

International Consensus Statement: Spontaneous Cerebrospinal Fluid Rhinorrhea

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Background: The association between spontaneous cerebrospinal fluid (CSF) leak/rhinorrhea and idiopathic intracranial hypertension (IIH) has been increasingly recognized over the last years. However, considerable variability of opinion regarding the assessment, investigations, and management of patients with spontaneous CSF rhinorrhea remains.

Methods: A consensus group was formed from experts from Europe, Asia, Australia, South and North America. Following literature review and open discussions with members of the panel, a set of 61 statements was produced. A modified Delphi method was used to refine expert opinion with 3 rounds of questionnaires and a consensus group meeting in Santo-Rhino meeting in September 2019.

Results: Fifty statements (82% of total) on spontaneous CSF leak and IIH reached consensus. In 38 of 50 statements, the median response was 7 (strongly agree) and in the 12 remaining statements the median response was 6 (agree). Eleven statements were excluded because they did not reach consensus and one new statement was added during SantoRhino meeting. The final statements refer to patient history and clinical examination ("History taking should include presence of headache, tinnitus and visual defects"), investigations (role of Thin Slice Computed Tomography and CISS/FLAIR sequences in Magnetic Resonance Imaging), principles of management (watchful waiting or measures to reduce ICP are supplementary but cannot subsitute surgical closure), surgical technique, intraoperative, early postoperative and long term management.

Conclusion: We present fifty consensus statements on the diagnosis, investigation, and management of spontaneous CSF rhinorrhea based on the currently available evidence and expert opinion. Although by no means comprehensive and final, we believe they can contribute to the standardization of clinical practice. Early diagnosis, prompt surgical closure of the defect, assesment for and treatment of potentially co-existing idiopathic intracranial hypertension in a comprehensive multidisciplinary approach are essential in order to successfully manage spontaneous CSF rhinorrhea, reduce associated morbidity and prevent recurrence. © 2020 ARS-AAOA, LLC.

Key Words:

idiopathic intracranial hypertension; IIH; spontaneous CSF leak; rhinorrhea; consensus article |

How to Cite this Article:

Georgalas C, Oostra A, Ahmed S, et al. International consensus statement: spontaneous cerebrospinal fluid rhinorrhea. Int Forum Allergy Rhinol. 2021;11:794–803.

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however, the representation of 11 different countries and 4 continents produced a diversity of voices and encouraged **Methods**

The development of this consensus statement consisted of 9 steps: (1) panel recruitment including vetting of potential conflicts of interest; (2) determination of clinical evidence gaps through a literature review; (3) qualitative survey and development of initial set of statements with open feedback from members of the panel; (4) survey development and administration (first iteration); (5) revision of ambiguous survey questions and removal or adaptation of remaining statements; (6) re-survey (second iteration); (7) data aggregation and analysis; (8) a consensus meeting during the Santo-Rhino conference (September 2019, Santorini Island, Greece; https://www.santorhino.eu/); and (9) third iteration with production of final statements.

open and healthy discussions.

The expert panel convened included a variety of disciples spanning 11 countries and 4 continents panel chair (C.G.), along with designated panel members, led the survey and manuscript development using the modified Delphi method.19

Literature review

Clinical gaps in the literature were sought through existing guidelines or evidence-based reviews. A supplemental search that included systematic reviews (including metaanalyses) or clinical practice guidelines in English from PubMed and The Cochrane Library from 2000 to 2019 using the search terms "spontaneous CSF leak - rhinorrhea AND idiopathic intracranial hypertension" was also included. The gaps in literature were used as a framework for the Delphi surveys.

Creation of initial set of statements

Following literature review and open discussions with members of the panel, an initial set of 61 statements was produced. These statements were separated into 6 clinical areas: (1) clinical examination; (2) investigations; (3) management; (4) surgical technique; (5) intraoperative and immediate postoperative management; and (6) long-term management.

