APTA

American Physical Therapy Association

April 1, 1999

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RE: APTA Response to ECRI January 23, 1998 Letter and October 14, 1998 Memorandum from Dr. Kamerow (AHCPR), Center for Practice and Technology Assessment

Dear Dr. Whyte:

In April, 1996, ECRI prepared a technology assessment for HCFA entitled Electrical Stimulation for the Treatment of Chronic Wounds". On the basis of the ECRI assessment, HCFA issued a national coverage decision denying Medicare reimbursement for the use of electrical stimulation (ES) for the treatment of wounds. The American Physical Therapy Association (APTA) and five named individuals filed civil action against the Secretary of HHS and the HCFA Administrator and were successful in obtaining an injunction of HCFA's national coverage decision (November, 1997). In January, 1998, at HCFA's request, ECRI wrote a letter to HCFA addressing the Court's decision. (ECRI's letter focused only on two specific technical issues in the Court's decision). On August 8, 1998, HCFA requested an AHCPR Center for Practice and Technology Assessment opinion on ECRI's evaluation of the court's decision. When it discovered that HCFA had made such a request of AHCPR, APTA submitted materials to AHCPR that telephone communication confirmed would not be part of AHCPR's evaluation since these were materials HCFA had not forwarded to the agency. These materials included an APTA position paper; APTA's proposed coverage policy (submitted to HCFA at the request of the HCFA); the court decision; correspondence from primary investigators in five electrical stimulation studies clarifying the treatment received by the control groups in each of the studies; four studies of electrical stimulation in the treatment of wounds; an excerpt from the AHCPR *Clinical Practice Guideline* #15 relative to electrical stimulation; two lists of references (totaling 57 articles); and four relevant case studies involving wounds of Medicare beneficiaries treated with electrical stimulation.

The purpose of this letter is to follow up on our meeting of January 13, 1999, to discuss literature relative to the use of electrical stimulation of the treatment of wounds since it was HCFA's expressed intent to issue a coverage decision based on scientific evidence relative to this issue. During this meeting, APTA representatives submitted a list of 28 references (attached) that represented controlled trials and randomized controlled trials that studied the effectiveness of the treatment of wounds. During the meeting, APTA discussed 13 of those CTs and RCTs as well as one yet-to-be published meta-analysis of 15 studies relative to the same issue. Also at that meeting, there was some discussion of the AHCPR *Clinical Practice Guideline* #15, *Treatment of Pressure Ulcers,* as well as the ECRI letter of January 23, 1998 and the AHCPR Center for Practice and Technology Assessment letter reviewing the ECRI evaluation. During this meeting, HCFA requested APTA's official response to the AHCPR review and the ECRI letter. This letter represents APTA's official response to those documents.

ECRI Letter of January 23, 1998

In a January 23, 1998 letter, at HCFA's request, ECRI analyzed the U.S. District Court decision regarding electrical stimulation in the treatment of wounds. ECRI did not dispute the key findings in the Court's opinion or the Court's conclusion that the ECRI report and other evidence in the administrative record did not support, and indeed "ran counter" to, HCFA's non-coverage decision. Rather, the ECRI letter addressed only the "specific technical issues" mentioned in a footnote in the Court's opinion. Unfortunately, the ECRI letter, while purporting to address what the Court termed a "definitional inconsistency" in the record, only confuses the issue further. Indeed, ECRI admits to imprecision and unfortunate wording in the technology assessment. In an effort to clarify, ECRI states that the terms "no therapy and minimal therapy are functionally equivalent." They also go on to state that the terms "passive therapy", "concomitant standard therapy", and "minimal therapy" mean the same thing. On the second page of their letter, ECRI acknowledges that "conventional care" includes topical agents, oral meds and pressure devices. Moreover, ECRI goes on to give these regimens as examples of "concomitant therapy", which it states carries the same meaning as "minimal therapy" and "passive therapy." In essence, ECRI's discussion of operational definitions results in equivalency of the terms "passive therapy", "concomitant standard therapy", "minimal therapy", "no therapy" and "conventional care".

