

Performance of the fixed pressure valve with antisiphon device SPHERA® in the treatment of normal pressure hydrocephalus and prevention of overdrainage

Efeito da válvula de pressão fixa com antisifão SPHERA® no tratamento da hidrocefalia de pressão normal e prevenção de hiperdrenagem

Renan M. Pereira¹, Mariane T. Suguimoto¹, Matheus F. Oliveira², Juliana B. Tornai³, Ricardo A. Amaral⁴, Manoel Jacobsen Teixeira^{3,5}, Fernando Campos Gomes Pinto³

ABSTRACT

Normal pressure hydrocephalus (NPH) is characterized by the triad of gait apraxia, dementia and urinary incontinence associated with ventriculomegaly and normal pressure of cerebrospinal fluid. Treatment is accomplished through the implantation of a ventricular shunt (VPS), however some complications are still frequent, like overdrainage due to siphon effect. This study analyses the performance of a valve with anti-siphon device (SPHERA®) in the treatment of patients with NPH and compares it with another group of patients with NPH who underwent the same procedure without anti-siphon mechanism (PS Medical® valve). 30 patients were consecutively enrolled in two groups with 15 patients each and followed clinically and radiologically for 1 year. Patients submitted to VPS with SPHERA® valve had the same clinical improvement as patients submitted to VPS with PS Medical®. However, complications and symptomatology due to overdrainage were significantly lower in SPHERA® group, suggesting it as a safe tool to treat NPH.

Keywords: normal pressure hydrocephalus, cerebrospinal fluid shunt technology, complications.

RESUMO

A hidrocefalia de pressão normal (HPN) é caracterizada pela tríade de sintomas de apraxia de marcha, demência e incontinência urinária. O tratamento padrão é realizado através de derivação ventricular, porém várias complicações são frequentes, como a hiperdrenagem secundária ao efeito sifão. Este estudo avaliou o resultado da válvula SPHERA® no tratamento desses pacientes em comparação com um grupo controle (PS Medical®). 30 pacientes foram consecutivamente alocados em dois grupos de 15 e seguidos por 1 ano. Pacientes com a válvula SPHERA® tiveram o mesmo grau de melhora clínica em comparação ao grupo controle, no entanto as complicações diagnósticas e sintomatologia secundária à hiperdrenagem foi significativamente inferior no grupo da válvula SPHERA® group, sugerindo-a como uma ferramenta segura e aplicável.

Palavras-chave: hidrocefalia de pressão normal, derivações líquóricas, complicações.

Normal pressure hydrocephalus (NPH) is a neurological syndrome which manifests typically between 60 and 80 years of age, characterized by a triad of symptoms consisting of gait apraxia, dementia and urinary incontinence, associated with ventriculomegaly (detected radiologically) and normal pressure of the cerebrospinal fluid (CSF)^{1,2,3}.

NPH can be divided into two categories: idiopathic and secondary. The secondary NPH occurs in the context of neurological events such as subarachnoid hemorrhage (SAH), intraventricular hemorrhage caused by trauma or aneurysm rupture and meningitis. In contrast, idiopathic NPH usually occurs between the sixth and eighth decades

¹Universidade Anhembi Morumbi, Sao Paulo SP, Brazil;

²Hospital do Servidor Público Estadual de São Paulo, Departamento de Neurocirurgia, Sao Paulo SP, Brazil;

³Universidade de São Paulo, Hospital das Clínicas, Instituto de Psiquiatria, Divisão de Neurocirurgia Funcional, Grupo de Hidrodinâmica Cerebral, Sao Paulo SP, Brazil;

⁴Universidade de São Paulo, Hospital das Clínicas, Instituto de Psiquiatria, Grupo de Estudos sobre Álcool e Drogas, Sao Paulo SP, Brazil;

⁵Universidade de São Paulo, Faculdade de Medicina, Departamento de Neurologia, Sao Paulo SP, Brazil;

Correspondence: Matheus Fernandes de Oliveira; Rua Loefgren, 700 / apto 103; 04040-000 São Paulo SP, Brasil; E-mail : mafernoliv@yahoo.com.br

Conflict of interest: There is no conflict of interest to declare.

