



Original Article

ANF therapy[®] for pain management, feasibility, satisfaction, perceived symptom reduction and side effects: a real-world multisite observational study

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Abstract. [Purpose] Non-invasive and drug-free interventions for pain are being developed. One of them is ANF (which stands for “Amino Neuro Frequency”) Therapy[®], which consists in the application of carbonized metal devices on a patient’s skin. We aimed to: 1) test perceived changes in pain intensity after ANF application, 2) record frequency and severity of side effects, 3) assess clinician and patient satisfaction, 4) explore effects on swelling and range of motion (ROM). [Participants and Methods] In this real-world multisite observational study, N=113 physical therapists in 45 countries, applied ANF to N=1,054 patients (Mage=45.2, 56.2% female) with pain complaints. Demographic data, pain intensity (NRS-11), effects of ANF on swelling and ROM, clinician and patient satisfaction and side effects were collected. [Results] Main pain locations were: low back (14.9%), knee (12.4%), neck (10%), and shoulder (9.6%). Pre-treatment pain intensity was high (Mean=7.6, SD=1.9). It significantly decreased post-treatment (Mean=3.1, SD=2.0), $t(1053)=7.25$, with a large effect size (Cohen’s $d=2.2$). Swelling decreased and ROM increased. Average satisfaction with ANF was 92/100. Patients often experienced mild side effects (42.3%): dry mouth, headache and fatigue. [Conclusion] Results show large effect sizes, high satisfaction, and mild and short-term side effects. This is very promising but should be interpreted with caution considering the study limitations.

Key words: ANF therapy[®], Pain, Swelling

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INTRODUCTION

Adequate pain management is a global health priority¹⁾ and a fundamental human right²⁾. Pain effects on quality of life and disability are well-documented³⁾ as well as the significant economic impact on the patients and healthcare systems^{4, 5)}. However, access to appropriate management is not universal^{6, 7)} and the available treatment options have shown limited efficacy. One of the most widespread ways of treating persistent pain is administering medication⁸⁾, which is often helpful short-term, but is not exempt from considerable side effects, specially opioids⁹⁾, including elevated misuse and dependence rates^{10, 11)}.

Consequently, there is a need for increasing research on the development of non-pharmacological (i.e., drug-free) therapies for pain management. In this regard, ANF (which stands for “Amino Neuro Frequency”) therapy is an intervention with only infrequent and mild side effects and great benefits observed at a clinical level, but which efficacy has not yet been tested in a scientific manner. Recent systematic reviews have shown that other frequency-based therapies, such as administering

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low-intensity and low-frequency electromagnetic fields¹²⁾ or interferential currents¹³⁾ are effective for pain management, however, those therapies are not widely available and require specific training and complex infrastructure to be administered. This is the first time the effects of ANF therapy in particular have been tested.

Regarding the safety of the treatment, a Post Market Surveillance program to ensure the safety, quality, and performance has been conducted by the manufacturer since ANF started to be used in 2012, and several mild and short-term known side effects have been observed, specifically: headache, dry mouth, dizziness, light headedness, light flu-like symptoms, shivers, fatigue, general discomfort, runny nose, hives or skin issues, itching, nausea, vomiting, and diarrhea. A potential explanation for such symptoms is the overreaction or sensitivity of the body, which has been observed in similar frequency-based treatments¹³⁾ or the possibility that the treatment might potentiate medication effects and side effects by its effect on the endogenous opioid system¹⁴⁾.

This is the first study to scientifically assess and report on the effects of ANF, as well as its feasibility and satisfaction. We aimed to: 1) test perceived changes in pain intensity after ANF application, in the sample as a whole, and as a function of: sex, age, pain duration, location of the main pain complaint, type of issue, and presence or absence of other health problems; 2) record the frequency, severity and duration of any side effects, and 3) assess clinician and patient satisfaction. As an exploratory aim, we sought to explore the perceived effects of ANF on both swelling and range of motion (ROM) in the treated area. Based on prior clinician observations and patient reports, we hypothesized that patients treated with ANF would report significant reductions in pain intensity and mild-to-none side effects. Satisfaction from both patients and clinicians was expected to be high.

