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Assessment of depression in patients with terminal cancer and its implications in the Mexican context: A review*

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SUMMARY

Depression is one of the most common emotional problems in palliative patients. Due to the advanced nature of the disease, several physical symptoms presented by these patients overlap with symptoms of depression, making it difficult to evaluate and diagnose the problem. The aim of this paper was to conduct a narrative review of the main instruments used to assess depression when it occurs in palliative patients, with special consideration of the Mexican context. As proposed by the available data and the research literature, it is more appropriate to assess depression focusing on emotional rather than somatics aspects in palliative patients. Internationally, a number of studies on depression assessments place greater emphasis on anhedonia and such emotions as hopelessness, than on somatic aspects of depression. In Mexico, a considerable gap remains in the development of instruments for identifying depression in the palliative settings. Finally, we describe alternative assessment strategies of depression, which could be evaluated and considered in future palliative care settings.

Key words: Depression, cancer, palliative care.

RESUMEN

La depresión es uno de los problemas emocionales más frecuentes en pacientes con cáncer terminal. Debido a la evolución de la enfermedad, varios síntomas físicos presentes en los pacientes se pueden yuxtaponer y confundir con los síntomas que permiten identificar de manera taxonómica la depresión, lo cual dificulta la evaluación del problema. El objetivo de este artículo es realizar una revisión de los principales instrumentos utilizados para evaluar la depresión en pacientes con cáncer terminal, junto con sus implicaciones en el contexto mexicano. Con base en la información recabada se puede decir que es más pertinente realizar una evaluación de la depresión enfocada en los aspectos emocionales que en los somáticos. Actualmente existe una gran cantidad de instrumentos para evaluar la depresión que dan mayor énfasis a los aspectos de la anhedonia y las emociones que a los aspectos somáticos de la depresión. En México existe un enorme rezago en el desarrollo de instrumentos que permitan identificar estos síntomas. Se concluye señalando instrumentos alternativos para evaluar la depresión en pacientes con cáncer terminal, estos instrumentos podrían ser evaluados y considerados en un futuro en el contexto de la medicina paliativa.

Palabras clave: Depresión, cáncer, tratamiento paliativo.

INTRODUCTION

Depression is one of the most frequent emotional problems in patients with advanced cancer.[1,2] A recent systematic review mentioned that there is a prevalence of up to 24% of patients affected by this condition,[3] however, depression has very wide ranges of prevalence from 1% to 69%,[4] largely due to the way in which it is conceptualized and measured.[5]

According to Wasteson et al.,[5] obtaining a reliable prevalence rate for depression is not possible without taking into account the following: 1. How the concept is defined; 2. The classifications made on the basis of such definitions; 3. The method used to assess it; and 4. The difficulty in arriving to a consensus of how to understand depression in the palliative population.

There is controversy in terms of how to diagnose depression in patients with advanced cancer, due to different factors within this group itself. For this reason, we have presented a review which aims to describe how depression has been defined and assessed in terminal cancer patients,

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as well as the challenges posed by measuring this problem in Mexico.

DEFINITION OF DEPRESSION IN THE PALLIATIVE CONTEXT

The various articles that explore the subject of depression in patients with advanced illness can be broadly split into two groups: 1. Those that conceptualize depression as a psychiatric disorder diagnosed through a clinical interview[6] and 2. Those that assess the presence or intensity of depressive symptomatology, contributing to the patient's overall distress[7] or which consider the presence of anhedonia as a fundamental component.[8]

In studies where depression is approached as a disorder according to the DSM-IV criteria,[9] prevalence ranges of between 9%-16%[3] have been reported. When it is treated as a problem with mood measured by direct questions, a median prevalence of 40% is obtained.[4] When the presence of depressive symptomatology is explored through questionnaires such as the Hospital Anxiety and Depression Scale (HADS)[10] a mean of 29% is obtained.[4]

Two broad paradigms can be identified in defining depression in palliative care:[5] the first refers to a categorical definition, in which taxonomic criteria are used to identify the problem in the patient, for example, based on the DSM-IV or the International Classification of Diseases *tenth version* (ICD 10). The problem with this type of definition is that the population with advanced cancer can very often develop physical symptoms as a part of the natural development of the disease, or as a consequence of its medical treatment. Since these get juxtaposed with the physical symptoms considered as criteria to identify depression, it becomes difficult to detect and identify if the depressive symptom as such is present, or if it reflects the development of the physical illness, or as a side effect of treatment.[4,11]

