

## Reducing stress symptoms in patients undergoing MRI: preliminary observations on the use of a low-dose preparation

Alberto Laffranchi <sup>a</sup> and Carlo Modonesi <sup>b</sup>

<sup>a</sup> Department of Diagnostics and Imaging Radiotherapy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

<sup>b</sup> Cancer Registry and Environmental Epidemiology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy

Corresponding author: Alberto Laffranchi, [alberto.laffranchi@istitutotumori.mi.it](mailto:alberto.laffranchi@istitutotumori.mi.it)

### Abstract

Patients undergoing magnetic resonance imaging (MRI) often experience unexpected anxiety episodes. This raises the question of ensuring the success of the diagnostic examination, which is crucial especially for cancer patients. In hospital practice, the solution to that problem is often based on the administration of benzodiazepines. However, this option may be accompanied by adverse events, so patients must be monitored for a too long period of time, with negative effects on the daily work of health care services. Adopting an approach borrowed from integrative medicine, we tested a homeopathic product commonly used in the treatment of emotional and behavioral disorders, and we observed interesting results that deserve to be confirmed by further studies.

**Keywords:** Anxiety; MRI; Cancer Patients; Homeopathy; Integrative Medicine

**Citation:** Laffranchi, A, Modonesi, C, 2019, "Reducing stress symptoms in patients undergoing MRI: preliminary observations on the use of a low-dose preparation" *Organisms. Journal of Biological Sciences*, vol. 3, no. 1, pp. 43-47. DOI: 10.13133/2532-5876\_5.9

## 1. Introduction

The comparative analysis aimed at assessing the differential effectiveness of alternative pharmacological treatments is a growing research field. This is good news. First, because a reproducible approach to the evaluation of different types of drugs has long been considered highly desirable from an evidence-based perspective. Secondly, because the extremely diverse areas in which the current clinical practice takes place call for empirical and non-controversial assessments of therapies.

In other words, the public health care system should adopt a more scientific and pragmatic attitude, setting aside the ambivalence and prejudice that have characterized old views about the use of non conventional medications (Morrison et al, 2000; Horrobin 2007; Ernst 1997). Many practitioners see integrative medicine

as a valid alternative to conventional therapies for the symptomatic treatment of minor health problems. Such therapies are becoming increasingly popular in many parts of the world for several reasons, while in Germany and other European Countries homeopathic remedies have been prescribed since the 1930s.

Moreover, the approach to biomedical research and innovation, particularly in a public health framework, should not be focused solely on avoiding market discrimination between different brands and commercial products. As it was acutely noted by the British medical scientist David Horrobin (2000) "All forms of therapeutics have their place and we should be grateful for the diversity of approach that so adds to the interest of the medical world" (Horrobin 2007).

In our opinion, the primary objective of a pragmatic health care science must be to improve patient condition as a whole by optimizing the work of physicians and health operators. At the same time, knowledge tools should be provided to enable health officials and deci-

sion makers to make appropriate choices. Pursuing the common good both at population and individual level is, after all, the essential requirement of a human-centered health care.

## 2. From qualitative to quantitative data

The work we present here aims to illustrate some promising results on the use of a low-dose preparation (commercial name: Homéogène 46) which has been given to cancer patients or patients suspected to have a cancer. As described below, during a period of observation on patients undergoing magnetic resonance imaging (MRI) at the Department of Diagnostics and Imaging Radiotherapy of the National Cancer Institute (Milan, IT), we collected a series of preliminary indications based on qualitative evidence that show significant benefits associated with the administration of that drug. Compared to conventional drugs used in similar diagnostic settings, such as benzodiazepines, the low-dose preparation help patients feel better during and after the examination, providing health professionals with a useful tool to optimize the performance of the diagnostic procedure. As with many homeopathic remedies, Homéogène 46 shows an attractive safety profile; however, as with most non-conventional medications, there is a need for adequate assessment of effectiveness and tolerability in specifically designed studies. Based on these assumptions, we believe that it is worthwhile to plan further investigations to verify whether the qualitative findings reported here can be confirmed by more exhaustive data.

