Received: 17 November 2020 / Revised: 20 November 2020/ Accepted: 28 November 2020 /Published online: 9 December 2020

Original article

JOURNAL OF APPLIED COGNITIVE NEUROSCIENCE

Predictors of favorable response to implanted of ventriculoperitoneal shunt in patients with idiopathic normal pressure hydrocephalus

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Abstract

Introduction: The indication of a ventriculoperitoneal shunt (VPS) is discussed in patients with idiopathic normal pressure hydrocephalus (iNPH), due to the heterogeneity of the response to treatment and the risks involved in neurosurgery. Objective: To search for clinical factors and complementary studies in order to determine predictors of a favorable response to the VPS placement in patients with iNPH. Methodology: A retrospective study of patients with probable iNPH (according to international guidelines) treated with VPS assisted in a neurological clinic from January 2014 to January 2017 was conducted. A univariate statistical analysis of the variables considered as possible prognostic factors was performed. Results: 58 patients were included. Women presented 3.68 times more chances of improvement after the VPS (p=0.019). Good response to the gait test was associated with better response to the VPS (p=0.024). Conclusions: Female sex and good response to the gait test could be considered as predictors of a favorable response to the VPS placement in patients with iNPH. A prospective study is necessary to achieve a homogeneous diagnostic evaluation and a more extensive longitudinal follow-up to evaluate the clinical evolution in this group of patients.
Keywords*:* Idiopathic normal pressure hydrocephalus; ventriculoperitoneal shunt; cognitive impairment; gait disorder; neurosurgery

Predictores de respuesta favorable a la colocación de derivación ventriculoperitoneal en pacientes con hidrocefalia normotensiva idiopática

Resumen

Introducción: La indicación de la derivación ventriculoperitoneal (DVP) se discute en pacientes con hidrocefalia normotensiva idiopática (HNTi), debido a la heterogeneidad de la respuesta al tratamiento y los riesgos que conlleva la neurocirugía. Objetivo: Búsqueda de factores clínicos y estudios complementarios, para determinar predictores de respuesta favorable a la colocación de DVP en pacientes con HNTi. Metodología: Estudio retrospectivo de pacientes con probable HNTi (según guías internacionales) tratados con DVP asistidos en una clnica neurológica desde enero de 2014 hasta enero de 2017. Se realizó un análisis estadístico univariado de las variables consideradas como posibles factores pronósticos. Resultados: se incluyeron 58 pacientes. Las mujeres presentaron 3,68 veces más posibilidades de mejora tras la DVP (p=0,019). La buena respuesta a la prueba de la marcha se asoció con una mejor respuesta a la DVP (p=0,024). Conclusiones: el sexo femenino y la buena respuesta a la prueba de la marcha podrían considerarse predictores de una respuesta favorable a la colocación de la DVP en pacientes con HNTi. Es necesario un estudio prospectivo para lograr una evaluación diagnóstica homogénea y un seguimiento longitudinal más extenso para evaluar la evolución clínica en este grupo de pacientes.
Palabras clave: Hidrocefalia normotensiva idiopática; derivación ventriculoperitoneal; deterioro cognitivo; trastorno de la marcha; neurocirugía

Introduction

In 1965, Hakim and Adams first described Normotensive Hydrocephalus (NPH) as a condition characterized by the clinical triad of gait disorder, urinary incontinence, and memory impairment, associated with the presence of normal Cerebrospinal Fluid (CSF) pressure in Lumbar Puncture (LP), enlarged cerebral ventricles and improvement after ventricular shunt surgery (Adams, Fisher, Hakim, Ojemann & Sweet, 1965; Halperin et al., 2015). This triad is present in less than 60% of patients and its individual components are not specific: gait disturbances due to many other etiologies occur in 20% of people over 75 years of age; there is urinary incontinence in 18% of men and 38% of women older than 60 years; the prevalence of mild cognitive impairment and dementia is approximately 35% in people older than 70 years; and the ventricles tend to enlarge with age and in patients with neurodegenerative disorders (Espay et al., 2017).