Delphi method

The Delphi method¹⁹ was utilised: This is a standardized technique to define expert opinion in a way that an equal input from each expert is obtained while minimizing bias. Authors were asked to state their opinion of the statements in a 7-point Likert scale as follows: 1 = strongly disagree; 2 = disagree; 3 = somewhat disagree; 4 = neither agree nor disagree; 5 = somewhat agree; 6 = agree; and 7 = strongly agree.

espite initial hesitance in establishing a link,¹ evidence D has gradually accumulated that idiopathic intracranial hypertension (IIH) is associated with spontaneous cerebrospinal fluid (CSF) leaks.²⁻⁷ Patients with IIH and those with spontaneous CSF rhinorrhea both tend to be female and overweight and share specific radiographic findings, such as empty sella,⁶ abnormalities of the optic sheath complex, globe flattening, encephaloceles, arachnoid pits, enlarged Meckel's cave,8 and dural ectasia.9 However, patients with spontaneous CSF rhinorrhea do not usually complain of the typical symptoms associated with IIH.¹⁰ Hence, the diagnosis of concurrent IIH is usually confirmed following closure of the skull-base defect: This may lead to increased intracranial pressure (ICP) and initiate the typical symptoms of increased ICP.10

Understanding the link between IIH and spontaneous CSF leaks is not of academic interest only: it has important management implications. This link suggests that controlling increased ICP may improve the results of spontaneous CSF leaks repair and reduce recurrence rates.⁷ However, there is significant discrepancy - a form of an "academic disconnect"- between the otolaryngology, neurosurgical,¹ and neurology literature regarding the management of spontaneous CSF leaks¹¹⁻¹³. A significant number of oto-laryngologists and neurosurgeons do not acknowledge the link to IIH,¹⁴⁻¹⁸ hence missing the change of diagnosing and treating IIH early.

An expert panel was convened, consisting of endoscopic skull-base surgeons, otolaryngologists, and neurosurgeons with interest in IIH and spontaneous CSF rhinorrhea from 11 countries (United States, Brazil, United Kingdom, Australia, Italy, Greece, France, Belgium, Turkey, Austria, and Cyprus) with the aim of producing a common set of statements referring to the assessment, investigations, and management of spontaneous CSF rhinorrhea associated with IIH. The size of the group was party dictated by the need to meet in person in order to finalize the consensus document. We do recognize that this could potentially introduce bias;

Received: 13 May 2020; Revised: 8 September 2020; Accepted: 8 September 2020 DOI: 10.1002/alr.22704 View this article online at wileyonlinelibrary.com.

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Potential conflict of interest: None provided.



FIGURE 1. Iterations.

Consensus was achieved when:

- 80% of votes fell within 2 upper categories (6 agree or 7 strongly agree)²⁰
- 2. AND there was no more than 1 outlier in the opposite direction (3 somewhat disagree, 2 disagree or 1 strongly disagree)
- 3. AND there was no more than 1 panel member who skipped the question.

The Web-based software, Survey monkey (San Mateo, CA) was used for sending the question rounds to the experts. For all questions within the survey, there was an option for free text so that the participants could both state the reason they disagree and suggest amendments. An e-mail address was requested in the questionnaire in order to ensure follow-up, but answers were deliberately anonymized. Our Delphi process consisted of 4 rounds. In the first round, the initial 60 statements were sent using an electronic questionnaire. Consensus was reached in 36 statements, whereas another 24 statements were amended following comments supplied by the authors and sent for second iteration. Consensus was subsequently reached in 11 of them. The third iteration took place in person at the Santo-Rhino consensus meeting in September 2019, where all statements were again discussed, fine-tuned, and 1 new statement was added. Following the meeting, there was a final (fourth) Delphi round, during which 13 controversial statements were sent in a third electronic questionnaire out of which another 3 reached consensus (Total 50) (Fig. 1).

Results

A total of 50 statements, grouped into 6 categories, reached final consensus (Tables 1-6). In 38 of 50 statements, the median response was 7 (strongly agree) and in the 12 remaining statements the median response was 6 (agree). Eleven statements were excluded because they did not reach consensus and 1 new statement was added during SantoRhino meeting.

Discussion

Spontaneous CSF leaks can be challenging, both in their diagnosis and localization as well as their long-term management. Our panel reached strong consensus (median 7) in the vast majority of statements, reflecting the strength of recommendations and of overall agreement. This was most prominent in the areas of management (principles of management, surgical technique, intraoperative and early postoperative and long-term management), where every single one of the 25 statements reached strong consensus (median of 7).

History and clinical examination

CSF rhinorrhea should be suspected in cases of unilateral watery rhinorrhea, especially if triggered by changes in posture or following head trauma or skull-base surgery. The 2 statements: CSF rhinorrhea should be suspected in rhinorrhea associated with salty rather than sweet taste and rhinorrhea that continues during bedtime, did not reach consensus. It was believed that both answers are not specific enough to help with the diagnose of CSF rhinorrhea.

