developed. As a result, more uncertainty regarding the performance of euthanasia may exist among French-speaking physicians.

Alternatively, French-speaking physicians perform continuous deep sedation until death more often than their Dutch-speaking colleagues. This practice, better known as palliative or terminal sedation, has enjoyed growing acceptance among medical professionals but has also been criticized for its potential use in hastening death.[6] Our study shows that a life-shortening intention was present in some instances: in 2.4% of French-speaking physicians and in 0.7% of Dutch-speaking physicians. The criticism, thus, seems to hold. These findings, however, also raise the question whether less inclination to perform euthanasia leads to more continuous deep sedation with a life-shortening intention. Our data are inconclusive, and further research on this matter is needed.

We conclude that French-speaking physicians in Brussels seem more reluctant to perform euthanasia than their Dutch-speaking colleagues; the former more often opt for continuous deep sedation until death, which, in some cases, is carried out with a life-shortening intention.

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References

1. Ministry of the Brussels Capital Region, Directorate of Study and Regional Statistics. Recent demographics of the Brussels Capital Region. [Dutch]. Brussels, Belgium: IRIS, 2002. 64.

2. Law concerning euthanasia. Belgian official collection of the Laws. [Dutch]. Available from: https://portal.health.fgov.be/pls/portal/docs/pageinternet_pg/homepage_menu/gezondheidzorg1_menu/overlegstructuren1_menu/commissies1_menu/euthanasia1_menu/publicaties105_hide/publicaties105_docs/loi_euthanasie.pdf. Accessed: December 16, 2009.

3. Federal Control and Evaluation Committee on Euthanasia. Second report to Parliament. January 1, 2006-December 31, 2007. [Dutch and French]. Available from: https://portal.health.fgov.be/pls/portal/docs/page/internet_pg/homepage_menu/gezondheidzorg1_menu/overlegstructuren1_menu/commissies1_menu/euthanasia1_menu/publicaties105_hide/publicaties105_docs/g6635%20rapport%20euthanasie%20nl31-29%20oct_0.pdf. (only in Dutch). Accessed December 16, 2009.

4. Van den Block L, Deschepper R, Bilsen J, et al. Euthanasia and other end-of-life decisions: a mortality follow-back study in Belgium. BMC Public Health 2009;9:79.

5. Ganz FD, Benbenishty J, Hersch M, et al. The impact of regional culture on intensive care end of life decision making: an Israeli perspective from the ETHICUS study. J Med Ethics 2006;32(4): 196–199.

6. Levy M, Cohen S. Sedation for the relief of refractory symptoms in the imminently dying: a fine intentional line. Semin Oncol 2005;32:237–246.

Targeting Diuretic Use for Malignant Ascites—Two Case Reports Highlighting the Value of the Serum-Ascites Albumin Gradient in a Palliative Setting

To the Editor:

Malignant ascites is a distressing, debilitating, and common complication occurring in up to half of all malignancies.[1,2] Repeated paracentesis is widely recognized as the mainstay of treatment but benefits tend to be short-lived and the procedure can be associated with fatigue and hypotension.[2] Studies have shown that patients with ascites formed because of liver metastases, termed central ascites, tend to respond to diuretics and that identification of such patients can allow targeted diuretic use.[2] The serum-ascites albumin gradient (SAAG) is a simple test that can accurately distinguish the mechanism of formation of malignant ascites.[3] Two cases are described where the SAAG was successfully used to guide the use of diuretics in the control of ascites.

Case 1

An 84-year-old woman with pancreatic cancer was referred with progressive symptomatic ascites. She also had marked peripheral edema with lymphorrhea. The patient had been on spironolactone 50 mg for four weeks, increased from the 25 mg that she had been taking for

three weeks. This had not been further increased as she had experienced transient dizziness when it was originally started. She wanted paracentesis and it was performed without complication. Five liters of fluid was drained over the course of six hours and a further six liters in the four days after removal of the drain before the site healed. The patient was well throughout and her symptoms improved.

A sample of the fluid was sent for albumin level and her SAAG was calculated to be 17 (serum albumin 24 g/L−ascitic albumin 7 g/L). This was suggestive of a central cause for the ascites, and, therefore, her spironolactone was increased to 100 mg and furosemide 20 mg was added, in the hope of reducing the rate of reaccumulation. The patient tolerated these adjustments and has remained on these doses for four months with no significant reaccumulation of her ascites and resolution of her peripheral edema.

Case 2

A 77-year-old woman, with a clinical diagnosis of cholangiocarcinoma, underwent paracentesis of 17 L of fluid over 48 hours in the local hospital, with significant symptomatic benefit. She was discharged on spironolactone 100 mg daily, but after discharge, deteriorated and was seen by the specialist palliative community team nine days after paracentesis. At this point, her ascites had reaccumulated and was large but not tense. She still had a stoma bag over the drain site, which had continued to collect a few milliliters daily. This fluid was sent for albumin level. Her SAAG was calculated to be 18 (serum albumin 22 g/L−ascitic albumin 4 g/L). Her diuretics were increased to spironolactone 200 mg, and furosemide 20 mg daily was added. The ascites reduced clinically and remained stable until her death nine weeks later.