The ECRI letter attempts to defend its statement that "there were no comparative studies of ES vs. conventional therapy." Again, however, ECRI completely misses the point: electrical stimulation is adjunctive therapy and, therefore, it is appropriate and meaningful to compare conventional care plus electrical stimulation to conventional care alone. Indeed, it would be unethical (and also impractical) to halt conventional care when electrical stimulation is introduced as a treatment regimen. It is widely known that it would be considered unethical for studies to be done using human subject design that compared the studied procedure to no treatment at all. The absence, therefore, of so called "head-to-head" studies is understandable and expected. Given ECRI's apparent acknowledgement that no patients should go untreated, its statement that "one's study must contain a group of patients that received only electrical stimulation and a group that received only conventional therapy" defies common sense and practical reality. The existing studies of ES do compare ES to conventional care in the only way that is practical and appropriate from a patient care standpoint, and ECRI does not dispute the fact that, as the Court noted, "the ES studies are about as good as one usually gets in this area." Therefore, the ECRI statement that there are no comparative studies of electrical stimulation vs. conventional care is wrong, and the letter's suggestion that a study must compare "ES alone vs. conventional therapy" in order to be "comparative" continues to miss the point.

October 14, 1998 ACHPR Center for Practice and Technology Memorandum

The AHCPR Center for Practice and Technology Assessment memorandum also falls short in adding to the meaningful discussion of this issue. That memorandum provides a short, two-paragraph discussion of the ECRI evaluation of the U.S. District Court memorandum and order, and then a four-page discussion of documents APTA submitted to AHCPR when it discovered HCFA had requested this AHCPR analysis. Dr. Kamerow's letter discusses three sections of a four-section APTA position paper and four published articles pertinent to the use of electrical stimulation in the treatment of chronic wounds.1

Unfortunately, Dr. Kamerow's letter contains numerous errors which detract from, rather than contribute to, a better understanding of the central issue, i.e., the effectiveness of electrical stimulation in the treatment of chronic wounds. For example, on page 2, Dr. Kamerow states ECRI used "the terms 'passive therapy', 'concomitant standard therapy' and 'personal therapy' to all mean the same thing." This terminology further distorts the discussion referenced hereinabove relative to the use of terms by ECRI. The term "personal therapy" is not used by ECRI nor does it appear in any of the materials reviewed by Dr. Kamerow. One is therefore at a loss to discover where that term came from. And it does nothing to help clarify the analysis, or aid in the discussion, of the central issue.

Dr. Kamerow also errs in several ways in his discussion of his own agency's *Clinical Practice Guideline* #15, *Treatment of Pressure Ulcers* (AHCPR, 1994). He correctly represents that the AHCPR panel recommendation supporting the use of electrical stimulation in the treatment of wounds was made on the basis of "Level B evidence", but he incorrectly characterizes Level B evidence as "observational studies". AHCPR *Clinical Practice Guideline* #15 states that Level B strength of evidence is considered to exist when "results of two or more **controlled clinical trials** on pressure ulcers in humans provide support, or when appropriate, results in two or more controlled trials on an animal model provide indirect support" *(Clinical Practice Guideline* #15, *Treatment of Pressure Ulcers,* AHCPR, 1994, page 18). Dr. Kamerow goes on to write that the total number of patients in these clinical trials were "only 147".

Dr. Kamerow then claims that because of this small number, these trials "were not adequately powered studies or persuasive because of other methodological flaws." In statistics, lack of "power" means that a study did not detect a significant difference between groups when a significant difference did indeed exist. This is a so-called Type II error, and can occur if a sample size is too small to detect a small, but real, effect. However, the studies that Dr. Kamerow claims contained "only 147" subjects **did** detect significant differences between electrically stimulated groups and non-stimulated groups.

Therefore, the claim of inadequate power is an unjustified criticism. Moreover, Dr. Kamerow's "review" mentions "other methodological flaws" in these studies, but fails to specify the nature of such alleged flaws.

Moreover, it is important to note that in the recent article published in January of 1999 *Ostomy/Wound Management,* 1999; 45(supplIA): 94S-106S, Dressings and Adjunctive Therapies: AHCPR Guidelines Revisited, Lisa G. Ovington, PhD, CWS, which we previously submitted to you, Dr. Ovington concludes that the strength-of-evidence rating for electrotherapy in stage 3 and 4 recalcitrant pressure ulcers "should perhaps advance from B to A based on the five original randomized controlled trials plus the 1994 trial." It should be noted that the 1994 AHCPR *Clinical Practice Guideline* #15 defined a strength-of-evidence rating of A on the basis of "results of two or more randomized controlled clinical trials on pressure ulcers in humans." It is clear that the literature supporting electrical stimulation in the treatment of pressure ulcers warrants a strength-of-evidence A rating. As mentioned, APTA submitted four published articles to AHCPR when it was discovered that HCFA had requested an analysis of materials by AHCPR. The four studies were: Wood, et al; Stefenovska et al; Stiller, et al; and Kloth and Feedar. We discuss below these studies as relevant to the AHCPR comments.