NPH was described as a potentially reversible cause of gait disorder and dementia and NPH is now separated into idiopathic NPH (iNPH) and secondary NPH (sNPH) (Halperin et al., 2015). Ventriculoperitoneal Shunt (VPS) surgery is considered the standard of care for patients with sNPH, but in iNPH, its response is variable (Halperin et al., 2015; Relkin, Marmarou, Klinge, Bergsneider & Black, 2005; Mori et al, 2012; Andersson, Rosell, Kockum, Söderström & Laurell, 2017; Toma, Papadopoulos, Stapleton, Kitchen & Watkins, 2013; Vanneste, Augustijn, Dirven, Tan & Goedhart, 1992). Post VPS benefits in patients with an initial diagnosis of iNPH persist in only one-third of patients, with a known revised diagnosis in more than 25% of patients (Alzheimer's disease, Lewy body dementia, and Progressive supranuclear palsy). Previously reported cases of NPH with "dual" pathology (that is, developing a "second" disorder) likely represent ventriculomegalic presentations of selected neurodegenerative disorders in which the benefits of VPS may be short-lived, with consequent unfavorable risk-benefit ratio *(*Espay et al., 2017; Saper, 2017). In addition to this, the pathophysiology of iNPH is controversial. There are new considerations in this regard, like alterations in cerebral blood flow with ischemia secondary to a phenomenon of the last meadow at the subependymal/periventricular level, irreversible compression of the projection fibers of the frontal regions and reduced clearance of CSF with an accumulation of toxic degradation products that leads to neurotoxicity (Bräutigam, Vakis & Tsitsipanis, 2017; Martín-Láez et al, 2018; Ringstad, Vatnehol & Eide, 2018). It is proposed that once a point of no return has been reached in any of these pathophysiological mechanisms, the therapeutic intervention may not have a modifying effect of the disease's course or not represent a solution for all of them. Then, the problem no longer lies only in achieving an accurate diagnosis, but also in its timing.

In this context, searching for clinical factors and complementary studies in order to determine the predictors of a favorable and sustained response to the VPS placement in patients with iNPH is substantially important (Halperin et al., 2015; De Mol, 1985) This is the main objective of this study.

Methodology

A retrospective review of medical records of patients with probable iNPH (according to international guidelines) treated with VPS assisted in a neurological clinic from January 2014 to January 2017 (Relkin et

al., 2005; Mori et al., 2012; Andersson et al., 2017). Clinical data and complementary studies were recorded (brain MRI and CT, gait test post-lumbar puncture) (Gallagher, Marquez & Osmotherly, 2019). Clinical response was evaluated with the Modified Rankin Scale (mRS) at baseline and 12 months follow-up, dichotomously: equal or better than the previous mRS (Bruno et al., 2010). For MRI evaluation, clinical signs were dichotomized: Positivity was defined as an abnormal Evans index (greater than 0,3), an acute callosal angle (less than 90º), the presence of at least one DESH (disproportionately enlarged subarachnoid space) (Relkin et al., 2005; Mori et al., 2012; Andersson et al., 2017). Positive lumbar puncture was defined as a more than 20% change in walking speed or the number of steps before and after the puncture) (Gallagher et al., 2019). A univariate statistical analysis of the variables considered as possible prognostic factors was performed.

Results

58 patients were included, 33 men and 25 women (M:W 1,3:1). The mean age was 73,2 (SD 7,5). All patients presented with a gait disorder and 46.5% of them had a history of falls. 84.5% had some degree of associated cognitive impairment and 87.9% had urinary disorders, urination urgency being the most frequent.

Table 1.
Analysis of clinical factors and complementary studies evaluated in relation to mRS at 12 months of follow-up from VPS placement

Clinical factors		
Sex (N = ?)	Women 3.68 times more chances to improve	p = 0.019
Age	Without statistical correlation	p = 0.2
Time of evolution from the onset of symptoms	No statistical correlation at 3 and 12 months of follow-up.	p = 0.9-0.7
Gait dysfunction		p = 0.5-0.7
Urinary disorder		p = 0.4-0.8
Cognitive impairment		p = 0.8-0.7
MMSE	Without statistical correlation	OR 1.13
Complementary studies		
Evans Index	Without statistical correlation	p = 0.09
Callosal angle	Each degree of increase in the angle of the callus was associated with a 5% reduction in the possibility of improvement, although this effect was not significant.	p = 0.08
DESH	The presence of DESH was associated with the reduction of 1 in mRS in 56.25% of the patients, without reaching statistical significance.	p = 0.2
Fazekas score	Without statistical correlation	p = 0.75
Gait test (with LP)	Patients with good response to the gait test had a better response to the VP shunt.	p = 0.024

MMSE: Mini-mental state examination. DESH: disproportionately enlarged subarachnoid space hydrocephalus. LP: lumbar puncture.

Among the clinical factors: women presented 3.68 times more chances of improvement after the VPS (p = 0.019), while age, time of evolution of the clinical manifestations and MMSE had no correlation (Table 1). Regarding the complementary studies: good response to the gait test was associated with better response to the VPS (p = 0.024) and each degree of increase in the angle of the callosum was associated with a 5% reduction in the possibility of improvement, although this effect was not significant (p = 0.08); the Evans index had no prognostic correlation (Table 1). In 19 of 58 patients, Disproportionately Enlarged Subarachnoid Space Hydrocephalus (DESH) data was available: in 3 it was negative and in 16 positive. Of the 3 negatives, one year of follow-up (after VPS) were unchanged (according to mRS); of the 16 positives: 9 had improved 1 point in mRS at one year of follow-up (56.25%) and 6 were unchanged (43.75%) and none got worse. However, none of these findings were statistically significant.