PARTICIPANTS AND METHODS

Procedures. The study, a single-arm observational study, consisted in a review of the data routinely collected in 113 physical therapy clinics during therapy sessions in which the clinicians applied ANF Therapy. The study was first presented to the Ministry of Health of Denmark and was considered minimal risk and exempt of a full ethics review. Clinicians obtained consent from their patients. Only data from patients who consented was included in the analyses. The study complies with the Declaration of Helsinki. Neither clinicians nor patients received economic compensation for sharing their data with the study.

The ANF tool is a small device made of a polymerization mixture (PET) of ethylene glycol and terephthalic acid with 22.8% carbon metallic fragments embedded on the top surface in order to store and transfer frequency in the form of sub-harmonic signals. It is bonded with a skin-friendly adhesive. After a complex process, this thin metal layer of the device has exactly the amount of pure carbonized metal to hold electrical frequencies. This combination is hypothesized to allow the device to be charged with frequencies and also to send, receive and reflect the frequencies within the body. The devices (Fig. 1) can be charged with different oscillation, speed and wave forms, therefore, aiming to target different neurons, cells and organs. They should not be applied on open wounds or reddened skin.

ANF therapy[®] consists of more than 130 devices with unique frequencies and functions. The device is activated and starts emitting the frequency when applied on the skin, facilitated by the human infrared heat and sunlight. The ANF Therapy Method, is a Patented Model U202032252, ES1259974: developed by Dr. Mikel H-G Hoff. This method guides certified healthcare professionals in how to utilize the ANF device to approach and alleviate injuries and diseases in a holistic manner, chronic pain being one of the main ones.



Fig. 1. Placement of ANF Therapy devices on a patient's back.

All participating clinicians received standard training by the company ANF Academy, consisting in 30.5 hours of classes and 16 hours of practice. At the training, ANF therapists learned to design ANF protocols. Then, clinicians proceeded to implement the new technique as part of their practice and shared de-identified data from their sessions, so the instructors would assess whether the protocols were correctly designed. Only data from first treatment sessions were included to avoid summation or habituation effects. After the training finished in March 2021, data collection started. The deadline the clinicians had to provide the data in order to graduate from the class was December 2021. ANF Academy signed an agreement with the University of Málaga, Spain, to have a team of external senior scientists conducting an independent analysis of the results and interpreting the data.

A typical ANF session follows the ANF Therapy Method and consists of 3 stages: 1) Assessment of the patient, 2) ANF Device application, and 3) Re-assessment. During the Assessment stage, the ANF Therapist examines the patient's body searching for the root cause of the pain or symptom (this may include the nervous, cardiovascular, lymphatic, and musculo-skeletal systems). Based on the outcomes, the ANF therapist designs a personalized ANF protocol, which is a combination of ANF Devices. During stage 2, the ANF therapist applies the ANF Device on clean and dry skin, ensures the patient is hydrated and controls the patient's response. The re-assessment occurs 10 to 60 minutes afterwards. No other co-interventions (e.g. physical therapy) are applied in the session.

Measures. Demographic and clinical data. Clinicians collected information about: sex, age, main complaint, duration of the problem, and general health status of their patients.

Pain intensity. Pain intensity was assessed at the beginning and end of the session by asking patients to report on their pain with a Numerical Rating Scale (NRS-11) where 0 is "No pain" and 10 is "The worst possible pain", which is the gold standard for pain intensity assessment¹⁵.

Swelling and Range of Motion (ROM). Changes in swelling and ROM after ANF application were visually inspected by the clinicians and reported on a 7-point Likert scale, ranging from "Very much worse" to "Very much improved".

Clinician and patient satisfaction. Satisfaction with the ANF protocol and its results was assessed by asking the patient, and with clinician self-report, using a 0–100 satisfaction scale where 0 means "Not satisfied" and 100 means "Very satisfied".