The second definition –also called dimensional– considers depression as a general phenomenon in which the patient shows an increase in the level of depressive symptoms in the patient, without them having to fully meet the taxonomic criteria for identification, and which can even leave aside the physical symptoms of depression, primarily focusing on the emotional symptoms.[5] The primary problem with this definition is that it is difficult to distinguish between depression, fear, and normal or expected decline due to the knowledge of death being near.[5] The European clinical guide for palliative care recommends the combined use of taxonomic and emotional criteria in order to be able to identify depression, placing emphasis on anhedonia above the somatic aspects of depression.[11]

The majority of assessments of depression in patients with terminal cancer has been conducted through instruments, which can be classified into 1. One- or two-question assessments, and 2. Assessment questionnaires. The contents of both of these types of assessment can be explained as follows:

1. One- or two-question assessment

This has been widely used in both the clinical sphere and in research within the palliative population.[12] It consists of directly asking the patient if he or she consider themselves depressed or with a low mood; it is considered particularly useful to obtain rapid information about the patients' mood and they are used more often as a screening tool than as a means to establish a diagnosis. Studies that use this type of question can overestimate rates of depression.[4,13]

Two recent reviews[12,14] described the psychometric properties of assessing depression by means of one or two questions or the combination of questions with scales (Table 1).[8,13,15-23] Contradictory information was reported in assessments that used one or two questions, given that while one study reported 100% sensitivity and specificity to detect different types of depressive disorders,[17] three others reported low sensitivity for detecting minor affective disorders but high sensitivity for detecting major depressive disorder.[15,19,20] When the question was accompanied with an analogous visual scale, it did not increase the likelihood that a patient without depression would have a negative test result, but it did increase the sensitivity of the assessment.[15,16]

One study described how assessments of depression by means of a question are not the most advisable for Spanish-speaking populations, given that there is a negative cultural connotation around the term "depressed" which causes patients not to report feeling that way. As such, the authors do not advise its use and recommend the use of the term "discouraged".[24]

Finally, a meta-analysis was conducted of the studies which assessed depression this way, and the conclusion was that the use of this type of assessment should only be for screening purposes; its use was not recommended for research purposes.[12,14]

2. Assessment questionnaires

These are instruments that have better psychometric properties and that usually assess a wider spectrum of emotional incapacity, using a greater number of questions (usually between 5 and 20 per instrument).[12] In this category, five instruments have been described which directly assess depressive symptomatology but which are usually used as screens to assess the presence of depression. The first is a short version of 13 questions on the Beck Depression Inventory, which assesses depressive symptomatology in patients with chronic illnesses and which correlates highly (r=.96) with the original instrument of 21 questions.[17] It has been used in two studies of patients with advanced cancer; but

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Table 1. Assessment of depression with one or two questions