Authors declare that SPHERA® valves applied in the study were legally donated by HPBio company – São Paulo, in accordance with ethics committee of Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo (CAPPESQ 10992).

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of life and does not have its pathophysiological mechanisms completely understood^{4,5,6}.

Once NPH is a rare case of reversible dementia, it is essential to have an adequate clinical assessment, early diagnosis and proper treatment in such cases 4-7. Standard treatment is accomplished through the implantation of a ventricular shunt, offering the possibility of significant neurological improvement^{7,8,9}.

Different types of ventricular shunts are possible, but the most common is the ventricular peritoneal shunt (VPS), performed by using a thin catheter whose interior flow is unidirectional (craniocaudal) due to the presence of a device coupled to the valve system, which communicates the cerebral ventricles with the peritoneal cavity, where the excess CSF is drained^{4,5,6,7}.

Complications related to VPS procedure are mainly biological and mechanical, and the infection is still the most feared figure in the case of biological complications. Among mechanical complications (such as proximal shunt obstruction, headache, dizziness, slit ventricle syndrome, subdural or extradural hematomas, secondary paralysis of cranial nerves and craniosynostosis), the most frequent and important are attributed to changes related to the strength of drainage system, which results in excessive CSF drainage. This phenomenon is called siphon effect^{10,11,12,13,14}.

In general, the siphon effect occurs due to the increased flow of CSF from the ventricles drained after postural changes such as sit or stand up. This phenomenon is due to the increased hydrostatic pressure (HP) and perfusion pressure (PP) of the drainage system. However, there are reports in the literature that some physiological mechanisms, such as increased intra-abdominal pressure (IAP) and the reduction of intracranial pressure (ICP) during postural changes has a preventive effect on the siphon effect^{10,11,12,13,14,15,16}.

Many of CSF drainage systems have been designed to prevent excessive drainage such as adjustable valves, flow-regulated valves and gravitational antisiphon valves (the latter two valves not only controlled by differential pressure, but also under the influence of gravity as the position the body)^{17,18,19,20,21,22,23}.

This study aims to evaluate the performance of a valve with anti-siphon device (SPHERA® - Figure 1)²⁰ in the treatment of patients with NPH and compare it with the performance observed in another group of patients with NPH who underwent the same procedure (VPS), but whose valves had no anti-siphon mechanism.

METHOD

The research project was approved by the ethics committee of Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo (CAPPESQ 10992).

Sample

Eighty nine patients with normal pressure hydrocephalus were selected and had their medical profiles retrospectively

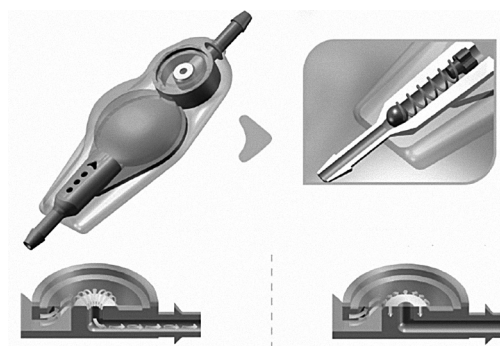


Figure 1. SPHERA® Valve.

analysed. Patients presented with clinical (dementia, urinary incontinence, gait apraxia) and radiological (cranial tomography or magnetic resonance imaging demonstrating ventriculomegaly; Evans index > 0.3). They were admitted in the group of Cerebral Hydrodynamics, Division of Functional Neurosurgery, Institute of Psychiatry, Hospital das Clínicas, Faculty of Medicine, University of São Paulo (HC - USP), from September 2008 to July 2012, treated by ventriculoperitoneal shunt (VPS).

Inclusion criteria were: age between 60 and 95 years old, clinical and radiological diagnosis of normal pressure hydrocephalus and improvement after lumbar puncture (Tap test).

Exclusion criteria were: presence of severe systemic diseases.

Procedures

Selection of patients

All patients were selected after clinical and radiological evaluation. The radiological criterion used to evaluate ventricular size was the ratio of Evans, which is the ratio between the maximum width of the anterior horn of the lateral ventricles and the maximum width of the skull (internal board of the parietal bones). Hydrocephalus is defined by an index greater than or equal to 0.3 index.

