The impact of the double blinded randomized control trial *Brave Dreams* on the nursing staff

Clara Todini,[1] Michela Zanandrea[2]

[1]Pediatric Nursing, La Sapienza University, Rome; [2]University-Hospital of Ferrara, Updating and Training Service, Nursing Degree Course, Ferrara, Italy

Abstract

The objective of this study is a qualitative pilot survey to evaluate the impact of the double-blinded randomized controlled surgical trial *Brave Dreams* on the nursery staff. Chronic cerebrospinal venous insufficiency (CCSVI) is a condition frequently associated to multiple sclerosis, and characterized by impaired venous drainage of the brain and spinal cord as a result of outflow obstruction in the extracranial venous system. The trial was of paramount importance, because the main objective was to test whether re-establishing a correct venous drainage could have therapeutic implications for multiple sclerosis patients, when the disease was associated to CCSVI. Basically, Brave Dreams assessed the efficacy and safety of percutaneous transluminal angioplasty of extracranial veins.

To assess the impact of the trial on the nursery staff, an ad hoc questionnaire was used to test a sample of 8 nurses. The tests investigated 5 macro areas: i) managing of patient assistance; ii) how the research team trained the nursery staff; iii) unmasking efficacy; iv) the overall satisfaction of the nursery staff; v) possible introduction of subjects that explain the methodology of clinical trials during degree nursing education. Data analysis showed that assistance in a trial context must be personalized and based on *primary nursing* principles. It also showed that staff training was extremely satisfying and helpful to the study successful outcome. Furthermore, it showed that each patient was convinced to have undergone a percutaneous transluminal angioplasty, and not a sham procedure. Moreover, the survey showed a strong synergy between the patients and the nursery staff involved in the study. Our conclusions are to examine in depth the notions of professional deontology, ethical behavior and patients' psychology whenever nurses are called to take part in clinical randomized trials.

Introduction

Multiple sclerosis is a chronic degenerative inflammatory disease of the central nervous system, with an unknown etiology[1,2] as well as the most common disease that causes disability among young people. Chronic cerebrospinal venous insufficiency (CCSVI) is a condition characterized by impaired venous drainage of the brain and spinal cord as a result of outflow obstruction in the extracranial venous system, mainly caused by intraluminal obstacles, defective valves, hypoplasia, and/or compression of the internal jugular veins and/or azygos vein. This condition was first described associated to a group of patients affected by multiple sclerosis (MS).[3,4] Furthermore, the CCSVI research extended to other neurodegenerative diseases even more complicated the scientific picture. Recent studies reveal that CCSVI, initially described by Zamboni in multiple sclerosis (MS) patients, is also associated to Parkinson, Alzheimer, Ménière syndrome, and sudden sensorineural hearing loss, and even present in healthy controls.[5-8] However, independently from the problem of imaging CCSVI, which prevents to reliably collect solid epidemiologic data, the knowledge about the pathology characterizing the jugular venous wall in CCSVI condition has been recently increased by a number of papers. The challenging hypothesis of *Brave Dreams* trial was to open the venous obstruction by the means of percutaneous transluminal angioplasty in patients with MS associated with CCSVI, in order to verify if the improvement of venous drainage could in turn improve the clinical outcomes of the diseases.[9] The proposal to add an endovascular treatment to the current therapies for the multiple sclerosis created an important scientific controversy which involves vascular and neurological sciences, respectively.[4] Hence originated the need of an experimental study in order to evaluate the efficacy and safety of percutaneous transluminal angioplasty of extracranial veins in patients affected by multiple sclerosis. The trial, done in double-blinded, implied the randomization of patients into two groups; respectively the experimental group who underwent the intervention, and the control group to a simulated intervention.[5] The nurses, assisting the patients during the trial, were specialized in surgery and faced for the first time in their lives a double-blinded trial. This is the main reason that inspired the will to investigate the influence of *Brave Dreams* on the nursing assistance component of this study.

Correspondence: Clara Todini, Pediatric Nursing, La Sapienza University; and Pediatric Short-Stay Emergency Observation Unit/Pediatric Emergency Department, Umberto I Hospital, Rome, Italy. E-mail: clara.todini@libero.it

Key words: Brave Dreams trial; randomized control trials; chronic cerebrospinal venous insufficiency; multiple sclerosis; chronic cerebrospinal venous insufficiency; nursing.