Side effects. Three categories of adverse events were created: 1) detox symptoms or mild side effects (presence or absence, intensity and duration), specifically: headache, dry mouth, dizziness, light flu-like symptoms, shivers, fatigue, general discomfort, runny nose, hives, itching, nausea and vomiting; 2) severe reactions (presence or absence): life-threatening illness or injury, permanent impairment of body structure or body function, hospitalization, medical or surgical intervention (not planned), 3) unexpected positive benefits (assessed with an open-ended question: "Have you experienced any unexpected positive effects?"). Side effects were assessed during the session with a questionnaire and at the following session.

Participants: Therapists. Study clinicians were licensed therapists (mostly physical therapists). A total of 113 therapists (healthcare professionals with >2 years' experience) from 45 countries participated in the study. Sixty-five of them (58%) were female.

Patients. Patients were people with a pain complaint who attended the clinics and were 18 years old or older. The only exclusion criterion was to have a severe comorbidity (e.g. cancer). Inclusion and exclusion criteria were purposefully kept broad to enhance external validity.

Data analysis plan: To test the study hypotheses, we compared pre and post-session scores on the main outcomes using paired samples t-tests (as it is indicated for large samples irrespective of their distribution¹⁶), both for the total sample and several subgroups, created as a function of: sex (males and females), age [young adults (18–39 years), middle-aged adults (40–59 years), senior adults (60–79 years), older adults (above 80 years)], pain duration, main complaint bodily location, presence or absence of other health issues. We then calculated the effect sizes of such changes using Cohen's ds. Analyses of covariance (ANCOVAS) were conducted to test the between-participant effects of sex, age, presence of chronic pain and presence of other health issues on pre to post-treatment differences on pain intensity. Percentages were computed to test for changes in swelling and ROM. Finally, means and standard deviations, percentages and frequencies were computed for reported satisfaction and side effects. All the analysis were conducted using IBM SPSS 26 for Mac (IBM corporation, Armonk, NY, USA)¹⁷.

RESULTS

Description of the sample. Therapists provided data for 1355 patients. From them, 301 (22%) cases were excluded for the following reasons: 168 (12%) patients did not provide consent for their data to be shared, 55 (4%) were minors, 4 (0.3%) had cancer, 55 (4%) were follow-up sessions, 11 (0.8%) were duplicates, and in 8 (0.6%) of the cases the therapist did not complete the form correctly. The remaining sample (N=1,054; mean age=45.2 years, SD=14.6, range 18–99 years; N=592, 56.2% female) was included in the analysis. Participants were recruited from 45 different countries, with most of them living in Australia N=198 (19%), USA N=141 (13%), Romania N=103 (10%), and Kuwait N=96 (9%).

The most frequent location of the main pain complaint was: low back N=157 (14.9%), knee N=131 (12.4%), neck N=105 (10%), and shoulder N=101 (9.6%). Pre-treatment pain intensity was high on average (Mean=7.6, SD=1.9), about half of the patients reported having a chronic pain problem (i.e., pain lasting over 3 months: N=472, 44.8%), followed by patients reporting a pain problem that lasted from a few days to a month (N=322, 30.6%). In addition to their pain problem, about

half of the sample N=507 (48.1%) reported the presence of other health issues, such as: orthopedic complaints, low-grade inflammation or autoimmune disorders. About a quarter of the sample N=251 (23.8%) was taking medication for their pain (analgesic or anti-inflammatory) at the time of the visit. See Table 1 for the full demographic and clinical information.

ANF effects on pain intensity: As expected, pain intensity was significantly reduced after ANF treatment in the sample as a whole. It decreased significantly from pre-treatment (Mean=7.6, SD=1.9) to post-treatment (Mean=3.1, SD=2.0), $t(1053)=72.5$, $p<0.001$ with a large effect size (Cohen's $d=2.2$).