## 3. Magnetic resonance and tolerability

MRI is an increasingly important technology used in biomedical practice and research. Unfortunately, the fundamental role played by this examination in the diagnostic pathway of many patients comes up against some tolerability problems. The diagnostic procedure is often perceived as stressful or even insidious by the most susceptible subjects. Anxiety, for example, is a typical symptom of those people who refuse or fear to enter the confined space of the machine with the obvious restrictions of movement implied in the execution of the examination. Even the sound emitted by the machine scan is a significant element of disturbance for many patients (Van Minde *et al*, 2014).

Almost 40% of people undergoing a magnetic resonance test show moderate to high levels of anticipatory anxiety, while a fraction of patients (5% to 10%) experience panic or claustrophobia. The scarce tolerability of MRI can be further exacerbated by the need to apply head and neck coils to the patient (Van Minde *et al*, 2014). Another problematic aspect is that anxiety attacks in patients, before or during the examination, may lead to low diagnostic accuracy, poor quality of the imaging output, up to the refusal to repeat a MRI in the future. Furthermore, patients' negative experiences linked to this diagnostic procedure may affect their perceptions of the quality of care (MacKenzie *et al*, 1995; Dantendorfer *et al*, 1997).

Psychological methods have been proposed to manage some critical individual reactions related to the magnetic resonance test (Lukins *et al*, 1997; Munn *et al*, 2013). Although these strategies can be helpful in reducing patient stress, they are not always suitable for routine use because they increase the duration of the examination and require greater investments in health professional staff. Thus, the most common solution is to administer sedative products based on benzodiazepines (Pinel 2000). Although sedation with benzodiazepines makes it possible to improve patient performance during the MRI test, such an option is not without its problems.

## 4. Side effects of benzodiazepines

As emphasized from a growing biomedical literature, benzodiazepines are no longer recommended. These molecules are considered inappropriate due to their well-known negative effects, observed especially in the elderly. Benzodiazepines cause memory troubles and increase the risk of falls, fractures and various types of accidents. Recent evidence shows that even the sporadic use of these drugs is associated with relevant health hazards (Tannenbaum 2015). In the diagnostic context of magnetic resonance, the administration of benzodiazepines requires that patients be prepared and monitored even after the conclusion of the examination, due to side effects of the treatment (Grey *et al*, 2000). The result is an additional and unavoidable commitment by health care operators who must carefully monitor all patients and particularly outpatients. In fact, it is strictly not recommended driving cars or performing other complex activities after taking benzodiazepines (Brennan *et al*, 1988; Murphy *et al*, 1997).

## 5. Case report

### 5.1 Materials and methods

Given the above difficulties linked to the use of benzodiazepines, our staff at the Department of Diagnostics and Imaging Radiotherapy of the National Cancer Institute decided to test a different approach. A simple protocol was implemented to manage the procedure of magnetic resonance and assess the potential benefits both for patients and the work of medical staff. The protocol was based on treating patients with Homéogène 46 several minutes before entering the MRI machine. Homéogène 46 is a low-dose preparation developed by Laboratoire Boiron, used in the treatment of sleeping disorders or to control states of irritability, mild anxiety and states of agitation. The composition of a Homéogène 46 tablet is the following: Datura stramonium 3 DH - 1.2mg; Hyoscyamus niger 3 DH - 1.2mg; Passiflora incarnata 3 DH - 1,2mg; Ballota foetida 3 DH - 1,2mg; Nux moschata 4 CH - 1.2mg; to 0.0012 g; Excipient q.b. at 0.20 g. Each patient recruited in the study had to met at least one of four eligibility criteria: 1) patients with no sedation who explicitly asked for sedation to perform the MRI test; 2) patients with no sedation who refused to enter the MRI machine; 3) patients with no sedation who asked to stop the examination due to the sudden appearance of anxiety and agitation during the centering phases; 4) patients with no sedation who had used benzodiazepines in previous MRI tests.