After confirming the diagnosis of normal pressure hydrocephalus, patients underwent a Tap test, whose steps were as follows:

- 1) The patient was analyzed according to gait and cognitive pattern;
- 2) Then, a lumbar puncture was performed with removal of approximately 40-50 ml of cerebrospinal fluid (CSF);
- 3) After about 180 minutes, the patient was again analyzed according to gait and cognitive pattern.

From 89 patients initially selected, only 34 presented with improvement after Tap test, being then included in the study. Four patients among the 34 presented with severe systemic diseases, being then excluded from study. After all, 30 patients participated, being consecutively divided in group 1 (anti-siphon) and group 2 (without anti-siphon), both groups with 15 patients. Allocation was performed consecutively, without randomization.

Ventricular shunt

One group was selected for the implantation of fixed pressure (medium and low pressure) with anti-siphon mechanism membrane (SPHERA®, HPBIO, São Paulo, Brazil) valve. SPHERA® valve operates by a mechanism coupled with a coil spring and a ruby ball (ball and spring mechanism). According to the characteristic of the spring, four levels of pressure difference ensures a physiological flow of CSF: extra low (1 to 3 cm H₂O) and low (3 cm H₂O -7), medium (7 to 11 cm H₂O) and high (11 to 14 cm H₂O). The body of the prosthesis measures 42 x 14 x 6.5 mm. Its proximal portion contains the valve mechanism, the central part is the digital camera for pumping and punch, and the distal part contains the anti-siphon mechanism membrane. When the distal pressure becomes negative, the membrane temporarily occludes the system, avoiding excessive drainage. This occurs when the patient is in the standing position (up to - 50 cm H₂O) or additionally during inspiration in patients with ventriculo-pleural shunt (up to - 8 cm H₂O).

The other group was subjected to similar procedures, but without anti-siphon mechanism (PS Medical® valve, Medtronic).

The criterion for the choice of opening pressure of the implanted valves was the final value of CSF pressure measured after completion of the Tap test. Low pressure valves were implanted in patients who had values lower than 4 cm H₂O, medium pressure in patients with values between 5 and 10 cm H₂O and high pressure in patients with values greater than 10 cm H₂O.

Postoperative follow-up

Patients were evaluated for a year after surgery, according to pre-established routine outpatient visits: 10 days after surgery to removal of stitches, three months, six months and one year after surgery. Follow-up criteria were:

- Clinical: comparison of pre and post neurological surgery, presence of signs and symptoms of malfunction or excessive drainage system (headache, positional headaches, nausea, vomiting, visual changes, altered level of consciousness);
- Radiological: pre and postoperative CT, immediately after surgery and after three months. Signs of CSF hypodrainage (Evans index > 0.3) and signs of CSF overdrainage (subdural collections > 1 cm) were evaluated.

Scales

The following scales were used for clinical and radiological assessment of the patients:

1) Mini Mental State Examination (MMSE)^{21,22}

Objective: To evaluate cognitive changes.

Score: 0 to 30 (higher is better).

2) Japanese NPH Scale (NPH Scale)²³ – Figure 2

Objective: scoring patients according to clinical characteristics of NPH triad.

Score: 0 to 12 (higher is worse).

Statistics

According to the nature of the variables the data were analyzed by the absolute and relative frequency and applied the following tests: Kolmogorov-Smirnov test, t-test, Mann-Whitney and Wilcoxon. The value of 5% ($p < 0.05$) was adopted as the threshold for rejecting the null hypothesis with a confidence interval of 95%.

RESULTS

Anthropometric data

Of the 30 patients, there were 23 men and 7 women. In group 1 (SPHERA®), age ranged from 60 to 85 years (mean 71 years) and Body Mass Index (BMI) ranged from 18 to 30 kg/m² (mean 24.8 kg/m²). In group 2 (PS Medical®), age ranged between 60-79 years (mean 70 years) and BMI ranged from 21 to 36.8 kg/m² (mean 26 kg/m²). There was no statistical difference between the mean age and BMI between groups.

Twenty-five patients had complete clinical triad, 2 patients had gait apraxia and urinary incontinence, 2 patients had gait apraxia and dementia and 1 patient had only dementia. All patients had communicating hydrocephalus according to CT and MRI, and Evans index ranged from 30% to 49% (mean 39.8%).