1. The Wood article (reference #19) described use of ES in the treatment of 43 ulcers in 41 patients with a chronic ulcer refractory to standard nursing care (unspecified) compared with sham treatment of 31 ulcers in 30 patients. The study was performed using a common protocol.

Dr. Kamerow's comment: In essence this study demonstrated 58% *of the ES treatment ulcers healed in* 8 *weeks* vs *only one* (3%) *healed in the untreated group. The study demonstrated that ES promoted healing (which concurs with the ECRI report) but says nothing about what further treatment may have accomplished in the untreated control patients. "*

Dr. Kamerow's comment is not in reality a substantive criticism, He takes the paper to task for not "prophesizing" what further treatment may have accomplished in what he labels "the untreated control patients." However, there were no untreated control patients, since all patients received, as Dr. Kamerow indicated, "standard nursing care". The experimental group received, in addition to this standard care, a course of electrical stimulation clearly specified in the paper. Moreover, since almost all patients in the control group had not shown any improvement over the eight weeks of the study (as summarized by Dr. Kamerow), criticism for not attempting to guess what might have happened had they continued receiving this standard treatment seems immaterial and unjustified.

2. The Stefenovska article (reference #20) described use of ES in addition to conventional treatment (unspecified) in 100 treated patients and 50 non-ES patients as controls. The data strongly supported the hypothesis that ES contributed to the faster healing of decubitus ulcers.

Dr. Kamerow's comment: "The authors took great pains to emphasize that the initial pretreatment lesions had great variability and that it was impossible to vary only one parameter."

The following text is taken from the conclusion of the article:

> "In the work presented, we have paid particular attention to the role of only one parameter: electric currents yes or no? We have been compiling data for six years and we are now able to say that the AC current we have applied had a stronger influence on healing than all other parameters. Furthermore, an arbitrarily chosen wound has a chance of healing twice as fast when treated with AC treatment. In practice, however, this means that it is possible that some wounds will not benefit at all, while others will heal at even more than twice the normal rate. Can we say then that we have proved the efficacy of AC treatment in pressure sore healing? The answer is no because it does not hold true for every sore: the truth is simply only for simple systems, and not for systems as complex as biological ones. In these systems, what is true is true only under certain circumstances. Therefore, we have to acquire data for all particular cases.

> A further explanation for acquiring new data is that we may wish to optimize the treatment, for example, to find the optimal stimulation current, primal electrode placement, or to determine whether it is optimal to stimulate only two hours a day or whether it is better to apply ES overnight. It is clear that the quantity of experimental data we need is vastly increasing."

Dr. Kamerow's comment: "I *agree with the authors that the efficacy of AC treatment for pressure ulcers is not proven and more data are needed."*

It is interesting from the above that despite the paper reporting such obvious benefits of electrical stimulation, Dr. Kamerow focuses on one comment by the authors and concludes that the paper does not show efficacy of electrical stimulation. However, upon more in-depth analysis it is clear that the authors were describing what is meant by the term "average". That is, on average the healing rate of ulcers treated with electrical stimulation was double that of the non-ES group. The authors go on to say this average doubling means that some ulcers might not heal, while others might actually heal four times quicker. Since the "average" means that not all ulcers heal at the same rate, it is impossible to predict which ulcer will heal more rapidly or which ulcer will heal more slowly. Dr. Kamerow parlays this simple statement of statistical fact into meaning that this study has not shown efficacy, when in fact it has. ("An arbitrarily chosen wound has a chance of healing twice as fast when treated with AC treatment").

3. The Stiller article (reference #18) was a RCT involving 31 patients, each having a recalcitrant ulcer. Eighteen patients were randomized to active ES treatment and 13 to the placebo group. Eight treatment centers participated in the trial, and the different centers applied varying ancillary treatments in addition to the daily treatment with the active or placebo ES device (which were indistinguishable to patients and investigators). Results demonstrated statistically significant improvement in healing in patients treated with the active device. Fifty percent of the ES treated ulcers healed or markedly improved compared with none in the placebo group.

*Dr. Kamerow's comment: "These positive results await confirmation in trials with larger numbers of patients. The treatment of*18 *patients in* 8 *different centers is inherently problematic."*

Dr. Kamerow states the number of patients studied (he reduces the original 31 to 18), and then claims that these are not enough. He then states that since this was a multicenter trial, this treatment "is inherently problematic". Clinical research literature abounds with multicenter studies since results indicate that findings are not peculiar to a particular location but have generalizability, which is a strength. Lastly, while Dr. Kamerow states: "These positive results await confirmation in trials with larger numbers of patients", he apparently ignores the two previous studies that total 221, plus the previous 147 mentioned at the beginning of his summary. Therefore, even if no other clinical research papers in this area are considered (and there are indeed many more), Dr. Kamerow's review of these four papers describes sample sizes of 147, 31, 150, and 71, for a total of 399 patients.