The low-dose preparation was proposed and administered directly by the doctor who performed the magnetic resonance imaging or by nursing staff (under medical supervision) after a brief informative interview about the homeopathic product. Outpatients who had already taken benzodiazepines on their own initiative were excluded, as well as were hospitalized patients who had already been given benzodiazepines in the ward or patients who explicitly had refused to take any drug. Patients were recruited from December 2007 to April 2018 and treated with Homéogène 46. The effectiveness of the treatment was assessed in terms of 1) effectiveness of the drug in controlling stress symptoms, and 2) effectiveness of the drug in facilitating the complete execution of the test without slowdowns. In other words, the beneficial effect of the treatment should have been extended for as long as necessary to complete the diagnostic procedure. The quality of the radiograms was evaluated and used as a more or less good outcome parameter. Assessing the quality of the imaging output,

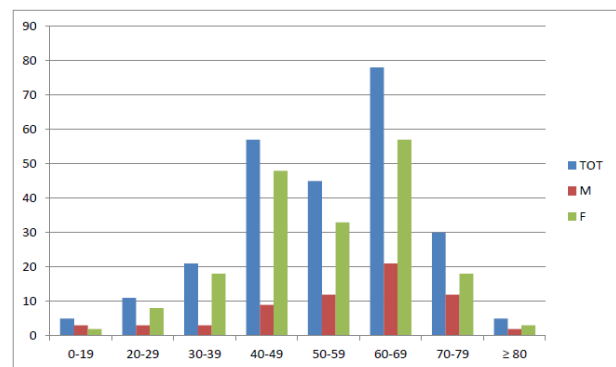
three levels of medical reporting were obtained: i) totally reportable output, ii) partially reportable output, iii) not reportable output.

AGE	M	F	FREQ (%)	CUM FREQ (%)
0-19	3	2	5 (2%)	5 (2%)
20-29	3	8	11 (4.4%)	16 (6.3%)
30-39	3	18	21 (8.3%)	37 (14.7%)
40-49	9	48	57 (22.6%)	94 (37.3%)
50-59	12	33	45 (17.9%)	139 (55.2%)
60-69	21	57	78 (31%)	217 (86.1%)
70-79	12	18	30 (11.9%)	247 (98.0%)
≥ 80	2	3	5 (1.9%)	252 (100%)
TOT	65	187	252	252

**Table 1: Age class and gender.** Eligible patients grouped by age class and gender (frequency and cumulative frequency). Note that 158 (63.2%) patients were aged over 50 years.

The time required by the procedure was also estimated, taking into account that in the daily diagnostic practice an average duration of 30-40 minutes is considered desirable.

Subjective reactions were also recorded by developing an unstructured free survey presented to patients after completing the diagnostic procedure. This informal tool has been designed to collect patients' spontaneous reactions and perceptions, as well as their level of satisfaction. Not being a mandatory task for patients, the survey has been used only to have their personal and immediate feedback.



**Fig. 1: Age distribution.** Frequency distribution of age of the 252 eligible patients. Mean = 54.5 years; median = 56 years; range = 9-88 years.

### 5.2 Results

In the table 1 and figure 1, basic statistical information about the target patients included in this study is shown.

From 2 to 4 sublingual tablets of Homéogène 46 were given to 244 out of the 252 subjects included in the treatment (65 males; 187 females; mean age 54.5 years). With the exception of the dosage (depending on individual weight), the homeopathic drug administration has been standardized regardless of whether the

patients were hospitalized or outpatients. No patient was forced or persuaded in any way to take the homeopathic product. Eight patients previously identified for taking the low-dose preparation, were treated with benzodiazepines or were not treated at all, according to their request (these subjects were excluded from those treated with Homéogène 46). The MRI was interrupted in six cases (2.5%), while the radiograms of four patients (1.6%) treated with Homéogène 46 were only partially reportable. For other 234 patients, the imaging output was completely reportable. The low-dose preparation Homéogène 46 appeared to be effective in 95.9% of patients without showing any side effects. The average time required to complete the diagnostic procedure was 32 minutes.