Comment

Maintenance of patients with ascites due to liver cirrhosis on high doses of diuretics is well established and generally well tolerated.[4] Combination diuretics are generally used to minimize the interval between starting treatment and natriuresis, with starting daily doses of spironolactone 100 mg and furosemide 40 mg.[4,5] These are adjusted according to clinical response and electrolyte balance up to "ceiling" doses of spironolactone 400 mg and furosemide 160 mg.[4,5] Studies demonstrate that 90% of cirrhotics have a successful diuresis in combination with a restricted sodium diet of 2000 mg/day.[5]

The morbidity associated with cirrhosis can be likened to patients with advanced malignancy, and yet, use of diuretics by physicians treating malignant ascites is extremely varied. The risk of their burden is often felt to outweigh their unpredictable benefit.[6] It is of note that in both cases described, clinicians involved were wary of increasing diuretic doses for this reason, yet both patients tolerated the higher doses well and had clinical benefit.

Malignant ascites is thought to be formed in four ways. Approximately half of all cases seen are thought to have developed because of peritoneal seeding and are termed peripheral ascites. Chylous ascites is reported to account for around one-fifth of cases, being formed as a result of tumor infiltrating the retroperitoneal space and obstructing lymphatic flow. Central ascites, accounting for 15% of cases, is the most physiologically similar to primary hepatic failure, as it is caused by extensive hepatic metastases.[2] The remaining cases are because of a combination of these causes. Because malignant central ascites formation can be likened to ascites formation in hepatic failure, it is postulated that such ascites should be responsive to diuretics. Pockros et al.[7] undertook a prospective study that confirmed that patients with ascites because of massive hepatic metastases responded to diuretics but those with peripheral or chylous ascites failed to respond. The study also demonstrated that the mechanism of ascites formation could be accurately predicted by measurement of the SAAG.

The SAAG is a well-established measurement in ascites and has been shown to have a differential diagnostic accuracy of 97%.[3] In central ascites, the SAAG is usually greater than 11 g/L and this type is the most likely to respond to diuretic therapy. Peripheral ascites and chylous ascites have a SAAG of less than 11 g/L, and there is no evidence to suggest that diuretic therapy is helpful in controlling the ascites. In fact, Pockros et al.[7] demonstrated a higher frequency of diuretic-related complications within the lower gradient group.

The cases described demonstrate the potential benefit of using the SAAG as a guide for diuretic trial or titration. The measurement is

a simple one and may allow diuretic use to be targeted, both reducing potentially burdensome trials in patients unlikely to respond and allowing confident titration in those with central ascites where the benefits may be significant. Further formal work within the malignant ascites population would allow the development of protocol guidance.

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References

1. Campbell C. Controlling malignant ascites. Eur J Palliat Care 2001;8(5):187–189.

2. Doyle D, Hank G, Cherny N, Calman K, eds. The Oxford textbook of palliative medicine, 3rd ed. Oxford, UK: Oxford University Press, 2005.

3. Runyon B, Montano A, Akriviadis A, et al. The serum-ascites albumin gradient is superior to the exudates-transudate concept in the differential diagnosis of ascites. Ann Intern Med 1992;117: 215–220.

4. Runyon B. Management of adult patients with ascites due to cirrhosis: an update. Hepatology 2009; 49:2087–2107.

5. Yamada T, Alpers DH, Laine C, Owyang C, Powell DW, eds. Textbook of gastroenterology, 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 1999.

6. Lee CW, Bociek G, Faught W. A survey of practice in management of malignant ascites. J Pain Symptom Manage 1998;16:96–101.

7. Pockros PJ, Esrason KT, Nguyen C, Duque J, Woods S. Mobilization of malignant ascites with diuretics is dependant on ascitic fluid characteristics. Gastroenterology 1992;103:1302–1306.

A New Combination Cream for the Treatment of Severe Neuropathic Pain

To the Editor:

Neuropathic pain may be quite resistant to drug treatment. In the case of intractable pain, rational polypharmacy is now well established.[1] The treatment of patients suffering from neuropathic pain with rational polytherapy seems to have the highest likelihood of success.[2] A variety of treatment modalities, such as percutaneous electrical nerve stimulation (PENS) or transcutaneous electrical nerve stimulation (TENS), can be administered together with drugs, potentially allowing use of lower and better-tolerated doses. The same outcome may be possible with the use of topical therapies. The following case did not respond well to our rational polytherapy until a novel combination topical cream, consisting of isosorbide dinitrate (ISDN) 0.4%, capsaicin 0.075%, and lidocaine 3%, was added.

Case

A 62-year-old man suffered from intractable neuropathic pains in both feet and hands since 2003. The diagnosis was painful diabetic polyneuropathy. Glucose levels were within range as a result of treatment with glimepiride 4 mg daily and metformin 500 mg three times a day. Because of the pain, his function was severely compromised. He scored 6 on the Douleur Neuropathique 4 questionnaire (total score 10), which corresponds to severe neuropathic pain. The patient described his pain as burning and excruciating. On the dorsal side of his right foot, he experienced a painful feeling as if a clamp was squeezing his foot (a "clamp pain"). Walking barefoot and sitting increased the pain. The symptoms worsened as the day progressed. Total score on the short-form McGill Pain Questionnaire was 26 (total score 45), the score on the visual analogue scale (VAS; 0–100 mm) was 98, and on the 11-point Brief Pain Inventory scale, the score for pain in the last 24 hours was 10 (0–10).

The treatment consisted of pregabalin 75 mg daily and topical capsaicin 0.075%. Neither of these medications had any effect on the pain