Acknowledgements: we thank the nursing involved personnel of the Day Surgery Care Unit of Ferrara's University-Hospital, Italy, and Mrs. Ornella Antoniolli, nursery staff responsible, for allowing and facilitating this study.

Conflict of interest: the authors declare no conflict of interests.

Received for publication: 26 June 2018.
Revision received: 24 September 2018.
Accepted for publication: 25 September 2018.

Veins and Lymphatics 2018; 7:7662
doi:10.4081/vl.2018.7662

Materials and Methods

There has been done a descriptive qualitative survey on June 2017 addressed to the nursery population in the Day Surgery care unit of the Ferrara University-Hospital.

Survey construction

In order to do this, there was used a yes-and-no questionnaire, 12 items, overall (Table 1).

Inclusion criteria

The inclusion was based on having participated actively in all the phases regarding the intervention day of the study, as follows: reception in the surgical ward, post-operative management and discharge. Specifically, the nursing staff arranged the patients in their rooms, explained in detail how the day would take place and clarified any further doubts. Then they advised the auxiliary staff dedicated to the transfers into the Interventional Radiology Unit. After about two hours, patients returned to the day surgery ward with mandatory bed restraints. From this moment on, that is the post-operative phase, the nurses scrupu-

lously noted the vital parameters of each patient, drew blood samples for the analysis of the blood count and coagulation, examinations necessary for the assessment of possible bleeding. During the discharge phase, after having assisted Professor Zamboni staff during the postoperative echo-color-Doppler, the nurses evaluated and lightened the compressive medication of the patients. Finally, the nurses dealt with the therapeutic education of the latter, instructing the patients on how to practice self-administration of low molecular weight heparin at home over the next 21 days.

Data analysis

Nurses joined in voluntary after being wholly informed on the survey aims. The sample dimension is of 8 nurses, each of who filled in the questionnaire anonymously and autonomously. Each question in the questionnaire (Table 1) also included a *motivation*, which could be filled out if any of the interviewed nurses wanted to add something more. From the above reasons, key words have been underlined. Subsequently, the questions were grouped by common themes, in accordance with a methodology previously described, which allowed us to identify 5 *domains* emerged from the post-hoc analysis:[6-8] managing and improvement of the assistance; patient and nursing staff training; successful result of masking; satisfaction; nursing degree education program.

Results

The sample was composed entirely of female nurses, aged between 40 and 65 years, with at least 20 years of experience in the surgical area, who for the first time faced a double blinded experimental context. Each topic included specific questionnaire questions, as follows:

i) Managing and improvement of the assistance

- *Do you think that something has changed in the nurses role with regard to a typical Day Surgery intervention?,* 63% replied *NO*, 37% replied *YES*.
- *Is there anything you would have done in a different way for a better service during the assistance phases?*, 75% replied *NO*, 25% replied *YES*.
- *In your opinion, does this trial contest show any new needs of assistance?*, 38% replied *NO*, 62% replied *YES*.

ii) Patient and nursing staff training

- *Have the operative instructions the research team gave before the study took place been clear?* 100% replied *YES*.
- *Do you think that patients and their relatives were well trained?* 100% replied *YES*.
- *Do you think that the preparatory training addressed to all the healthcare staff was satisfying?* 100% replied *YES*.

iii) Successful result of masking

- *Did patients and/or their relatives somehow try to violate the double blind method?* 88% replied *NO*, 12% replied *YES*.
- *Have there been any indirect questions to let leak anything related to the trial?* 63% replied *NO*, 37% replied *YES*.
- *Did any patient show firmly that they had never undergone percutaneous transluminal angioplasty?,* 100% replied *NO*.

iv) Satisfaction

- *Do you think that patients were motivated even if there was the possibility for them not to undergo the intervention?* 100 % replied *YES*.
- *Did you find participating such an ambitious clinical study gratifying?* 100% replied *YES*.

v) Nurse degree education

- *In your opinion, should preparation to the trial context be inserted in the nursing degree course?* 100% replied *YES*.

The participants answered all the above questions, *YES* and *NO*. Few nurses did not integrate closed questions with a motivation, but the majority did it. From the latter it has been shown how, each nurse involved in the trial, has provided optimal assistance to these patients, considering them in a holistic way, and having the foresight to give particular attention to what is the emotional and relational dimension, given the fragility of the context. The entire nursing staff also expressed extreme satisfaction at the time of the training prior to the implementation of the study, clearly illustrated by the PI and his research team. It also emerged that the research team has fully exposed the study to patients, testified by the fact that they have never, apart from an isolated case, asked questions or tried to violate the integrity of the experimentation and therefore with the successful masking. Therefore, overall satisfaction was expressed by nursing staff, but also by patients, who demonstrated a strong motivation, evidenced moreover by the fact that as many as 97% of them have completed the study, including follow-up[9-11] (Table 2).