## 6. Conclusion

In general, treating patients with Homéogène 46 allowed the medical staff to perform the diagnostic test without problems. Furthermore, the low-dose preparation made the patients calm and highly manageable, without experiencing any side effects both during the examination and after its conclusion. Outpatients treated with Homéogène 46 who had gone to the hospital unaccompanied, were able to return home alone.

The effective management of the MRI by the medical and nursing staff allowed a clear evaluation of the imaging output. What's more, the average time per patient required for the complete execution of the diagnostic test was not greater than that commonly necessary for patients not requiring any drug.

The low cost of the product along with its simple and rapid administration, the quality of the imaging output, the absence of side effects, and the short duration of the diagnostic test seem very promising. The information available today is consistent with a possible use of the product in diagnostic settings similar to that discussed above.

To conclude, we argue that a better understanding of the pharmacological properties of Homéogène 46 is necessary by carrying out investigations specifically designed to test its effectiveness. For many authors, the randomized controlled studies represent the gold standard to reduce the sources of bias that often negatively influence clinical research. However, studies carried out in the field of integrative medicine are associated with specific difficulties that often make them less suitable to a randomized controlled design. The problem is that some relevant principles and variables of the integrative medicine cannot be properly included into

this design. Just to give a simple example, let's think about the importance that integrative medicine assigns to biopsychological factors, personality traits, social relations, placebo effect etc. within the complex picture of human health and disease.

In order to reduce these problems and to preserve the wide spectrum of the integrative medicine methods, we suggest a non-randomized observational design.

## Ethical approval

This study has been approved by the Bioethics Committee of the National Cancer Institute, Milan (IT). All subjects included in the study provided informed consent before their agreement. The present work has been designed by the MeTeCo Group (Medicine e Terapie Complementari in Oncologia), operating since 1998 at the National Cancer Institute (Milan, IT).

## Conflict of interest

The Authors declare no competing interests.

## References

- Brennan SC, Redd W, Jacobsen PB, Scorr O, Heelan R, Sze GK, et al, 1988, Anxiety and panic during magnetic resonance scans. *Lancet*, 2(8609):512.
- Dantendorfer K, Amering M, Bankler A, Helbich T, Prayer D, Youssefzadeh S, Alexandrowicz R, Himhof H, Katschnig H, 1997, A study of the effects of patient anxiety, perceptions and equipment on motion artifacts in magnetic resonance imaging. *Magn Reson Imaging*, 15(3):301-6.
- Ernst E, 1997, Homeopathy, past present future. *Br J Clin Pharmacol*, 44: 435-437.
- Grey SJ, Price G, Mathews A, 2000, Reduction of anxiety during MR imaging: a controlled trial. *Magn Reson Imaging*, 18(3):351-5.
- Horrobin D, 2007, A brief history of homeopathy. *J Roy Soc Med*, 100: 2, 65-66.
- Lukins R, Davan IG, Drummond PD, 1997, A cognitive behavioural approach to preventing anxiety during magnetic resonance imaging. *J Behav Ther Exp Psychiatry*, 28(2):97-104.
- MacKenzie R, Sims C, Owens RG, Dixon AK, 1995, Patients' perceptions of magnetic resonance imaging. *Clin Radiol*, 50(3):137-43. 8.
- Morrison B, Lilfort RJ, Ernst E, 2000, Methodological rigour and results of clinical trials of homeopathic remedies. *Perfusion*, 13: 132-138.
- Munn ZJ, 2013, Interventions to reduce anxiety, distress and the need for sedation in adult patients undergoing magnetic resonance imaging: a systematic review. *Int J Evid Based Health*, 11: 265-274.

- Murphy KJ, Brunberg JA, 1997, Adult claustrophobia, anxiety and sedation in MRI. *Magn Reson Imaging*, 15(1):51–4.
- Pinel JPJ, 2000, *Biopsychology*. Need-ham Heights, Allyn & Bacon, Boston.
- Tannenbaum C, 2015, Inappropriate benzodiazepine use in elderly patients and its reduction. *J Psychiatry Neurosci*, 40(3): E27–E28
- Van Minde D, Klaming L, Hans W, 2014, Pinpointing moments of high anxiety during an MRI examination. *Int J Behav Med*, 21:487–495.