Table 1 shows the scores obtained by using the Japanese scale for NPH while performing Tap-test, after 3 months and 12 months after surgery.

GAIT DISTURBANCE	
0.....	absent
1.....	unstable, but independent gait
2.....	walking with one cane
3.....	walking with two canes or a walker frame
4.....	walking not possible
DEMENTIA	
0.....	absent
1.....	no aparent dementia, but apathetic
2.....	socially dependent, but independent at home
3.....	partially dependent at home
4.....	totally dependent
URINARY INCONTINENCE	
0.....	absent
1.....	absent, but with pollakisuria or urinary urgency
2.....	sometimes only at night
3.....	sometimes, even during the day
4.....	frequent

Mori K. 2001

Figure 2. Japanese scale for NPH.

Table 1. Normal pressure hydrocephalus (NPH) Japanese scale during Tap test and follow-up.

Group	Best before Tap test	Best after Tap test	After 3 months	After 12 months
Group 1 – anti-siphon (n = 15)				
NPH scale	8 (5-12)	7 (2-12)	8 (4-12)	6 (1-12)
Group 2 – without anti-siphon (n = 15)				
NPH scale	6 (2-11)	5 (2-8)	4 (0-10)	6 (0-12)

Group 1 (SPHERA® valve)

Of the 15 patients who constituted group 1, 12 were men and 3 were women. Medium pressure valves were implanted in 10 patients and low pressure valves (SPHERA®, HPBIO) in 5 patients.

Clinical evaluation

After one year of follow up, 10 patients had clinical improvement (10/15 = 66%), 2 patients (2/15 = 13%) remained unchanged compared to the preoperative period and 3 patients (3/15 = 20%) showed clinical worsening after one year of monitoring. During cognitive assessment by MMSE, the best results (mean and variation) before and after the Tap test, after 3 months and after 1 year were 14 (8-22), 14 (2-23), 14 (3-26) and 15 (9-27), respectively.

Radiological evaluation

Eleven patients showed no signs of parenchymal bleeding or subdural collections after one year of surgery (Figure 3). Two patients presented 45 days and 6 months after surgery subdural chronic hematomas in the right cerebral hemisphere, both in the right frontoparietal region. In the first case, there was 2 cm in the greatest thickness. In the second case, it was observed thickness of 1.5 cm and minimum deviation from the midline to the left. In both cases there was need for surgical drainage without changing valves.

Table 2 shows the radiographic patterns presented by patients in group 1.

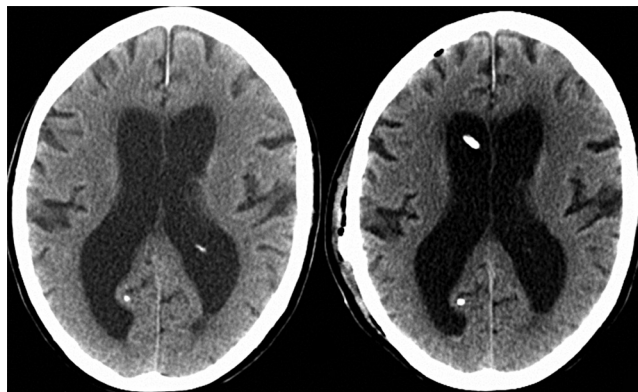


Figure 3. Pre and post operative images of a typical normal pressure hydrocephalus patient of group 1.

Table 2. Radiological evaluation in group 1.

	< 3 ms	3 months	6 months	9 months	12 months
Subdural hematomas > 1 cm	1	-	1	-	-
Subdural hematomas < 1 cm	-	-	-	-	-
Ventricular enlargement	-	-	-	1	-
Hemioventricle	-	-	1	-	-
Slit ventricle	-	-	-	-	-

Group 2 (PS Medical® valve)

Of the 15 patients who constituted group 2, 11 were men and 4 were women. 12 medium pressure valves and 3 low pressure valves (PS Medical®, Medtronic) were implanted.

