Suppression of Pain Sensation Caused by Millimeter Waves: A Double-Blinded, Cross-Over, Prospective Human Volunteer Study

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We conducted a double-blinded, randomized, cross-over, prospective trial to evaluate the pain relief effect of millimeter waves (MW) under experimental conditions. The cold pressor test was used as a model of tonic aching pain. Twelve healthy male volunteers were exposed to an active medical MW generator and to a disabled sham generator with at least 24 h between exposures. Characteristics of continuous-wave electromagnetic output from the active generator were: wavelength 7.1 mm, incident power density 25 mW/cm², and duration of exposure 30 min. MW produced a significant (P < 0.05) suppression of pain sensation, with an average 37.7% gain in pain tolerance and a 49.3% increase in pain sensitivity range (the latter being the difference between pain tolerance and pain threshold values). Of the 12 volunteers, 7 (58.3%) reacted to the active MW generator with an increased pain tolerance, and the individual reactions varied from 120% to 315% comparison with their own preexposure levels. MW therapy can potentially be used as a supplementary or alternative treatment for pain relief. Implications: Pain management is still a significant medical problem. In a double-blinded, experimental setting, we confirmed that low-intensity millimeter wave therapy can reduce pain sensitivity in healthy human volunteers and can potentially be used as a supplementary or alternative treatment for pain relief.

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Electromagnetic millimeter waves (MW) within the range of frequencies 37–78 GHz at incident power levels <25 mW/cm² have been used for medical purposes in several Eastern European countries for more than a decade. Until now, this treatment modality has been practically unknown to Western physicians. Our analysis of the available literature revealed that the most common effects of MW therapy are sedation and pain relief, which are reported by most patients and doctors involved in this treatment (1). This is a very important feature, and, if proven successful, medical MW generators could become valuable supplementary or alternative means of providing relief in various pathologic conditions characterized by pain.

However, with very few known exceptions (2), clinical results with the use of MW were not obtained in a double-blinded manner, which precludes separating placebo effects and experimental biases from the MW treatment procedure. Thus, before organizing large-scale clinical trials, we conducted a relatively small double-blinded study aimed at investigating the possible pain relief effect of MW in healthy human volunteers. The cold pressor test was used as a measure of sensitivity to experimental pain. The results of our study are described below.

Methods

Twelve volunteers participated in the study. The volunteers were either employees or students of the Center for Biomedical Physics, Temple University School of Medicine, who were informed about the physical and biological properties of MW relevant to human health and who freely gave their consent to participate in the study. The protocol of this study was approved by our institutional review board. The eligibility criteria for volunteers were: healthy adults (>18 yr old); no use of pain relievers at least 24 h before testing; and baseline response time in cold pressor test <2 min.

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Because gender differences can affect sensitivity to certain nociceptive stimuli (3), female volunteers were not included in this study. All volunteers were healthy men 18–65 yr old (mean age 37.3 ± 4.9 yr). None was a chronic pain sufferer or was taking medication of any kind, including vasoactive drugs or substances.

We slightly modified the cold pressor tests described previously (4–6). The tests were conducted in the same room with an ambient temperature 20–22°C. After the initial measurement of arterial blood pressure and pulse rate, the volunteer put his nondominant hand into a warm water bath (37.0 ± 1.0°C) for 2 min to equalize the initial hand temperature. Immediately thereafter, the same hand was immersed up to the wrist in an open position into a cold water bath containing melting ice (1.0 ± 0.5°C). To ensure the uniform distribution of cold water within the bath, a magnetic stirring bar was used.

Each volunteer was instructed to report sensations according to a scale placed in front of him. The operator conducting the test recorded the patient’s reports in the protocol using computer-generated time stamps. The time of immersion of the hand into the cold water was registered as the initial point (0); records were then made for the time to each of the following sensations: cool, cold, very cold, pain 1 (the onset of pain), and pain 2 to pain 10 (intolerable pain, hand withdrawal). The following two variables were the main end points for evaluating the effect of MW: time to reach the stages pain 1 (Pain threshold) and pain 10 (Pain tolerance). The third variable, pain sensitivity range, was calculated as the difference between the values of pain tolerance and pain threshold as defined by Wolff (7).