Study	Number of participants	Description	Results	Reliability	Sensitivity	Specificity
Akechi et al. (2006).	209 patients with terminal cancer.	Two questions were assessed: Are you depressed? Have you lost interest [in things]? These were compared with the Hospital Anxiety and Depression Scale (HADS).	The HADS is better for assessing adjustment disorders (AD) and major depression (MD) in a joint way than just the two questions. The two questions and the HADS are useful when only MD needs to be identified.	Not reported	AD+MD .47 Only MD .93	AD+MD .96 Only MD .92
Akizuki et al. (2003).	295 patients with cancer, only 42% with advanced cancer.	The following question was used: "Please grade your mood during the past week by assigning it a score from 0 to 100, with a score of 100 representing your usual relaxed mood", and the distress thermometer was used to assess AD and MD.	The single-question interview was effective in assessing both AD and MD, but it performed worse than the HADS.	Not reported	.84	.61
Chochinov et al. (1997).	197 patients with terminal cancer.	One question was used to assess depression; two questions to assess depressive mood (DM) and lack of activities; one scale to assess DM and this was compared with the Beck Inventory.	The one-question interview was effective to identify DM and this result was better than using analogous visual scales.	Not reported	1.00	1.00
Kawase et al. (2006).	282 patients with advanced cancer but who were receiving radiotherapy.	One question was used: Are you depressed? And this was compared with a semi-structured interview based on DSM-IV criteria.	The one-question assessment did not have enough specificity.	Not reported	.42	.86
Lloyd-Williams et al. (2003).	74 palliative patients.	One question was used: Are you depressed? And this was compared with a semi-structured interview based on DSM-IV criteria.	The one-question assessment did not have enough sensitivity or specificity.	Not reported	.55	.74
Payne et al. (2007).	167 palliative patients, 74% due to terminal cancer.	Two questions were assessed: Are you depressed?, Have you experienced loss of interest in things or activities you normally enjoy? These were compared with a semi-structured interview based on DSM-IV criteria.	The assessment allowed the professionals to identify MD in palliative patients.	Not reported	.90	.67
Teunissen et al. (2007).	79 patients with advanced cancer.	Depression and anxiety in patients and the physical symptoms reported were assessed with the HADS, one single question, and ESAS.	The assessment of a single question for depression showed high sensitivity for depression.	Not reported	.61	.94
Noguera et al. (2009).	100 Spanish-speaking patients with terminal cancer.	The best term in Spanish to identify depression was assessed by means of one question, the HADS, and numeric verbal scales.	The use of the word 'discouraged' in place of 'depressed' showed greater sensitivity and specificity.	Not reported	.80	.70
Meyer et al. (2003).	45 patients with advanced cancer.	Mood over the past week was assessed in terms of depression or low mood with Likert options, and this was compared with a semi-structured interview based on DSM-IV criteria.	It was recognized as potentially useful to assess depressive symptoms in the palliative population.	X=0.935	PPV (100%)	NPV (96%)
Jefford et al. (2004).	100 patients, 60% of whom were palliative.	Participants were asked: "In the past two weeks, have you felt unhappy or depressed?"	The questions had moderate properties for assessing depression in palliative patients.	K=.21	.67	.75
Ohno et al. (2006).	160 patients with cancer.	They were asked if they were depressed and given three options: yes, I am depressed; no, I am not depressed; or neither.	It had high sensitivity in patients with terminal cancer.	Not reported	.93	.31

HADS = Hospital Anxiety and Depression Scale; MD = Major Depression; AD = Adjustment Disorder; PPV = Positive Predictive Value; NPV = Negative Predictive Value.

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Table 2. Assessment of depressive symptomatology by means of instruments

Study	Participants	Description	Results	Reliability	Sensitivity	Specificity
Chochinov et al. (1997).	197 patients with terminal cancer.	The Beck Depression Inventory of 13 questions was compared with one question to assess depression; two questions to assess depressive mood (DM) and lack of activities; and one scale to assess DM.	The instrument showed moderate sensitivity and specificity and low inter-reliability.	Not reported	.79	.71
Love et al. (2004).	227 women with stage IV breast cancer.	Both the Beck Depression Inventory and the HADS were applied in order to identify depression.	The two scales allowed the identification of depression but the Beck allowed the identification of major and minor depression, albeit with low specificity.	K=.17	.84	.63
Hopko et al. (2008).	33 patients with different types of cancer.	Different instruments were applied to assess depression (Beck, CES-D, semi-structured interviews).	All the instruments used had predictive properties to identify depression; however, the Beck instrument and CES-D were recommended due to their psychometric properties.	.90	1.00	.79
Katz et al. (2004).	60 patients with head and neck cancers.	Different instruments were applied to assess depression (Beck, HADS, CES-D).	The three instruments were recommended to be used to assess depression, however the HADS instrument presented the best psychometric properties.	Not reported	1.00	.85
Lloyd-Williams et al. (2000).	100 palliative patients.	The Edinburgh Postnatal Depression Scale was applied to palliative patients to identify psychometric characteristics.	The instrument was considered reliable to measure depression in palliative patients largely due to its assessments of desperation, worry, and guilt in place of physical symptoms.	α=.78	.81	.79
Lloyd-Williams et al. (2002).	50 palliative patients.	The Edinburgh Postnatal Depression Scale was applied to palliative patients over 12 weeks to identify the development of depression and the characteristics of the instrument employed.	The scale proved useful for identifying depression over a period of weeks in palliative patients.	α=.81; K= .77	Not reported	Not reported
Lloyd-Williams et al. (2007).	246 palliative patients.	The Edinburgh Postnatal Depression Scale was applied to palliative patients and an even shorter version of the questions was obtained.	After the application, 6 questions were obtained from the original scale, and depression could be identified from these.	α=.78	.72	.74
Hopwood et al. (1991).	81 patients with stage IV breast cancer.	Two instruments were applied, the HADS and the Rotterdam Symptom Checklist in order to identify psychiatric morbidity.	Both questionnaires showed average values of predictability to identify affective problems, among them depression.	Not reported	.75	.75
Le Fevre et al. (1999).	79 palliative patients.	Two instruments were applied; the HADS and the General Health Questionnaire to identify psychiatric morbidity. These were compared with semi-structured psychiatric interviews.	The HADS performed better than the general health questionnaire to identify depression in palliative patients.	Not reported	.77	.85
Lloyd-Williams et al. (2001).	100 palliative patients.	The HADS was applied and compared with a semi-structured interview for depression.	The HADS was recommended to assess depression in combination with another instrument.	α=.78	.54	.74
Akechi et al. (2006).	209 patients with terminal cancer.	The HADS was compared with two questions: Are you depressed? Have you lost interest [in things]?	The HADS is better to assess adjustments disorders (AD) and major depression (MD) than the two questions alone.	Not reported	.86	.69
Akizuki et al. (2003).	295 patients with cancer, 42% of whom had advanced cancer.	The HADS was used as a comparison instrument to be able to identify depression.	The HADS showed high sensitivity for identifying depression.	Not reported	.92	.57