Clinical evaluation

After one year of follow-up, 8 patients (8/15 = 53%) showed clinical improvement, 2 patients (2/15 = 13%) remained unchanged compared to the preoperative period and 5 patients (5/15 = 33%) showed clinical worsening after a year of monitoring.

During cognitive assessment by MMSE, the best results (mean and variation) before and after the Tap test, after 3 months and after 1 year were 22 (13-29), 20 (1-30), 16 (2-29) and 21 (10-30), respectively.

Radiological evaluation

Five patients had chronic subdural hematoma > 1 cm during follow-up (Figure 4). One in the first month (frontoparietal region, measuring 2.1 cm); two after two months (both right frontoparietal region without midline deviation or ventricular compression, one measuring 1.2 cm, and the other measuring 1.4 cm); one after three months (in the right frontal parietal region measuring 1.1 cm without midline deviation or ventricular compression) and one six months after surgery (bilateral frontoparietal region, measuring 1.2 cm).

Four of the five largest hematomas that occurred in the first six months required reoperations for hematoma evacuation and replace valves for high-pressure valves (three cases after 2 months of surgery) and closure of the shunt system by occlusion of catheter (one patient 3 months after surgery). The remaining case was approached conservatively.

One patient had slit ventricles syndrome after six months of surgery without midline deviation or ventricular compression (Figure 5). We opted for a conservative approach.

Table 3 presents the radiographic patterns presented by patients in group 2.

Comparison between groups

In both groups, there was clinical improvement after one year ($p = 0.005$) and that was superior in Group 1, however without statistical significance ($p = 0.059$). NPH scale after one year revealed statistical significant difference in both groups ($p = 0.005$), while Evans index did not differ in both groups ($p = 0.105$).

Overdrainage complications were significantly lower in Group 1 ($p = 0.042$). The need for reoperation in the first year after surgery in both groups is presented in Table 4. There was a smaller number of reoperations in Group 1, not statistically significant ($p > 0.05$).

Table 5 presents the causes of emergency room care in the HCFMUSP during the first year after surgery of patients in groups 1 and 2. There were fewer clinical complications in group 1 ($p = 0.05$).



Figure 4. Pre and post operative images of a subject of group 2 who developed subdural hematoma after ventricular peritoneal shunt.

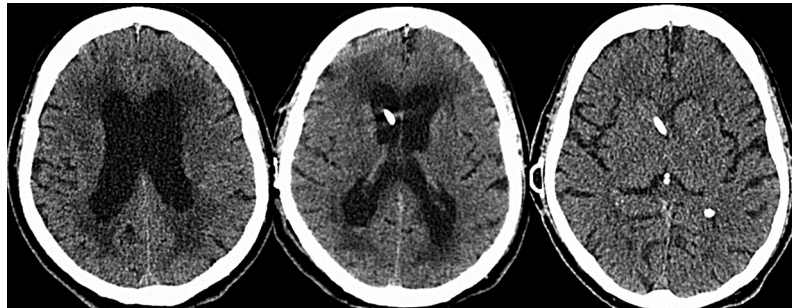


Figure 5. Pre and post operative images of a subject of group 2 who developed slit ventricle syndrome after ventricular peritoneal shunt.

Table 3. Radiological evaluation in group 2.

	< 3 ms	3 months	6 months	9 months	12 months
Subdural hematomas > 1 cm	2	2	1		
Subdural hematomas < 1 cm	-	-	2	-	-
Ventricular enlargement	-	2	1		
Hemoventricle	-	-		-	-
Slit ventricle	-	-	1	-	-

Table 4. Reoperation after 1 year.

	3 ms	6 months	9 months	12 months
Group 1	1	-	1	-
Group 2	4	-	-	-

Table 5. Reasons for emergencial medical evaluation during the first year after surgery in groups 1 and 2.

Symptoms/Signs	Group 1 (n = 15)	Group 2 (n = 15)
Headache	2	4
Impairment of level of consciousness	1	5
Dizziness	1	3
Falls	1	2
Behavior changes	2	3
Vomiting	1	2

DISCUSSION

Normal pressure hydrocephalus is one of the few causes of dementia with potential for reversal of symptoms. Hakim and Adams in 1965 described the classic triad that can characterize disease in varying degrees of combination^{1,2,3}.