Discussion and Conclusions

The results of the present pilot study are below discussed by sub setting the Survey per domain.

Managing and improvement of the assistance

It was noticed that in a trial context, the

Table 1. The complete copy of the 12 items' questionnaire.

	Questions
1.	Do you think that something has changed in the nurses' role with regard to a typical Day Surgery intervention?
2.	Is there anything you would have done in a different way for a better service during the assistance phases?
3.	In your opinion, does this trial contest show any new needs of assistance?
4.	Have the operative instructions the research team gave before the study took place been clear?
5.	Do you think that patients and their relatives were well trained?
6.	Do you think that the preparatory training addressed to all the healthcare staff was satisfying?
7.	Did patients and/or their relatives somehow try to violate the double blind method?
8.	Have there been any indirect questions to let leak anything related to the trial?
9.	Did any patient show firmly that they had never undergone percutaneous transluminal angioplasty?
10.	Do you think that patients were motivated even if there was the possibility for them not to undergo the intervention?
11.	Did you find participating such an ambitious clinical study gratifying?
12.	In your opinion, should preparation to the experimental contest be inserted in the nursing degree course?

role of nurses did not change but the self-awareness of belonging to an assisting profession did. The majority of nurses assert to have done an excellent assistance, personalized and based on *primary nursing* principles, aiming to satisfy new assistance needs. There appeared a greater sagacity towards patients due to the delicateness of the route taken, putting the patient in a room with less people than usual and allowing relatives to enter beyond visiting hours; thus, major attention was paid to the psychological and relational aspect.

Patient and nursing staff training

All nurses showed themselves to be totally satisfied with the training they were given formerly by the principal investigator and the other components of the research team, and emphasized its priority and necessity to the positive result of the study i.e. to reach the goal. As far as patients and relatives training is concerned, they were found to be more prepared and educated in study matters and about the rules to be followed. Furthermore, nurses state that none of the patients showed doubts or suspects about the activities lead during the hospitalization and that they had no difficulties at all in doing their duty.

Successful result of masking

The most crucial step of a double-blinded study in surgery, *i.e.* unmasking, was solved in this study. Apart from an only case in 70 patients treated in the Ferrara University-Hospital, none of the patients insisted or put any questions directly or indirectly, to understand which group they were randomized. The study showed that the patients tried to understand what was happening through the nurse behavior instead of putting questions to them. The most important thing is that the nursery staff testimony shows that each of them was convinced of having being randomized to the PTA intervention, which is crucial to the successful result of this study.

Satisfaction

Guided by a spirit of love and dedication for the sake of the people, all the nurses felt that all the patients had constantly been motivated. The patients who underwent this study strongly believed that, this contribution would help other people with the same problem. They were aware that only through a clinical trial the National Health System could recognize the intervention making it accessible to all. According to the nurses, this motivation comes as a result of the hope and serenity of those who face resolutions confidently and not only for their own sake. Taking part in a clinical trial not only gives hope to other people facing the same problems as yours, but it also gives a huge contribution to the scientific community. Being part of a clinical study so well structured, bearing an important purpose, made nurses feel gratified. They also state to have felt as being an active part of the clinical team.

Nursing degree education program

All the nurses involved were of the opinion that it is mandatory to introduce the role of nursing staff in clinical experimental trial context during the degree course. They also stated that it is crucial a deeper study of all the notions related to the professional deontology, to the ethical behavior as well as to the study of patient's psychology inserted in a clinical trial. This is crucial to the optimal communication approach, to the management and assistance of patients who are subject to a clinical blinded experimental study.