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Table 2. Continued

Study	Participantes	Descripción	Resultados	Reliability	Sensitivity	Specificity
Jefford et al. (2004).	100 patients, 60% of whom were palliative.	The HADS was used as a comparison instrument to validate an instrument that measured depression.	The HADS showed high specificity but low sensitivity.	K=.27	.48	.95
Love et al. (2004).	227 women with stage IV breast cancer.	The Beck Depression Inventory and the HADS were applied to identify depression.	The two scales allowed depression to be identified but only the Beck Depression Inventory of major and minor depression. In the case of HADS, there was low sensitivity but high specificity.	K=.17	.16	.97
Mystakidou et al. (2004).	120 palliative patients.	The Greek version of the HADS was validated.	The HADS was validated with an acceptable level of reliability.	α=.78	Not reported	Not reported
Ozalp et al. (2008).	183 patients, 30% with terminal cancer.	The Turkish version of the HADS was validated.	The HADS showed good values for sensitivity and moderate levels for specificity.	Not reported	.84	.55
Olden et al. (2009).	422 patients with terminal cancer.	The Hamilton Depression Rating Scale was validated and compared with the diagnosis of depression according to the DSM-IV.	The Hamilton Depression Rating Scale showed high values for sensitivity and specificity.	Not reported	.91	.91

HADS = Hospital Anxiety and Depression Scale; MD = Major Depression; AD = Adjustment Disorder.

low inter-reliability and moderate specificity were reported in these studies. However, due to the very low number of studies that have assessed it, no definitive conclusions have been drawn about its use; it is therefore necessary to carry out more investigations in order to recommend it (Table 2).[17,25]

The Center for Epidemiologic Studies Depression Scale (CES-D) is another option for assessing depression in patients with advanced cancer. It consists of 20 questions, and it has shown good internal consistency, sensitivity, and specificity. However, when compared with other instruments such as the HADS, lower psychometric properties are obtained, and as a results its use has been moderately recommended.[26,27]

Another instrument that has been used is the Edinburgh Postnatal Depression Scale (EPDS) which is a scale with ten questions that primarily focus on non-physical symptoms related to postpartum depression. For this reason, it has been applied to patients with terminal cancer, and in three studies, it has shown specificity, sensitivity, and reliability even higher than that reported in some works that use the HADS. The above results notwithstanding, more studies are necessary to be able to widely recommend its use.[28-30]

The Hospital Anxiety and Depression Scale (HADS) is one of the most widely used instruments for assessing depressive symptomatology in the palliative context.[5] It consists of 14 questions (seven for anxiety and seven for depression) and it has Likert-style response options. At the end of the nineties and after the turn of the century, works were carried out to validate the use of the HADS in the palliative population, presenting good reliability, sensitivity, and specificity.[31-34] Later, it was used in various studies as the "gold standard" to validate other types of instruments.[15,16,18,25,35]

Currently, its use is widespread for the assessment of depression in the palliative context; however, a systematic review advises that given the small number of patients used for the validation of the HADS in the palliative context, it is necessary to carry out more studies to conclusively validate its use. The parallel use of other instruments is recommended in the application of the HADS in order to identify depressive symptomatology in daily clinical practice.[36]

There are other more extensive instruments such as the Mood Evaluation Questionnaire (MEQ) which consists of 23 questions and has shown good internal consistency in patients with terminal cancer.[21,37] Given the number of questions in the instrument and the time taken to apply it, it is not recommended for routine use in palliative clinical practice.[12]