Regarding the effect of demographic or disease characteristics on the magnitude of pain reduction, sub-group t-tests a function of: sex, age, pain duration, bodily location of the pain, presence or absence of other health issues showed that pain intensity was consistently significantly smaller after the application of the ANF treatment ($p<0.001$) with large effect sizes

Table 1. Demographic and clinical characteristics of the patients

	N (%)
Age ^a (years)	
Young adult (18–39)	314 (29.8)
Middle-aged adult (40–59)	478 (45.5)
Senior adult (60–79)	173 (16.4)
Old adult (above 80)	20 (1.9)
Sex (female)	592 (56.2)
Main complaint location	
Abdomen	32 (3.0)
Ankle	50 (4.7)
Chest	11 (1.0)
Elbow	55 (5.2)
Face	18 (1.7)
Foot	43 (4.1)
Hand	13 (1.2)
Head	36 (3.4)
Hip	62 (5.9)
Knee	131 (12.4)
Lower arm	12 (1.1)
Low back	157 (14.9)
Lower leg	58 (5.5)
Middle back	17 (1.6)
Neck	105 (10.0)
Pelvis	17 (1.6)
Ribs	2 (0.2)
Sacrum	10 (0.9)
Shoulder	101 (9.6)
Upper arm	16 (1.5)
Upper back	18 (1.7)
Upper leg	55 (5.2)
Wrist	35 (3.3)
Time with pain	
Just happened	112 (10.6)
Few days to 1 month	322 (30.6)
1–3 months	146 (13.9)
3–6 months	109 (10.3)
6 months to 1 year	125 (11.9)
1–5 years	124 (11.8)
5–10 years	50 (4.7)
10–15 years	23 (2.2)
15–20 years	41 (3.9)

^aAge group was missing for 69 participants.

Table 1. Continued

	N (%)
Country of patient	
Algeria	5 (0.5)
Argentina	15 (1.4)
Australia	198 (18.8)
Austria	31 (2.9)
Bahrain	1 (0.1)
Belgium	2 (0.2)
Bosnia-Herzegovina	1 (0.1)
Brazil	9 (0.9)
Canada	15 (1.4)
Comoros	1 (0.1)
Croatia	16 (1.5)
Denmark	27 (2.6)
Egypt	4 (0.4)
France	56 (5.3)
Germany	12 (1.1)
Ghana	1 (0.1)
Hungary	11 (1.0)
India	6 (0.6)
Indonesia	17 (1.6)
Italy	4 (0.4)
Jordan	1 (0.1)
Kuwait	96 (9.1)
Lebanon	1 (0.1)
Macedonia	1 (0.1)
Mexico	2 (0.2)
New Zealand	32 (3.0)
Norway	4 (0.4)
Pakistan	1 (0.1)
Palestinian Territories	2 (0.2)
Philippines	1 (0.1)
Portugal	14 (1.3)
Romania	103 (9.8)
Saudi Arabia	16 (1.5)
Serbia	7 (0.7)
Singapore	17 (1.6)
Slovenia	25 (2.4)
South Africa	1 (0.1)
Spain	9 (0.9)
Sweden	63 (6.0)
Switzerland	18 (1.7)
Tunisia	1 (0.1)
Turkey	4 (0.4)
United Arab Emirates	41 (3.9)
United Kingdom	21 (2.0)
United States	141 (13.4)

^aAge group was missing for 69 participants.

(Cohen's d s=1.7–2.7). See Table 2 for details. ANCOVAs including the same variables (minus pain location due to the large variability) showed non-significant effects on pain reduction ($p>0.1$).

Side effects. In line with the hypotheses, no severe side effects were reported by any patient. Mild side effects were present in 446 (42.3%) of patients, and they were rated as low intensity in most cases $N=360$ (80.7%). The reported side effects matched the list of expected symptoms (known as “detox symptoms”). The most common were: dry mouth, experienced by 196 (18.6%) patients, headache $N=192$ (18.2%), and fatigue $N=141$ (13.3%). When present, they lasted from minutes to hours in most cases $N=343$ (76.9%). See a full list of side effects on Table 3. Additionally, a quarter of the sample $N=267$ (25.3%) reported experiencing positive effects after the administration of ANF, beyond the intended pain reduction, such as improving sleep quality or experiencing a sense of general relaxation.

Clinician and patient satisfaction with ANF. As hypothesized, both clinician and patient satisfaction levels were high. Specifically, clinicians reported an average satisfaction of 92/100 ($SD=13.2$), with 93.9% satisfaction levels of 70/100 or higher. Similarly, patients reported an average satisfaction of 93/100 ($SD=13.5$), with 94.3% showing satisfaction levels of 70/100 or higher.

