related with the ADHD.	8.72	9	0%	0	Agreement

Annex 1 | **Continuation**

no.	Item	Mean	Median	% outside of range of 3 points of where the median is located	Inter-quartile range	Result
	Block 3. Treatment of ADHD					
13	The treatment recommended by the clinical practice guidelines is the multimodal one.	8.64	9	1.69%	1	Agreement
14	The cognitive-behavioral therapy is recommended as initial treatment.	6.24	7	32.76%	2	Agreement 2nd round
15	A psychoeducational program for parents is recommended.	8.33	9	5%	1	Agreement
16	Children with ADHD require an individualized intervention program in the school that includes academic, social and behavior aspects.	8.20	8.5	3.33%	1.5	Agreement
17	Teachers need to receive training that enables them to detect and manage these children in the school.	8.55	9	1.67%	1	Agreement
18	The drug treatments approved in Spain include stimulant and non-stimulant drugs.	8.73	9	3.33%	0	Agreement
19	Children under 6 years of age can be treated with drugs.	7.83	8	5.17%	2	Agreement 2nd round
20	Pharmacological rest periods (therapeutic holidays) are recommended systematically in the treatment of ADHD.	2.73	2	20%	2	Disagreement
21	In some mild cases, a non-stimulant can be an alternative to psychotherapy.	2.71	2	31.03%	4	WITHOUT CONSENSUS
22	Rest periods should be performed to reevaluate the utility/need for pharmacological treatment.	6.67	7	31.67%	2.5	Agreement
	Block 4. Efficacy and response of the pharmacological treatment					
23	The pharmacological treatment is the most effective treated for ADHD.	7.67	8	15%	2	Agreement
24	Pharmacological treatment should be considered as first choice considering the age of the patients, severity of the symptoms, functional repercussion and characteristics and preferences of the family.	7.85	8.5	11.67%	2	Agreement
25	Of all the pharmacological treatments, the stimulant treatment is the one, in general lines, that has a greater efficacy in the control of the symptoms of ADHD.	8.34	9	5.08%	1	Agreement
26	Due to its efficacy, normally the stimulant treatment is generally chosen as the first choice of pharmacological treatment.	8.15	9	8.33%	1	Agreement
27	The stimulant drugs have a greater effect size.	8.05	9	10%	1	Agreement
28	Even though the non-stimulant treatment is generally considered less effective than the stimulant one, it is of first choice in some patients.	7.85	8	15.25%	2	Agreement

Annex 1 Continuation

no.	Item	Mean	Median	% outside of range of 3 points of where the median is located	Inter-quartile range	Result
	Block 4. Efficacy and response of the pharmacological treatment					
29	The time interval up to initiation of the response is an added value to any medication.	7.55	8	21.67%	2	Agreement
30	Within the non-stimulant treatments approved in Spain with the indication for ADHD, guanfacine has a lower time of initiation to response compared with atomoxetine.	7.25	8	30%	3.5	Agreement
31	Within the non-stimulant treatments, guanfacine presented greater efficacy in the control of the core symptoms of ADHD compared with other non-stimulant treatments approved in Spain with indication for ADHD.	7.03	7	36.21%	4	WITHOUT CONSENSUS
32	Guanfacine has a faster initiation of action than atomoxetine.	7.67	8	20.69%	2	Agreement
33	Addition of Guanfacine can improve the response compared with the continued isolated use of a stimulant when there is a suboptimal response to said long duration treatment.	7.49	8	16.95%	2	Agreement
34	In the studies, guanfacine has been shown to be effective both in the control of attention and in hyperactivity/impulsivity in comparison with the control group.	7.62	8	16.67%	2	Agreement
	Block 5. Pharmacological treatment action mechanisms					
35	Each drug has a unique action mechanism.	6.53	7	25.86%	2	Agreement 2nd round
36	The action mechanism does not affect the safety of each treatment.	2.70	3	16.67%	2	Disagreement
37	The action mechanism does not affect the efficacy of each treatment.	2.55	2	16.67%	2	Disagreement
38	The most accepted action mechanism within the stimulant treatments is that of inhibition - competitive inhibition of the synaptic catecholamine reuptake.	7.40	8	13.33%	2	Agreement
39	Atomexetine is a selective inhibitor of the pre-synaptic transporter of norepinephrine.	8.25	9	1.67%	2	Agreement
40	Guanfacine, although it is non-stimulant as is atomexetine, has a different action mechanism consisting in the stimulation of the alpha-2 adrenergic receptors.	8.52	9	1.67%	1	Agreement
41	Guanfacine and clonidine has a high affinity for the alpha-2 adrenergic receptors.	7.65	8	15%	2	Agreement
	Block 6. Pharmacological treatment and comorbidity in ADHD					
42	The comorbid disorders that often accompany ADHD are fundamental when choosing the type of treatment for the patient.	8.18	8	5%	1	Agreement
43	In general, non-stimulant treatments should be considered of first choice in patients with substance abuse.	6.33	7	24.14%	1	Agreement 2nd round