In this group of patients, we observed that of the 41 patients who improved after 3 months, only 24 (59%) maintained it at 1 year (p = 0.043) (Figure 1).

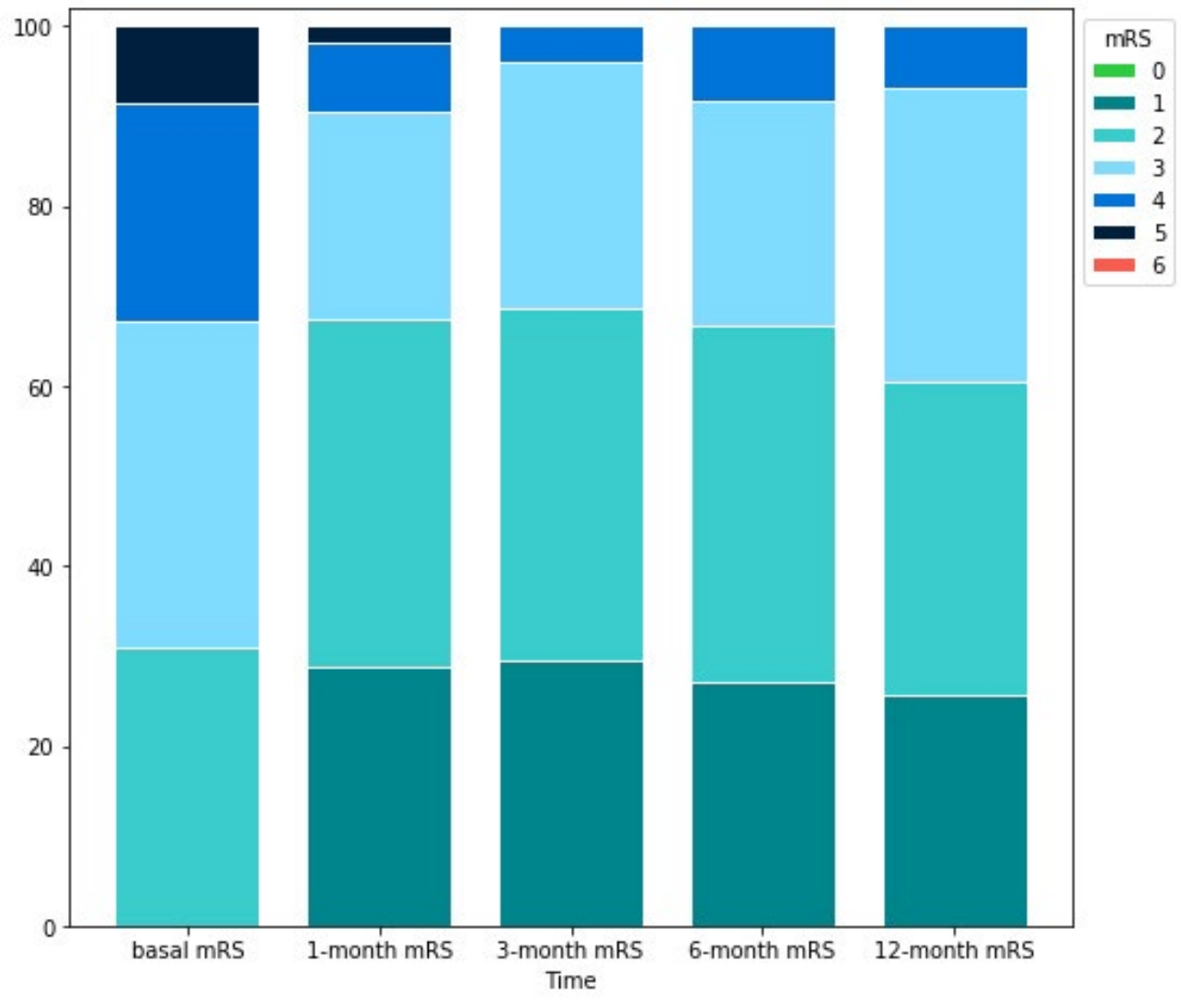

Figure 1. Follow-up of the patients (expressed as a percentage) from the VPS placement to 1, 3, 6 and 12 months, evaluated according mRS (0-6).
Source: Authors.

This research study has the following limitations: data collection was carried out retrospectively and, in some patients,, all the necessary clinical data and complementary studies were not available. The sequence of complementary studies carried out was not completely the same for all patients; this reveals the need for a homogeneous diagnostic evaluation appropriate to international guidelines. Also, it is important to consider that mRS was calculated indirectly by recording clinical evaluations.

Conclusions

Female sex and good response to the gait test could be considered as predictors of a favorable response to the VPS placement in patients with iNPH. A prospective study is necessary to achieve a homogeneous diagnostic evaluation and a more extensive longitudinal follow-up to evaluate the clinical evolution in this group of patients.

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