When the volunteer withdrew his hand, he took the metal probe of the digital thermocouple thermometer into his hand to measure the lowest temperature of the palm (which usually was displayed within 5–7 s) and the temperature of the palm 30 s after withdrawal. At the same time, the arterial blood pressure and heart rate were measured again.

Each volunteer underwent such a test six times with ≥24-h break between the tests. In the beginning, three baseline tests without exposure to MW were made to study the normal response of each individual. The first baseline test was intended to train the volunteers, and the results obtained in this test were not included in the data analysis. On completion of the baseline studies, the volunteers were consecutively exposed to an active and a sham MW generator in a random order, and the cold pressor test was performed after each exposure. The final test was performed to determine whether the volunteers developed a lower level of sensitivity to the cold stimulus as a result of multiple testing.

The Russian-made medical MW generators, Yav-1, used in this study emitted a continuous electromagnetic signal with a frequency of 42.25 ± 0.05 GHz (corresponding wavelength 7.1 mm) and incident power density of 25 ± 5 mW/cm². Chest skin in the lower third of the sternum was exposed to the generator for 30 min while the patient was sitting in an armchair. The waveguide of the generator was located at a distance of <1 cm from the skin surface. The order of exposure of volunteers to an active and sham generator was varied randomly.

The steady-state temperature increase on the surface of the sternum area skin exposed to the MW generator under the conditions of our study was 1.6 ± 0.2°C after 5 min of exposure. Because the heating rate was rather slow, this temperature increase was undetectable to the volunteers. A separate series of experiments demonstrated that volunteers were unable to feel whether they were exposed to an active or to an inactive generator. Of the 15 individuals who participated in that study, 8 felt nothing, and feelings of slight pressure or slight warmth at the site of exposure alternated in the remaining 7, regardless of whether they were exposed to the sham or the active generator.

Two identical devices were used for exposure to electromagnetic MW and sham exposure. The output of the sham generator was disabled, but all of the external features of both generators were the same. Neither the operator nor the patient knew which device was active during the study. The generators were marked 1 and 2, and the responses of the volunteers were analyzed based on their reaction to a certain generator, after which the code was revealed by the third person who did not participate in the study as a volunteer or an operator.

To determine whether experimental results were affected due to training, baseline response durations of the last test were compared with those of the preliminary tests (Tests 2 and 3). Had there been any increase in any subject’s baseline response duration, the subject would have been removed from the study. Using this criterion, no subjects were excluded from our study.

Comparison of baseline readings with the results of true and sham exposures was performed by using Wilcoxon’s signed-rank paired sample test (8). The level of significance was set at P < 0.05 for all tests.

Results

Possible side effects were monitored by observing the volunteers and by asking them questions about any reactions they could assign to the treatment. No toxic side effects of one-time exposure to MW were noticed. Of the 12 volunteers, 4 reported “sleepiness” during exposure to the active, but not to the sham, generator.
However, they were not asleep, and they were able to answer questions and follow instructions adequately.

We evaluated four variables as functions of exposure to MW in this study: arterial blood pressure, heart rate, palm temperature after withdrawal from the cold water as a sign of peripheral blood flow, and cold-induced pain sensitivity.

According to numerous experimental reports, arterial blood pressure and heart rate increase in response to the cold pressor test (7,9). Moreover, according to Fillingim and Maixner (10), the level of resting blood pressure correlates with thermal pain responses in men.

The pulse rate of volunteers measured within 1 min after hand withdrawal from the cold water was increased by 5.6% on average, and the mean increases in systolic and diastolic pressures were 3.7% and 7.0%, respectively. There was no significant influence of MW on these variables. Additionally, there was no correlation between the baseline arterial blood pressure and pain sensitivity in the cold pressor test.

The average palm temperature of the volunteers immediately after hand withdrawal was 12.8 ± 0.6°C; 30 s later, it increased to 16.6 ± 0.6°C. Exposure to either of the MW generators did not result in significant changes of palm temperature compared with the data from baseline tests. Thus, within this study, there were no meaningful effects of MW on heart rate, arterial blood pressure, or peripheral blood flow in the hand.