ANF effects on swelling and ROM: Swelling was a relevant issue in 462 (43.8%) patients; from them 325 (70.3%) showed significant improvement, 123 (26.6%) showed at least some improvement and only 14 (3%) experienced a lack of change after treatment. Regarding ROM, it was a relevant issue for 840 (79.7%) of patients, with 653 (77.7%) showing significant improvement and 169 (20.1%) showing at least some improvement. Only 18 (2.1%) experienced a lack of change after treatment. Information was not collected for the 592 patients for whom Swelling was not an issue and for the 214 for whom ROM was not relevant.

Table 2. Pre- to post-ANF treatment changes in pain intensity scores, as reflected by pre- and post-treatment scores, and effect sizes associated with these changes

Sub-group	Pre-treatment Mean (SD)	Post-treatment Mean (SD)	Effect size (Cohen's d)
Whole sample	7.6 (1.93)	3.1 (2.02) ***	2.2
Sex			
Females	7.6 (2.02)	3.1 (2.05) ***	2.3
Males	7.6 (1.82)	2.9 (1.98) ***	2.3
Age			
Young adults	7.3 (1.91)	2.9 (2.02) ***	2.2
Middle-aged	7.5 (1.97)	3.0 (2.01) ***	2.1
Senior adults	7.7 (1.99)	3.0 (2.05) ***	2.1
Pain duration			
Acute	7.7 (1.86)	3.1 (2.06) ***	2.4
Chronic	7.4 (1.95)	3.0 (1.92) ***	2.3
Main complaint			
Abdomen	6.3 (2.61)	2.2 (1.87) ***	1.7
Ankle	8.0 (1.77)	3.7 (2.15) ***	2.3
Elbow	7.8 (1.56)	2.8 (1.83) ***	2.9
Foot	7.6 (1.80)	3.2 (1.70) ***	2.2
Head	6.7 (2.60)	2.5 (2.10) ***	1.8
Hip	7.7 (1.74)	3.2 (1.90) ***	2.5
Knee	7.7 (1.73)	3.0 (1.94) ***	2.2
Low back	7.7 (1.59)	3.0 (2.00) ***	2.4
Lower leg	7.9 (1.52)	3.7 (1.92) ***	2.3
Neck	7.7 (1.88)	2.9 (2.00) ***	2.2
Shoulder	7.5 (1.90)	2.8 (2.09) ***	2.2
Upper leg	7.5 (1.98)	3.2 (1.83) ***	2.7
Wrist	7.9 (2.77)	3.3 (3.57) ***	2.3
Other health issues ^a			
No	7.7 (1.83)	3.2 (2.05) ***	2.3
Yes	7.4 (2.03)	2.9 (1.99) ***	2.3

t-tests were only conducted when sample sizes for the sub-group were $N>30$; the group with older adults and some pain locations were not analyzed. ***Significant change between pre-treatment and post-treatment $p<0.001$. ^aIn addition to their pain problem, some participants reported the presence of other health issues, such as: orthopedic complaints, low-grade inflammation or autoimmune disorders. ANF: amino neuro frequency.

Table 3. Side effects type and frequency

Side effects	N (%)
Dry mouth	196 (18.6)
Headache	192 (18.2)
Fatigue	141 (13.3)
General discomfort	72 (6.8)
Dizziness	67 (6.3)
Light flu-like symptoms	60 (5.7)
Itch	39 (3.7)
Shivers	30 (2.8)
Runny nose	30 (2.8)
Nausea	17 (1.6)

DISCUSSION

This is the first study describing the ANF therapy procedures and results in a systematic manner and providing a scientific view of the effects usually observed in clinics. All the results were in line with the hypotheses showing large effect sizes, high satisfaction of both clinicians and patients, and only infrequent mild and short-term side effects.

Specifically, pain intensity was significantly lower after ANF application, in line this is also observed in literature reviews of with other treatments that use electromagnetic fields¹²⁾ and interferential currents¹³⁾. This was observed in the sample as a whole, and was maintained when subgroups were created, which may indicate that ANF therapy is suitable for a wide range of patients, irrespective of their age, sex, or clinical features.