Patients with an active CSF leak may (infrequently) have symptoms of IIH (such as headache, visual defects,²¹ and pulsatile tinnitus²²) but may also display symptoms of decreased ICP such as orthostatic headache and neck stiffness.²³ Patients with spontaneous CSF leaks and IIH are usually obese (body mass index [BMI] > 30).^{24,25} Beyond nasal endoscopy, examination of the Eustachian tubes and of the tympanic membranes can show an otologic cause of CSF rhinorrhea, whereas an ophthalmology consultation (including fundoscopy) may show early signs of IHH.

The statement "Having the patient perform a modified Valsalva maneuver can be helpful in identifying a rhinology

#	Statement	Mode	Median	Range	Agree (%)	Strongly agree (%)
Ŧ	CSF rhinorrhea should be suspected in patients with unilateral watery rhinorrhea	7	7	5-7	12	82
2	CSF rhinorrhea should be suspected when rhinorrhea is triggered by changes in posture	9	9	5-7	47	47
с	CSF rhinorrhea should be suspected when rhinorrhea is triggered by head trauma or skull-base surgery	7	7	6–7	12	88
	History taking in patients with spontaneous CSF rhinorrhea should include symptoms of IIH such as:					
4	Presence of headache	7	7	4–7	29	53
5	Presence of visual defects	7	7	2–7	41	47
9	Presence of pulsatile tinnitus	7	7	3–7	38	50
7	Patients with an active CSF leak may also present with symptoms of decreased ICP including orthostatic headache and neck stiffness.	7	9	4–7	41	41
80	Patients with spontaneous CSF leak/ IHH are usually overweight (BMI > 25) and often obsese (BMI > 30)	Q	9	2–7	59	30
6	All patients with spontaneous CSF rhinorrhea should undergo a complete ENT examination including nasal endoscopy	7	7	2-9	9	94
10	Clinical examination of someone suspected of having CSF rhinorrhea should include otologic exam (fluid in the middle ear could indicate an otologic source for the CSF leak)	7	7	2-9	24	76
1	Examination of the Eustachian tube by endoscopy can be valuable when examining for an otologic source for CSF rhinorrhea	7	9	4–7	35	47
12	In patients with spontaneous CSF leak ophthalmologic assessment including fundoscopy for papilledema and assessment of visual fields is suggested	7	7	6–7	24	76

TABLE 1. History and clinical examination

BMI = body mass index; CSF = cerebrospinal fluid; CT = computed tomography; ENT = ear, nose, throat; ICP = intracranial pressure; IIH = idiopathic intracranial hypertension.

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CISS = constructive interference steady state; CSF = cerebrospinal fluid; CT = computed tomography; CTV = computed tomography venography; FIESTA-C = fast imaging employing steady-state acquisition cycled phases; FLAIR = fluid attenuation inversion recovery; ICP = intracranial pressure; IIIH = idiopathic intracranial hypertension; MRI = magnetic resonance imaging; MRV = magnetic resonance venography.

IADLE 2. Investigatio	S				
Statement	Mode	Median	Range	Agree (%)	St
Examination of the nasal fluid for beta2 transferrin/beta trace protein is an option if there is no obvious identifiable defect and/or mechanism of CSF leak	7	2	6–7	18	
All patients suspected of spontaneous CSF rhinorrhea should undergo a high resolution (<1 mm slice) CT scan of the sinuses and skull base without contrast	7	2	5–7	0	
In patients with suspected spontaneous CSF rhinorrhea a high resolution (<1 mm slice) T2 CISS/FIESTA-C and FLAIR or equivalent protocol MRI with coronal reconstruction should ideally be requested for the assessment of the area of leak as well as signs of IIH	7	2	5–7	18	
FIESTA-C/CISS and FLAIR sequences in MRI can help differentiate between CSF (bright in CISS and dark in FLAIR) and mucosal disease (bright in CISS, bright in FLAIR)	9	9	5–7	50	
Typical anatomical areas to examine for CSF leak in the CT scan include the lateral lamella/offactory cleft/ethmoid roof, the roof of the lateral recess of the sphenoid sinus (between foramen rotundum and vidian canal), the supraorbital ethmoid roof/frontal sinus posterior table and the planum sphenoidale as well as the posterior wall of sphenoid sinus and the temporal bone	7	2	6–7	24	
Patients with spontaneous CSF rhinorrhea/IIH may have multiple skull-base defects and areas of CSF	7	7	5-7	12	