A ventriculoperitoneal shunt is the procedure of choice for the treatment of NPH. Approximately 50-70% of patients report improvement after shunt. However, complications related to the procedure are still frequent and often severe, ranging from 13 to 40% of patients in the main series. The siphon effect, which occurs due to the increased flow of CSF from the ventricles drained after postural changes, like sit or stand, is being increasingly investigated in order to reduce complications^{4,5,6,7,8,9,10}.

Many CSF drainage systems have been designed to prevent excessive drainage such as adjustable valves, flow-regulated valves, and gravitational anti-siphon valves^{24,25}.

Several studies are known in this regard. The Codman Medos valve, for example, allows adjustment of the pressure in 18 levels between 30 and 200 mm H₂O. A series of 90 patients was published with satisfactory clinical results. Another retrospective study was published in 583 patients with hydrocephalus due to various causes who were treated with the Codman Hakim programmable valve. The proGAV valve (Aesculap) also has support in the literature^{26,27}.

The use of Strata® valve has been described previously, with a success rate of approximately 80% and 20% of

complications^{28,29,30}. Orbis Sigma[®] is a self-regulating valve and constant flow valve. Despite being probably one tool applicable in cases of NPH, the literature lacks studies corroborating results in these patients³¹.

Once complications related to CSF overdrainage are frequent and may be severe, the present study evaluated the performance of a valve with anti-siphon device (SPHERA[®]) in the treatment of patients with NPH compared to the performance observed in another group of patients with NPH who underwent the same procedure, but whose valves had no anti-siphon mechanism (PS Medical[®], Medtronic).

We evaluated 30 patients with NPH separated into 2 groups according to the type of valve used. We studied the clinical and radiological outcome, complications, reoperations, and symptomatology after a 1 year follow up. In group 1 (Anti-siphon), the improvement rate was 66 %, with 5 radiological complications and reoperation in 2 patients. In group 2 (without Anti-siphon), there was improvement in 53% of patients, with 11 complications and reoperation in 3 patients.

In both groups, there was clinical improvement after one year ($p = 0.005$) and that was superior in group 1, however without statistical significance ($p = 0.059$). Overdrainage complications were significantly lower in group 1 ($p = 0.042$). There was a smaller number of reoperations in group 1, not statistically significant ($p > 0.05$). Thus, SPHERA[®] valve was similar to the fixed pressure valve PS Medical[®] regarding clinical treatment and was superior in the management of overdrainage complications.

The use of valves with different pressures between the two groups (low and medium) were statistically significant ($p = 0.025$). Then a regression analysis was performed by controlling this variable. With this control, the variable "had complication" was significantly different between groups ($p = 0.049$).

As there were more patients in group 2 with medium pressure valves than in group 1, it was expected that the first presented with lower rates of overdrainage. However, in reality, a larger number of overdrainage complications happened in group 2, reinforcing the role of Anti-siphon device of SPHERA[®] valve in preventing such complications.

Some limitations should be considered. First, our analysis was a retrospective study without randomization in group allocation. The best study design to test hypothesis should be prospective and randomized. This methodological weakness surely brings bias which may interfere with inferences from study.

Additionally, when the patient is elderly, one should be cautious with the results of improvement of dementia after

shunt. The association with Alzheimer's disease and other dementia is known, sometimes without any improvement after shunt³².

Then, we did not use any objective functional scale to assess patients, such as the modified Rankin Scale and Barthel Index. Additionally, screening for shunt surgery was based on the results of Tap test. It was the only preoperative test used for the treatment of patients due to its applicability, validity and availability, as well as patient comfort, because hospitalization was not required during the protocol. Although with lower sensitivity (26-61%) compared to the infusion test (57-100%) and external lumbar drainage (50-100%), Tap test is feasible and its only great weakness is the potential loss of candidates for surgery³⁰.

Another important point is that the gold standard treatment for NPH is currently done with programmable valves^{9,20}. Thus, comparison of SPHERA[®] valve with a type of fixed pressure valve (PS Medical[®]) may decrease, but not invalidate the superiority of SPHERA[®] valve. Future trials comparing the latter with programmable valves will be needed to clarify these questions.