This study results show how active involvement of the nurses in the clinical trial can be crucial to the quality of assistance and to the maintaining of the study integrity as well as to the masking ethic. The result of the present study also shows that preparatory training specific for nursery staff is important for the successfulness of the survey. Furthermore, it was found out that the research team clearly showed the study to the patients, testified by the fact that they never asked questions or tried to interfere with the trial process (but one case), hence the unmasking positive result. Alternatively, we can deduce that the majority of patients was convinced of having been involved in the angioplasty group, i.e. in the treatment group, or we can deduce that the patients were highly motivated by the ethical need to maintain the unmasking integrity. On the other hand, these patients have shown a strong motivation, testified by the fact that 97% of them finished the study, follow-up included. [5] Therefore there has been expressed a total satisfaction by the nursery staff. Considering that the purpose of the clinical trial is to allow for scientific knowledge finalized to the prevention, diagnosis and treatment of the diseases, serious and motivating research in a hospital is not to be considered an obstacle to the nursing assistance, but a great opportunity for professional growth. From this point of view results show that the staff enjoyed very much the training session heading this study. The experimenters explained to the staff the purposes and the study modality. Staff could discuss criticality and could learn beforehand any possible risk, which could potentially have affected the Brave Dreams integrity. Interviews let us know that, after this preliminary work, the staff felt very much motivated and self-confident

Table 2. The questionnaire used to conduct this survey, and the percentage of YES and NO answers.

	Question	Yes (%)	No (%)
1.	Do you think that something has changed in the nurses' role with regard to a typical Day Surgery intervention?	37%	63%
2.	Is there anything you would have done in a different way for a better service during the assistance phases?	25%	75%
3.	In your opinion, does this trial contest show any new needs of assistance?	62%	38%
4.	Have the operative instructions the research team gave before the study took place been clear?	100%	0%
5.	Do you think that patients and their relatives were well trained?	100%	0%
6.	Do you think that the preparatory training addressed to all the healthcare staff was satisfying?	100%	0%
7.	Did patients and/or their relatives somehow try to ruin the double blind method?	12%	88%
8.	Have there been any indirect questions to let leak anything related to the trial?	37%	63%
9.	Did any patient show firmly that they had never undergone percutaneous transluminal angioplasty?	0%	100%
10.	Do you think that patients were motivated even if there was the possibility for them not to undergo the intervention?	100%	0%
11.	Did you find participating such an ambitious clinical study gratifying?	100%	0%
12.	In your opinion, should preparation to the experimental contest be inserted in the nursing degree course?	100%	0%

in participating to a clinical trial activity of a high level. Considering the frequency of clinical trials following the recommendations of the Evidence Based Medicine, we believe that it is important to prepare the nursing staff to these activities that involve them professionally starting from the degree course.

References

1. Noseworthy JH, Lucchinetti C, Rodriguez M, et al. Multiple Sclerosis. N Engl J Med 2000;343:983-52.
2. Frohman EM, Racke MK, Raine CS. Multiple sclerosis-the plaque and its pathogenesis. N Engl J Med 2006;354: 942-55.
3. Zamboni P, Galeotti R, Menegatti E, et al. Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 2009;80:392-9.
4. Zivadinov R, Bastianello S, Dake MD, et al. Recommendations for multimodal noninvasive and invasive screening for detection of extracranial venous abnormalities indicative of chronic cerebrospinal venous insufficiency: a position statement of the international society of neurovascular disease. J Vasc Interv Radiol 2014;25:1785-94.
5. Liu M, Xu H, Wang Y, et al. Patterns of chronic venous insufficiency in the dural sinuses and extracranial draining veins and their relationship with white matter hyperintensities for patients with Parkinson's disease. J Vasc Surg. 2015 Jun;61(6):1511-20.
6. Chung CP, Beggs C, Wang PN, et al. Jugular venous reflux and white matter abnormalities in Alzheimer's disease: a pilot study. J Alzheimers Dis 2014;39: 601-9.
7. Bruno A, Napolitano M, Califano L, et al. The Prevalence of Chronic Cerebrospinal Venous Insufficiency in Meniere Disease: 24-Month Follow-up after Angioplasty. J Vasc Interv Radiol 2017;28:388-91.
8. Tessari M, Ciorba A, Mueller LO, et al. Jugular valve function and petrosal sinuses pressure: a computational model applied to sudden sensorineural hearing loss. Veins and Lymphatics 2017;6:6707.
9. Zamboni P, Tesio L, Galimberti S, et al. Efficacy and Safety of Extracranial Vein Angioplasty in Multiple Sclerosis: A Randomized Clinical Trial. JAMA Neurol 2018;75:35-43.
10. Zamboni P, Menegatti E, Occhionorelli S, Salvi F, The controversy on chronic cerebrospinal venous insufficiency Veins and Lymphatics 2013;2:e14.
11. Zamboni P, Tesio L, Galimberti S, et al. Efficacy and Safety of Extracranial Vein Angioplasty in Multiple Sclerosis: A Randomized Clinical Trial. JAMA Neurol 2018;75:35-43.