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Exclude a transverse venous sinus stenosis with an MRV (or CTV if MRV not available) either initially or

Widening of the subarachnoid space around optic nerves and/or tortuous optic nerves

Posterior globe flattening

Dilated Meckel's cave

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Arachnoid pits/erosion of skull base

Empty sella

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Indirect features on brain CT/MRI suggesting increased ICP include:

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In patients suspected of spontaneous CSF leak/IIH, optical coherence tomography is an option for

assessing early changes

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#	Statement	Mode	Median	Range	Agree (%)	Strongly agree (%)
-	Patients with proven (radiologically/beta trace-beta transferrin) CSF leak should undergo closure, even if the leak is intermittent	7	7	6–7	19	81
2	Such patients should be operated as soon as feasible (in view of the risk of meningitis)	7	6	4–7	38	50
3	Once the diagnosis of a CSF leak is confirmed, the patient should be advised about the risk of meningitis and informed about its symptoms and signs	7	7	6–7	9	94
4	Watchful waiting or measures to treat the CSF leak by reducing ICP are supplementary and cannot substitute surgical repair of the anatomical defect, if established	7	7	5–7	41	53
5	Long-term treatment with oral antibiotics has not been shown to reduce the incidence of meningitis and should not be given routinely to patients with CSF leak (when there are no signs of infection)	7	2	6–7	35	65
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TABLE 3. Principles of management

CSF = cerebrospinal fluid; ICP = intracranial pressure.

International consensus statement

source for a CSF leak," did not reach consensus. Performing a modified Valsalva maneuver was even considered to be dangerous outside the operation theatre because it can lead, in cases of large defects, to pneumocephalus.^{26,27}

Investigations

In most cases appropriate imaging (high-resolution computed tomography [HRCT]^{28,29}, high-resolution magnetic resonance imaging-fluid attenuation inversion recovery [MRI-FLAIR] and fast imaging employing steady state acquisition [FIESTA] C/constructive interference steady state [CISS] protocols)^{29,30} will localize the defect. At the same time, they will identify indirect signs of IIH such as empty sella, arachnoid pits, skull-base thinning,³¹ and tortuous optic nerves with widened subarachnoid space32 Both nuclear cisternogram and CT cisternography do not provide a benefit over simple HRCT/heavily-weighted T2 MRI: however, they are more invasive, less sensitive, and associated with more complications, as shown in a recent metanalysis.³³ MRI cisternography does no longer involve intrathecal injection of contrast; instead it refers to heavilyweighted T2W and gradient sequences such as 3D T2 driven equilibrium radiofrequency reset pulse (DRIVE), balanced fast field echo (B FFE) (Philips, Andover, MA), CISS (Siemens Medical Solutions USA, Inc., Malvern, PA), FIESTA (GE Healthcare, Piscataway, NJ), prone highresolution MRI.

Comparing the signal in FLAIR and CISS can help differentiate between CSF (bright in CISS, dark in FLAIR) and inflammation/edema (bright in CISS, bright in FLAIR).

The use of beta trace³⁴ and/or beta2 transferrin is helpful³⁵⁻³⁹ to confirm the presence of CSF because they can detect 5 µL and 100 µL of CSF in 1 mL of nasal secretions, respectively. Beta2 transferrin test has a sensitivity and specificity of over 90% whereas beta trace protein is faster and cheaper to process and has a large CSF to serum ratio, favoring it as a marker for CSF (sensitivity over 90% and 100% specificity).^{35,38} The original statement "All patients suspected of CSF rhinorrhea should have the nasal fluid examined for beta trace protein or, if not available, for beta transferrin" did reach consensus but also many comments. Testing for beta trace protein is not readily available in the United States and 4 colleagues mentioned not testing for beta2 transferrin when the radiological and clinical signs are obvious for a CSF leak. Accordingly, we decided to change to the statement from the second Delphi round onward to "Examination of the nasal fluid for beta2 transferrin/beta trace protein is an option if there is no obvious identifiable defect and/or mechanism of CSF leak."