A linear relationship between shunt valve type and incidence of subdural hematoma remains unclear. Although there is limited evidence data generally assuming that subdural hematoma formation may occur as a consequence of excessive or too rapid CSF drainage, the use of flow-limiting valves or antisiphon devices to reduce the incidence of subdural hematomas has yet to be clearly proved.

We must highlight that SPHERA[®] valves applied in the study were donated by HPBio company. Finally, our results are tied to a 1-year follow-up. Although encouraging, they are still initial and further follow up must be documented.

In conclusion, SPHERA[®] valve showed satisfactory results, since the clinical improvement was observed in 66% of patients and complications were significantly less common because of Anti-siphon device.

Certainly, further studies are needed. However, SPHERA[®] valve is a safe and applicable tool in the treatment of NPH.

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References

1. Hakim S. Some observations on CSF pressure: hydrocephalic syndrome in adults with "normal" CSF pressure [these]. Bogotá: Universidade Javeriana da Faculdade de Medicina; 1964.
2. Wallenstein MB, McKhann GM 2nd, Salomón Hakim and the discovery of normal-pressure hydrocephalus. *Neurosurgery*. 2010;67(1):155-9. doi:10.1227/01.NEU.0000370058.12120.0E
3. Hakim S, Adams RD. The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure: observations on cerebrospinal fluid hydrodynamics. *J NeurolSci*. 1965;2(4):307-27. doi:10.1016/0022-510X(65)90016-X
4. Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. *Neurosurgery*. 2005;57(3 Suppl):S4-16.
5. Gallia GL, Rigamonti D, Williams MA. The diagnosis and treatment of idiopathic normal pressure hydrocephalus. *Nat ClinPract Neurol*. 2006;2(7):375-81. doi:10.1038/ncpneuro0237
6. Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T et al. Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients. *J Neurosurg*. 2005;102:987-97. doi:10.3171/jns.2005.102.6.0987
7. Pinto FC, Saad F, Oliveira MF, Pereira RM, Miranda FL, Tomai JB et al. Role of endoscopic third ventriculostomy and ventriculoperitoneal shunt in idiopathic normal pressure hydrocephalus: preliminary results of a randomized clinical trial. *Neurosurgery*. 2013;72(5):845-53. doi:10.1227/NEU.0b013e318285b37c
8. Siraj S. An overview of normal pressure hydrocephalus and its importance: how much do we really know? *J Am Med Dir Assoc*. 2011;12(1):19-21. doi:10.1016/j.jamda.2010.10.05.005
9. Oliveira MF, Pinto FC, Nishikuni K, Botelho RV, Lima AM, Rotta JM. Revisiting hydrocephalus as a model to study brain resilience. *Front Hum Neurosci* 2011;5:181. doi:10.3389/fnhum.2011.00181
10. Factora R. When do common symptoms indicate normal pressure hydrocephalus? *CleveClin J Med*. 2006;73(5):447-56. doi:10.3949/ccjm.73.5.447
11. Krauss JK, Faist M, Schubert M, Borremans JJ, Lücking CH, Berger W. Evaluation of gait in normal pressure hydrocephalus before and after shunting. *Adv Neurol*. 2001;87:301-10.
12. Verrees M, Selman WR. Management of normal pressure hydrocephalus. *Am Fam Physician*. 2004;70(6):1071-8.
13. Gleason PL, Black PM, Matsumae M. The neurobiology of normal pressure hydrocephalus. *J Neurosurg Clin N Am*. 1993;4(4):667-75.
14. Hebb AO, Cusimano MD. Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome. *Neurosurgery*. 2001;49(5):1166-84.
15. Maset AL, Castro SC, Camilo JR. Considerações hidrodinâmicas sobre a derivação líquórica: efeitos do cateter peritoneal. *Arq Bras Neurocir*. 2005;24(1):9-16.
16. O'Kane MC, Richards H, Winfield P, Pickard JD. The United Kingdom shunt registry. *Eur J Pediatr Surg* 1997;7 Suppl 1:S56.