4. The Kloth and Feedar article (reference #10) described a clinical trial involving treatment of patients and untreated controls all of whom were unresponsive to unspecified prior treatments. Necrotic tissue in both groups was debrided manually and with enzymes. Three patients in the control group were given sham treatments. Results of the study supported the hypothesis that ES enhances the rate and extent of wound healing, although additional studies are required to determine the optimal number and duration of treatments.

Dr. Kamerow's comment: "This study (of only 9 *patients) also supports the claim that ES promotes healing of skin ulcers. This concept is not contested by anyone. The issue for HCFA that has been highlighted by the ECRI report is the lack of persuasive evidence that ES is better than conventional or other alternative treatments. "*

Dr. Kamerow again misrepresents the number of patients in the study. In addition to the nine treated, there were seven "controls" to whom the ES was compared. All patients in the "treatment group" healed completely.

Patients in the "control group", none of whom had healed in the time the "treatment group" did (in many, the condition worsened), were then given ES. All in this "crossover group" healed in the next 8.3 weeks. Therefore, although Dr. Kamerow describes this as a study in nine patients, in actuality 100% closure was obtained in 16 patients. This experiment, therefore, is a classic crossover design and clearly demonstrates benefit. We would agree with Dr. Kamerow when he states that this is a study which "supports the claim that ES promotes healing of skin ulcers", and that this claim "is not contested by anyone." There is no question that ES is of benefit.

We find distressing Dr. Kamerow's comment that there "is the lack of persuasive evidence that ES is better than conventional or other alternative treatments" for these reasons. First, Dr. Kamerow's statement is not consistent with studies he reviewed. All four of the studies he reviewed, (plus the multitude of others that are in the literature but not reviewed here), compared ES to "conventional treatment", or to "standard nursing care" (depending upon terminology). The above-described difficulty with definitional terms notwithstanding (see discussion of ECRI review and opinion of court decision), these four papers describe with some detail, what is meant by "conventional treatment" or "standard nursing care." Moreover, all these patients had proven refractory to such treatment. Since these wounds had already been determined to be non-responsive to such treatment, we hold that this is "persuasive evidence that ES is better than conventional or alternative treatments." Second, as the Court's opinion makes clear, the evidence necessary for coverage need only show that electrical stimulation is effective; a finding of superiority is not required.

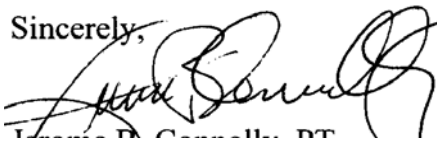
Summary/Conclusion:
In the relatively short meeting conducted on January 13 between HCFA representatives and representatives of the American Physical Therapy Association, 13 studies were discussed which contained a total "n" of 753 patients. In addition, the Franz-Gardner Meta-Analysis (submitted for publication) that included 15 studies (nine RCTs and six CTs) and an "n" of803 (591 treatment; 212 controls) concluded conservatively that ES provides a healing rate 144 percent better than the controls. It should also be noted that during our discussion, it was pointed out several studies involved the use of a crossover methodology employing ES when it was demonstrated that conventional care was not effective in closing a wound or when, despite conventional care, the wound was getting worse. In nearly every instance, the crossover methodology resulted in improved healing of the wound, and in many cases, the wound moved to full closure.

On the basis of an evidence-based review, it is shown then that there are improved health outcomes from using this therapy, that the benefits outweigh the risks and that there is evidence of improved health outcomes for not only some, but the majority of patients. Most types of electrical stimulation are more effective than minimal therapy (a term which ECRI itself used synonymously with "concomitant standard therapy").

Based on the foregoing discussion, on the review of the literature and the benefit to the considerably needy patient population, APTA urges HCFA to move rapidly toward the development of a positive national coverage policy decision which recognizes and reimburses for the use of electrical stimulation in the treatment of wounds as an adjunctive therapy when it has been shown that conventional care has failed.

APTA appreciates the opportunity to respond to these materials and opinions and remains willing to continue a dialogue with HCFA that will result in this positive coverage decision for this effective therapy which can benefit patients with intractable chronic wounds.

Sincerely,



Jerome B. Connolly, PT
Senior Vice President
Health Policy

[1] I would note in this regard that ACHPR had previously advised APTA that the material it submitted would not be part of AHCPR's evaluation since these were materials HCFA had not forwarded to that agency.

Attachment

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