Defects typically occur in the lateral lamella/olfactory cleft/ethmoid roof as well as the roof of the lateral recess of the sphenoid sinus^{25,39,40} (lateral to the foramen rotundum and vidian canal)⁴¹⁻⁴³—both areas of reduced weakness of the skull base. Additionally, the supraorbital ethmoid roof/posterior table of frontal sinus/planum sphenoidale as well as posterior wall of sphenoid sinus and the

TABLE 4. Surgical technique

#	Statement	Mode	Median	Range	Agree (%)	Strongly agree (%)
1	The use of intrathecal fluorescein is an option if the area of defect cannot be localized preoperatively or in suspicion of multiple areas of CSF leak and/or to confirm complete closure—if used, it should not exceed the maximum dose of 0.5 mg/kg of body weight, slowly administered.	7	7	3–7	29	59
2	The use of intraoperative neuronavigation with CT (with or without MRI fusion) is recommended in complex cases and can assist in localizing the area of bony defect and associated CSF leak	7	7	5–7	31	63
	A variety of techniques can be used for closure. Basic principles include:					
3	Accurate localization of the defect	7	7	6–7	6	94
4	Excision via bipolar cautery of the associated meningoencephalocele, if present	7	7	4–7	6	88
5	Removal of the mucosa around the defect and freshening of the defect edges	7	7	6–7	6	94
6	Application of graft materials (either homologous; pedicled or free tissue graft or heterologous) in 1 or more layers, using inlay or onlay technique	7	7	4–7	12	82
7	Securing and supporting the repair with absorbable or non-absorbable materials including glues and sealants	7	7	5–7	18	76

 $\mathsf{CSF} = \mathsf{cerebrospinal\ fluid;\ CT} = \mathsf{computed\ tomography;\ MRI} = \mathsf{magnetic\ resonance\ imaging.}$

TABLE 5. Intraoperative and early postoperative management

#	Statement	Mode	Median	Range	Agree (%)	Strongly agree (%)
1	As this is a clean-contaminated procedure a single prophylactic dose of intravenous antibiotic during the induction of anesthesia is strongly recommended. The use of antibiotics in the immediate postoperative period is an option.	7	7	6–7	18	82
2	The use of lumbar drain is an option: It can be used to inject fluorescein as well as to measure and reduce ICP following closure and inform IIH management; however, it requires robust monitoring and may be associated with tension pneuocephalus.	7	7	3–7	35	59
3	Patients should be admitted overnight and undergo monitoring of vital and neurological signs.	7	7	5–7	29	65
4	They are advised to remain recumbent for 12–24 hours following surgery in a 30-degree head elevation position.	7	6	2–7	38	50

 $\mathsf{ICP}=\mathsf{intracranial}\ \mathsf{pressure};\ \mathsf{IIH}=\mathsf{idiopathic}\ \mathsf{intracranial}\ \mathsf{hypertension}.$

#	Statement	Mode	Median	Range	Agree (%)	Strongly agree (%)
1	Patients with IIH may develop new symptoms (visual defects, headache) following defect closure	7	6	5–7	41	41
2	In cases with suspected (history/radiology) increased ICP, oral acetazolamide may be provided for 6 weeks postoperatively (until formal measurement of ICP)	7	7	4–7	24	59
3	The assessment of ICP should be considered (in recurrent CSF leak/or revision surgery) following defect closure: Either during the same admission or postoperatively and after the discontinuation of acetazolamide for at least 1 week.	7	7	5–7	18	65
4	Cases of secondarily increased ICP should always be excluded	7	7	4–7	29	53
5	The definitive management of increased ICP (>25 mm CSF/H ₂ 0) should always be undertaken in order to avoid recurrence of the leak and to avoid the long-term sequelae of IIH.	7	7	4–7	35	53
6	All overweight patients with IIH should be strongly advised to lose weight	7	7	5–7	24	71
7	The definitive management of IIH should always be undertaken in collaboration with a neurologist/neurosurgeon and could include either conservative measures (weight loss, acetazolamide) or surgical measures (CSF diversion procedures including lumboperitoneal or ventriculoperitoneal shunting)	7	7	2–7	18	71
8	Prolonged (4–6 weeks) CSF leak precautions should be instituted postoperatively to reduce the risk of recurrence. These include avoidance of nose blowing, bending over, strenuous activity or heavy lifting (>15 pounds/7 kg)	7	6	5–7	47	47
9	Flying is discouraged for the first weeks after surgery and diving for the first 6 months	7	7	1–7	18	76

TABLE 6. Long-term management

CSF = cerebrospinal fluid; ICP = intracranial pressure; IIH = idiopathic intracranial hypertension.