Annex 1 Continuation

no.	Item	Mean	Median	% outside of range of 3 points of where the median is located	Inter-quartile range	Result
	Block 6. Pharmacological treatment and comorbidity in ADHD					
44	In general, non-stimulant treatments should be considered of first choice in patients with tic disorder.	6,67	8	25.86%	2	Agreement 2nd round
45	In general, non-stimulant treatments should be considered of first choice in patients with anxiety.	6.85	7	27.12%	2	Agreement
46	In general, non-stimulant treatments should be considered of first choice in patients who have had adverse events to the treatment with stimulants.	8.05	8	8.33%	1	Agreement
47	Non-stimulant treatments are a good option when there has been previous experiences of lack of efficacy with stimulant treatment.	8.03	8	5.08%	1	Agreement
48	Non-stimulant treatments should be considered as first choice in patients whose family has a preference for this type of treatment.	6.91	7	17.24%	0	Agreement 2nd round
49	Non-stimulant treatments can be a therapeutic alternative in those patients who need a more constant and continued control over time (greater duration).	7.07	7.5	26.67%	2	Agreement
50	The non-stimulant treatments are the best therapeutic option in patients who have seizures / epilepsy.	5.90	7	37.93%	2	WITHOUT CONSENSUS
51	Non-stimulant treatments can be a therapeutic alternative when the patient has elevated irritability.	7.08	7	18.33%	1	Agreement
52	Non-stimulant treatments can be a therapeutic alternative when the patient has had episodes of emotional lability.	7.23	7	20%	1	Agreement
	Block 7. Adverse events to pharmacological treatment					
53	Before initiating the medication, it is recommendable to perform a physical examination that includes: blood pressure, heart rate, weight and height.	8.57	9	3.33%	0.5	Agreement
54	In general, the drugs for ADHD are safe and well tolerated.	8.37	9	1.67%	1	Agreement
55	The profile of side effects should be a criterion of choice of the drug.	8.02	8	8.33%	2	Agreement
56	The most frequent adverse events within the treatment with stimulant medications are: lack of appetite, headache and insomnia.	8.54	9	0%	1	Agreement
57	The most frequent adverse events of atomoxetine are: drowsiness, digestive problems and dizziness.	8.20	9	5%	1	Agreement
58	The most frequent adverse events of guanfacine are: drowsiness, headache and tiredness.	7.59	8	18.97%	2	Agreement

Annex 2 | **Alphabetical list of panelists participating in the Delphi survey**

Agüero, Cristina
Alcidor, Patricia
Almendral, Raquel
Alonso, Mercedes
Anta, Laura de
Barbero Aguirre, Pedro
Barragán Ortíz, Josefa
Barroso, Josep María
Blasco, Hilario
Burgos, Rafael
Cantó Diez, Tomás
Carballo, Juan José
Castelló Gascó, Javier
Chinchurreta, Nuria
Civeira, José
Correas Lauffer, Javier
Durán Forteza, Oscar
Espadas Tejerina, Marta
Espín, José Carlos
Fenollar Ibañez, Francisco
Fernández Fernández, Manuel
Figueroa, Ana
Flórez Menéndez, Gerardo
Gómez Sánchez, José Antonio
Gómez, Leticia
González Collantes, Ruth
Guijarro, Silvina
Hernández Otero, Isabel
Herreros, Oscar
Huertas, Abigail
López Pisón, Javier
Loro, Mercedes
Madruga Garrido, Marcos
Martínez Delgado, José Manuel
Martínez Raga, José
Martínez Valente, Joaquín
Mojarro Praxedes, María Dolores
Montoliu, Leonor
Monzón Díaz, Josué
Mulas, Fernando
Octavio, Inmaculada
Ortiz Guerra, Juan
Palanca, Inmaculada
Pando, Fuencisla
Pereira, César
Revert Marín, Laura
Rodríguez Díaz, Rocío
Rodríguez Hernández, Pedro
Ruiz Sanz, Francisco Carlos
Sagols, Audrei
Sans Fitó, Anna
Sanz de la Garza, César
Simón de las Heras, Rodrigo
Trillo, Mariano
Vega, Flora
Villar, Luis
Zapata, Maite

CONFLICT OF INTERESTS

AH has been a consultant and given lectures for Shire and Otsuka. TdS, in the last two years, has received support from Eisai, Esteve, Rubió, Shire, Nutricia and Ordesa to attend courses and congresses; has received fees from Eisai and Nutricia as speaker. JQ has participated as a speaker or advisor for Shire, Grunenthal and Janssen and has obtained research grants from Otsuka and Mutua Madrileña. PMR-L has been an advisor or speaker in medical training funded by Shire, Lilly, Janssen Cilag, Rovi, Juste; PMR-L has received help from Shire, Lilly, Janssen Cilag, Rovi, Juste to attend congresses of the specialty. JAA has been a consultant to Eli Lilly, Shire and Janssen Cilag; JAA has received research funds from the Ministerio de Sanidad, Instituto de Salud Carlos III, la Agència d'Informació, Avaluació i Qualitat en Salut (AIAQS) and the Fundación Alicia Koplowitz. AF-J has received support from Janssen, Eli Lilly, Rubio, Juste, Shire and Otsuka to attend courses and congresses as well as fees from Janssen, Eli Lilly, Rubio, Juste, Mead Johnson and Shire as a speaker; AF-J has carried out consulting activities for Janssen, Eli Lilly, Otsuka and Shire and has received fees or grants for studies from Janssen, Eli Lilly, Rubio and Shire; AF-J is a member of the Scientific Committee of the Federación de Ayuda al TDAH in Spain (FEAADAH), and collaborator/advisor of the Asociación de Niños con Síndrome de Déficit de Atención/Hiperactividad of Madrid (ANSHDA). JAR-Q has acted as advisor or consultant for Eli Lilly, Novartis, Shire, Lundbeck, Ferrer, Medice and Rubió in the last 3 years and has received traveling help for having participating in psychiatric meetings of Medice, Ferrer, Rubió, Shire and Eli Lilly; The ADHD Program directed by him received educational and research support without restrictions from the following pharmaceutical companies in the last 3 years: Eli Lilly, Shire, Rovi, Ferrer and Rubió.

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