The response of volunteers to the nociceptive stimulus was evaluated by pain threshold (Pain 1), pain tolerance (Pain 10), and pain sensitivity range data. Exposure to the active MW generator resulted in a statistically significant (P < 0.05) increase in pain tolerance by 37.7% and in pain sensitivity range by 49.3% (Fig. 1). Type and extent of individual reactions of the volunteers to MW treatment varied. Of the 12 subjects exposed to the active generator, 7 (58.3%) demonstrated an increase in pain tolerance by >20%. In two volunteers (16.7%), a decrease in pain tolerance of >20% was registered. The remaining three volunteers showed very little change in their response to the cold pressor test after MW treatment. There were no age differences in the group of volunteers “sensitive” to MW (mean age 38.2 ± 5.9 yr) and those “insensitive” to MW (mean age 34.7 ± 10.2 yr). Examples of individual responses are given in Figure 2.

Discussion

Our results indicate that, within the limits of our study, MW produce suppression of experimental pain sensation in healthy male volunteers.

Pain relief is the most common effect of MW therapy; it has been registered in 73%–100% of patients with heart disease, peptic ulcers, and phantom pain after amputations. Flaws of these and other studies include lack of double-blinded design, concomitant use of conventional drugs (including pain relievers), qualitative rather than quantitative analysis of the results, and failure to supply sufficient detail in publications (1,11). Each of the above criticisms can severely affect data validity. For example, the placebo effect alone can account for at least 33% of clinical improvement in patients with various diseases (12). In the present study, we sought to avoid these weaknesses by performing a randomized, double-blinded trial using healthy male volunteers who did not take any pain relievers and by providing quantitative results.

All myelinated nerve fibers become blocked at temperatures <5°C (13). Unlike other experimental conditions (electric shock, contact heat pulse, application of chemical nociceptive stimuli), the cold pressor test produces sustained activation of deep C-fiber receptors, mostly located along veins (14). This results in
Tonic aching pain, which mimics chronic pain better than experimental methods inducing acute pain (15). Furthermore, the cold pressor test is one of the most sensitive models for measuring opioid-induced analgesia in healthy volunteers (16). Using this test, significant correlation has been shown for the analgesic effect and plasma levels of morphine, whereas nonsteroidal antiinflammatory drugs with pain relief effects were indistinguishable from placebo in this model (17). Our previous findings demonstrated a possible involvement of opioids in the systemic whole body response to MW exposure: both the increase in duration of chemically induced anesthesia (18) and the suppression of experimental local pruritus in mice (19) were blocked by pretreatment with the opioid antagonist naloxone. Therefore, the cold pressor test is an appropriate model of pain adequate for quantitatively measuring the opioid-related effects of MW exposure.

Our results, obtained under double-blinded conditions, show that a single 30-min exposure to the MW generator produces a significant hypoalgesic effect in healthy male volunteers. The time of pain tolerance response in the cold pressor test increased by 37%, and duration of pain sensitivity range increased by almost 50% compared with the average baseline data for the same individuals. Such an effect correlates with data from uncontrolled, nonblinded clinical studies reporting pain relief in patients treated with MW therapy (1).

What is the possible mechanism of the observed effect of MW? To understand the interaction of low-power MW with any living system, including the human body, three main stages of such interaction should be identified: primary sensors of MW in the organism; pathways transmitting the signal to the regulating center(s); and biological and chemical substrates implementing the response to the electromagnetic stimulus. Because of the very shallow penetration depth of MW in water and water-containing media, MW are absorbed within a 0.3- to 0.5-mm layer of human skin (20). Unmyelinated free nerve endings can be found within this layer of skin throughout the human body (21). The ability of neurons of various organisms to react to low-power MW signals has also been shown in multiple experiments (22,23). Thus, nerve endings can possibly act as the primary receptors of MW.

If nerves are involved in the reception of this electromagnetic signal, it would be logical to hypothesize that neural pathways are used for its transmission to the corresponding regulatory center(s) in the body. Some clinical results indicate that the central nervous system participates in response to MW stimuli; for example, electroencephalogram changes were registered in healthy volunteers (24) and children with cerebral palsy (25) as a result of their exposure to MW. Our current findings that MW produce pain relief in an area of the body remote from the exposure site also suggest involvement of a certain central mechanism of transmitting the low-power electromagnetic signal and reacting to it.

In summary, using double-blinded, randomized, cross-over settings, we describe suppression of pain sensitivity in healthy male volunteers after their single exposure to low-intensity MW. Mechanisms of MW treatment and optimal treatment modes remain to be elucidated. This method can potentially be used as a supplementary or alternative treatment for pain relief.

References