temporal bone can be areas of spontaneous CSF leak.⁴⁴ It is not unusual for patients with spontaneous CSF rhinorrhea/IIH to have multiple skull-base defects and/or areas of CSF leak.⁴⁵ The intraoperative use of intrathecal fluorescein can be useful to localize the leak, identify multiple defects, and confirm watertight closure at the end of the procedure.³⁰ In cases of increased ICP, magnetic resonance venography (MRV) (or computed tomography venography [CTV]) may exclude transverse venous sinus stenosis,⁴⁶ and optical coherence tomography (OCT) may show early changes to the optic apparatus.⁴⁷

Management

There was a strong consensus of the panel that CSF leaks, even if intermittent, must be closed as soon as feasible,⁴⁸

and there is no role for a watchful waiting policy, or for ICPlowering procedures as a substitute for closure.^{49,50} Due to difficulty in logistics in different countries, we have to refrain from using a certain time frame because this is a required procedure but not an immediate emergency. Similarly, the long-term use of antibiotics has not been shown to reduce the incidence of meningitis and cannot substitute surgical closure.

Surgical technique and immediate management

There are a variety of materials and techniques that can be used to effectively close a defect—and there is little evidence that one is superior to another. Basic principles that apply include accurate localization, excision of associated meningoencephalocele (if present) and removal of mucosa around the bony defect.44,51 Additionally, the use of intraoperative navigation and/or intrathecal fluorescein can be useful in more complex cases. The use of lumbar drains is optional; the potential therapeutic benefit and measurement of opening pressures must be carefully weighed against its considerable complications.^{52,53} Day-case CSF leak repair is strongly discouraged, despite some limited and mostly anecdotal experience in its use,54 and admission overnight with appropriate monitoring is recommended. In complex cases (giant meningoencephaloceles, large defects, or multiple associated pathologies) the statement that a CT brain should be considered during the first 24 hours after surgery was rejected after the second Delphi round. Multiple experts had the opinion that clinical examination is more important and in the absence of clinical deterioration the CT scan can be performed later.

A significant part of our patients are obese with obstructive sleep apnea (OSA). Although there is very little evidence, most agree that the use of continuous positive airway pressure (CPAP) devices should be discouraged for the first 2 to 3 postoperative weeks,⁵⁵ depending to the size of defect as well as the severity of OSA.⁵⁶

Long-term management

Notably, patients may develop IHH symptoms (headache, visual defects) following defect closure,⁵⁷ and acetazolamide⁵⁸ may be useful postoperatively. However, patients may have longstanding intracranial hypertension without visual symptoms,⁵ which suggests that management of high ICP is needed even in the absence of symptoms in order to prevent subsequent CSF leaks. Patients with spontaneous CSF rhinorrhea should be considered for ICP assessment (either during admission or later postopera-

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tively and after the discontinuation of acetazolamide for at least 1 week) following closure of the defect, and if IIH is confirmed, this must be definitively managed^{50,59,60} (weight loss,⁶¹ acetazolamide, lumboperitoneal, or ventriculoperitoneal shunt⁶² in collaboration with a neurologist/neurosurgeon) in order to avoid recurrence,⁷ as well as to avoid complications of untreated IHH. Recent (2018) consensus guidelines on the management of IIH⁶³ provide a relevant flowchart: weight management advice should be offered for all patients with IIH, whereas patients without immediate threat to vision can be initially managed with acetazolamide. However, if vision is threatened, CSF diversion (preferably ventriculoperitoneal shunt, which has a lower reported revision rate as per meta analysis⁶⁴) or optic nerve sheath fenestration should be performed. Surgery is always indicated in cases where medical management does not adequately treat vision impairment or pressure remains elevated. The role of other medications (such as topiramate⁶⁵ an appetite suppressor that is also a carbonic anhydrase inhibitor⁶⁵) remains poorly defined: there is paucity of data on their use in patients with IHH.

Conclusion

In summary, we present fifty consensus statements on diagnosis, investigations and management of spontaneous CSF rhinorrhea based on currently available evidence and expert opinion. Although by no means comprehensive and final, we believe they can serve as a useful tool that will contribute to standardization of clinical practice. Early diagnosis and a comprehensive multidisciplinary approach are essential in order to successfully manage spontaneous CSF rhinorrhea and reduce the associated morbidity and recurrences.

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