Regarding side effects, they matched the known effects observed in the clinics. They were of mild severity, low intensity and short duration. This contrasts with the known effects of opioids¹⁸⁾, which include mild or moderate effects such as confusion, drowsiness, constipation or nausea, but also severe associated problems like depressed breathing and addiction problems⁹⁾. We also explored whether patients had experienced any other positive effects they associated with the ANF treatment, and we confirmed that about a quarter of the sample had improved sleep and experienced a sense of relaxation. This finding should be more exhaustively evaluated to confirm its reproducibility. Similar findings (i.e. patients experiencing fatigue or lightheadedness, but also improved sleep and general relaxation) have been reported in other non-pharmacological interventions for pain, such as acupuncture¹⁹⁾.

We also aimed to assess clinician and patient satisfaction with the ANF technique as a way to measure its feasibility, which was supported by over 94% of clinicians and patients being highly satisfied with ANF.

Finally, the effects of ANF on both swelling and range of motion (ROM) were positive. In patients where this was a treatment goal, 70% significantly decreased swelling and 78% significantly increased ROM. Future studies should use standardized measures, such as ROM angle measurement using a goniometer²⁰⁾ before and after the intervention, instead of relying on the clinician's observation of the change.

The findings of the present study should be interpreted in light of several limitations. First, the data were collected in a single session design is cross-sectional, which prevented us from learning about the long-term effects of ANF therapy. Second, the nature of the study is observational (single arm). Without systematically and randomly manipulating the treatment conditions, it is possible that some biases were undetected (including nocebo and placebo effects). Third, average income was not collected. All the patients had the financial ability to seek help at a specialized clinic, hence, it is possible that the results are not generalizable to patients with low income. Finally, some non-standardized measures were used to assess the study variables (such as the assessment of swelling and ROM). This prevents comparing those findings with ones obtained in other studies.

Despite the limitations, the study has important strengths. First, the large sample size allowed for capturing patient-to-patient variability and to conduct sub analysis based on demographic and clinical characteristics. Second, the study is multisite and international, allowing to include diverse patients from several cultural and racial backgrounds, which makes the results extensively generalizable. Third, the high number of clinicians applying the ANF protocol (N=113) ensures that there is not a "method effect" due to the characteristics or the skills of a specific therapist, and satisfaction levels support the feasibility of the ANF Treatment. Fourth, both patients and clinicians completed measures, avoiding a single-informant bias. Fifth, it is an ecologic real-world study, where clinicians administered the technique to patients as part of their clinics routine care, which avoids biases introduced by collecting data in more controlled environments (such as university laboratories)²¹⁾. On the other hand, to control for the quality of the included cases, the reported protocols were reviewed by the ANF Academy Manager (IH) and any case with a deviation from the standard instructions was excluded (0.6% of the cases). Sixth, adverse events

were transparently assessed and reported, which is a key aspect of any newly developed intervention which, unfortunately, is not often included in scientific works beyond what is strictly mandatory²²⁾.

The effects shown by this innovative treatment reinforce the idea that treatments targeting pain reduction have an effect on neural activity²³⁾. Other promising approaches in this line are neuro-modulatory treatments for pain²⁴⁾ which have an interesting line of research focused on neurofeedback²⁵⁾.

Future research is warranted for the assessment of ANF efficacy against a sham intervention (similar to what has been studied for acupuncture)²⁶⁾ in a randomized controlled trial (RCT), with double-blind assessment and a longitudinal design. This would allow for a follow-up of the duration of treatment effects, and of any adverse event. Studies including brain imaging would allow to better understand how ANF works in the pain network.

In conclusion, this study provides preliminary evidence showing that ANF therapy[®] is a safe, effective and feasible intervention that is liked by both clinicians and patients. More research is needed to determine its efficacy in a RCT and its long-term effects.

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Conflict of interest

RV has received scientific consulting fees from ANF Academy. IH works at ANF Academy. The rest of the authors have no conflicts of interest to declare.

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