One recent study demonstrated that the Hamilton Rating Scale for Depression has high reliability and validity in patients with terminal cancer; however, there are no other studies that corroborate this, and as such further research is needed in this field.[38]

ASSESSMENT OF DEPRESSION IN MEXICAN PALLIATIVE PATIENTS

No studies were found that had the aim of validating any instrument for identifying depression in Mexican palliative patients. There are a couple of studies that assess depression in primary caregivers, and in patients treated in palliative care using instruments validated in non-palliative Mexican populations.[39,40] In the study of Landa-Ramírez and collabo-

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rators,[40] depression was assessed in patients with terminal cancer using two cut-off points in the HADS instruments (national ≥7; international ≥11) and they reported that 67% of the patients presented depression with the national cut-off point; and 40% did so with the international cut-off point. However, this study assessed a small number of patients (59) and although it used the version of the HADS that was validated in Mexico, this validation was made in obese patients,[41] and because of this it is necessary to interpret this information with caution.

It is notable that there are not studies using valid instruments to measure depression in the Mexican context. This coincides with two articles that have recently mentioned that Mexican palliative patients face the problem of lack of hospital infrastructure which would allow them to receive necessary treatment during the last months of their life.[42] They also mention a scarce production of research and knowledge on the part of health staff in palliative care in Mexico, which seems to reflect little interest in this area among staff members. This could also reflect cumbersome methodologies and ethics implicit in carrying out such investigations during palliative care.[43] One recent study mentioned that there is important progress in palliative care in Latin America; however, there are still various challenges to overcome, among them a formal medical education which helps provide physical and psychosocial relief, and increases both patients' and primary caregivers' quality of life in palliative care.[44] The study also mentions strengthening the generation and distribution of knowledge which is applicable to the characteristics of the population being cared for.

FINAL CONSIDERATIONS

The aim of the present paper was to carry out a review of the primary instruments that are used to assess depression in patients with terminal cancer, along with its implications in the Mexican context. On the basis of the information presented, it seems clear that the best way of evaluating depression in this population is through the emotional condition of the patient, helped to a lesser extent by the use of somatic criteria of depression. At an international level, it is recommended to approach the problem of depression by means of combining one-and two-question tools with the use of an instrument that gives weight to conditions of anhedonia in depression (primarily the HADS). This should be supported to a lesser extent in somatic conditions of depression (such as those explored Hamilton scale). At a national level, there is a huge gap in terms of developing instruments with adequate psychometric properties to identify this emotional problem in patients with the economic, cultural, idiosyncratic, educational, and health characteristics of Mexican terminal cancer patients. If would therefore appear imperative to join together efforts for the development of these assessments.

In the nineties, various works attempted to assess depression in palliative patients using semi-structured interviews based on the DSM-IV; however, given the impossibility of identifying whether the physical symptoms reported were due to depression, the development of the illness, or as a side effect of treatment, it is recommended that these are not used regularly in daily clinical practice.[4] By the same token, although there are other instruments that have evaluated depression in the context of cancer, these efforts have not been validated in the palliative population or those with terminal cancer, and as such they were not included in the present paper.

It is important to mention that in other health contexts, the following strategies have been used to assess depression:

a) Functional analysis, which allows the organic and psychosocial factors involved in the emergence of depression to be accommodated and identified.[45]
b) Neuro-imaging assessments, which have been focused on studying brain structure changes in which an association has been found between major depression and an enlargement of the lateral ventricles; greater volume of cerebrospinal fluid; and a lower volume in the basal ganglia, thalamus, hippocampus, frontal lobe, orbitofrontal cortex, and gyrus rectus, and hippocampal volume during a depressive episode.[46]
c) Blood serum: a study recently described data that demonstrated the feasibility of diagnosing major depression with high levels of sensitivity (91%) and specificity (81%), by means of using an algorithm which analyzes the relationship of nine biomarkers obtained through blood serum (alpha-1 antitrypsin, apolipoprotein CIII, myeloperoxidase, tumor necrosis factor α receptor II, cortisol, epidermal growth factor, prolactin, resistin, and brain-derived neurotrophic factor). The study is still in the replication phase, but if these data are confirmed, it will allow for an analysis of major depression by means of a blood test.[47]

In none of the three strategies previously described were used to assess depression in patients with terminal cancer, they therefore represent an area of opportunity for developing future research. Finally, as has been described, there is no single method of assessment used in this population, and for this reason, it is recommended to use a combination of strategies in order to have greater certainty of information while adapting instruments for the Mexican population.

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