17. Kajimoto Y, Ohta T, Miyake H, Matsukawa M, Ogawa D, Nagao K et al. Posture-related changes in the pressure environment of the ventriculoperitoneal shunt system. *J Neurosurg*. 2000;93(4):614-7. doi:10.3171/jns.2000.93.4.0614
18. Kurtom, KH, Magram, G. Siphon regulatory devices: their role in the treatment of hydrocephalus. *Neurosurg Focus*. 2007;22(4):1-8. doi:10.3171/foc.2007.22.4.6
19. Maset AL, Castro SC, Camilo JR., Andrade JR., Xavier VEF. Hydrodynamic considerations on CSF shunting. Part IV: technology of shunting valves. *Arq Bras Neurocir*. 2009;28(3):87-96.
20. Pinto FC, Pereira RM, Saad F, Teixeira MJ. Performance of fixed-pressure valve with antisiphon device SPHERA® in hydrocephalus treatment and overdrainage prevention. *Arq Neuropsiquiatr*. 2012;70(9):704-9. doi:10.1590/S0004-282X2012000900011
21. Brucki SM, Nitrini R, Caramelli P, Bertolucci PH, Okamoto IH. Suggestions for utilization of the mini-mental state examination in Brazil. *Arq Neuropsiquiatr*. 2003;61(3B):777-81. [Portuguese]. doi:10.1590/S0004-282X2003000500014
22. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-98. doi:10.1016/0022-3956(75)90026-6
23. Mori K. Management of idiopathic normal-pressure hydrocephalus: a multiinstitutional study conducted in Japan. *J Neurosurg*. 2001;95(6):970-3. doi:10.3171/jns.2001.95.6.0970
24. Carmel PW, Albright AL, Adelson PD, Canady A, Black PML, Boydston W et al. Incidence and management of subdural hematoma/hygroma with variable- and fixed-pressure differential valves: a randomized, controlled study of programmable compared with conventional valves. *Neurosurg Focus*. 1999;7(4):e7. doi:10.3171/foc.1999.7.4.9
25. Reinprecht A, Czech T, Dietrich W. Clinical experience with a new pressure-adjustable shunt valve. *Acta Neurochir (Wien)*. 1995;134(3):119-24. doi:10.1007/BF01417677
26. Zemack G, Romner B. Seven years clinical experience with the Codman Hakim programmable valve : a retrospective study of 583 patients. *J Neurosurg*. 2000;92(6):941-8. doi:10.3171/jns.2000.92.6.0941
27. Meier U, Lemcke J. First clinical experiences in patients with idiopathic normal-pressure hydrocephalus with the adjustable gravity valve manufactured by Aesculap (proGAV (Aesculap)). *Acta Neurochir Suppl*. 2006;96:368-72. doi:10.1007/3-211-30714-1_76
28. Kondageski C, Thompson D, Reynolds M, Hayward RD. Experience with the Strata valve in the management of shunt overdrainage. *J Neurosurg*. 2007;106(2 Suppl):95-102. doi:10.3171/ped.2007.106.2.95
29. Lundkvist B, Koskinen LO, Birgander R, Eklund A, Malm J. Cerebrospinal fluid dynamics and long-term survival of the Strata valve in idiopathic normal pressure hydrocephalus. *Acta Neurol Scand*. 2011;124(2):115-21. doi:10.1111/j.1600-0404.2010.01432.x
30. Oliveira MF, Saad F, Reis RC, Rotta JM, Pinto FC. Programmable valve represents an efficient and safe tool in the treatment of idiopathic normal-pressure hydrocephalus patients. *Arq Neuropsiquiatr*. 2013;71(4):229-36. doi:10.1590/0004-282X20130007
31. Hanlo PW, Cinalli G, Vandertop WP, Faber JA, Bøgeskov L, Børgesen et al. Treatment of hydrocephalus determined by the European Orbis Sigma Valve II survey: a multicenter prospective 5-year shunt survival study in children and adults in whom a flow-regulating shunt was used. *J Neurosurg*. 2003;99(1):52-7. doi:10.3171/jns.2003.99.1.005
32. Hamilton R, Patel S, Lee EB, Jackson EM, Lopinto J, Arnold SE et al. Lack of shunt response in suspected idiopathic normal pressure hydrocephalus with Alzheimer disease pathology. *Ann Neurol*. 2010;68(4):535-40. doi:10.1002/ana.22015