**Original Article**

**Current State of Clinical Studies on Diagnosis and Treatment of Sudden Deafness in China**

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**Abstract**

Objective To evaluate the current status of clinical studies on diagnosis and treatment of sudden deafness (SD) in China by retrospective reviewing articles on SD published in Chinese journals in the past 5 years. Special attention is given to whether the diagnosis and treatment standards established in 1996 by the otolaryngology branch of Chinese Medical Association (the “1996 standard”) were followed. **Methods** The terms of "Sudden deafness" and "treatment" were used as the keywords in searching articles published between 2000 and 2004 in the Chinese biomedical literature database and Chinese journal network. Principles of evidence-based medicine were applied in reviewing the articles. **Results** Two hundreds and thirty-four articles were identified, including 176 between 2000 and 2002 and 58 between 2003 and 2004. Among the 176 articles published between 2000 and 2002, effects of medications were studies in 126 articles, of which only 26 (20.6%) followed the "1996 standards". Eighty-nine (70.6%) were reported based on controlled clinical trials (CCT) and 36 (28.5%) met the criteria of randomized controlled trails (RCT). Of the 58 articles published between 2003 and 2004, drug effects were evaluated in 25 articles, which were all based on the "1996 standards". However, there lacked placebo control, follow-up data or statistical analysis in these papers. Only 6 articles reported side-effects from pharmacological treatment. **Conclusions** While a significant number of articles on SD were published in the past 5 years, the "1996 standards" were followed only in a small number of them. The standards may not be appropriate in guiding research and need to be modified for improved guidance to SD management. Multi-center, RCTs should be a crucial part in studies on SD.

**Keywords** sudden deafness; therapy; evidence-based medicine; randomized controlled trials

Sudden deafness (SD) is a common otological condition. In 1996, the otolaryngology branch of Chinese Medical Association and the Editorial Board of Chinese Journal of Otolaryngology published its recommended diagnosis and treatment standards for SD (the “1996 standard”) in Shanghai. The standards define SD as sensorineural origin with unknown etiology. The diagnosis criteria include sudden onset, absence of clear precipitating causes, non-fluctuating sensorineural loss at middle or high frequencies, accompanying tinnitus, vertigo, nausea and vomiting, no recurrent attacks, and absence of damage to cranial nerves other than the VIIIth cranial nerve. By the standards, the effect of complete recovery from SD corresponds to normal or pre-disease level hearing thresholds over the frequency ranged from 250 to 4000 Hz; the effect of excellent treatment results represent a 30 dB or more improvement in the mean hearing threshold over the above-mentioned frequency range; regain of useful hearing is defined as mean threshold improvement over the same frequency range between 15 and 30 dB; and treatment resulting in less than 15 dB mean threshold improvement is considered ineffective.

There have been a large number of reports on the diagnosis and treatment of SD in the Chinese literature in recent years. Many studies have focused on pharmacological agents that dilate blood vessels, improve microcirculation and/or reduce blood viscosity, as well as anti-viral and neural nourishment agents. Other treatments that have been studied including physical therapies and hyperbaric oxygen therapies. The response rate for these treatments averages around 80% with significant variations between different treatments. Evalua-
tion of true treatment effects is difficult from these reports. To understand the current state of diagnosis and treatment of SD in China, it is of critical importance to analyze the reported treatment methods and results in a comparative manner. We have previously studied the literature data from 2000 to 2002. (Guo et al, 2004) In the current work, we have included literature data from 2003 to 2004 for a study covering the entire period from 2000 to 2004. Attention has been paid to whether the "1996 Standards" have been followed in these studies.

Materials and methods

The terms of "sudden deafness" and "treatment" were used as the key words in searching the Chinese biomedicine literature database and Chinese journal net from 2000 to 2004. The following aspects of the articles were analyzed: ① diagnostic and therapeutic protocols; ② study design; ③ selection of study subjects; ④ sample size; ⑤ randomized controls; ⑥ between-group comparison; ⑦ control techniques; ⑧ blinding methods; ⑨ criteria for treatment effects; ⑩ interventional procedures.

Results

1. General results: Two hundred and thirty four articles on SD treatment were identified. Of these, 176 were published between 2000 and 2002, including 126 articles on pharmacological treatment effects and 50 on correlation factors for prognosis and serum analysis. Of the 58 articles published between 2003 and 2004, 25 studied drug therapy effects, while the rest were review articles and studies on nursing issues or etiology of SD. Average treatment effective rates in the 234 articles ranged from 60.3% to 94.5%.

2. Diagnostic and treatment effect judgment standards: Most of these studies reported their criteria for judging treatment effects, but the diagnostic criteria were much less clear. Of the 126 articles on SD treatment published between 2000 and 2002, only 26 (20.6%) based their diagnostic criteria on the "1996 standards", and 38 (23.8%) had either their unique diagnostic standards or borrowed diagnostic standards from other studies. In contrast, all 25 articles on drug effects published between 2003 and 2004 noted that patient selection was based on the "1996 Standards".

3. Study design: Of the 126 articles from 2000 to 2002, 89(70.6%) were controlled clinical trials (CCT), including 36(28.6%) that described randomization methodologies consistent with randomized controlled trials (RCT). In 70 articles, a particular drug was used in addition to routine drug treatment protocols in the test group for comparison to a control group receiving only the routine protocol. Typical routine protocols included prescription Dan Shen (a Chinese herbal extraction compound), cytochrome C, Dextran, cortical steroids, adenosine triphosphate, etc, but they varied from study to study. Agents studied in the test group in some studies might be used in the control group in others. An example is the prescription Dan Shen, which was studied in the test group in 6 studies but used in the control group in another 24 studies. Average effective rate was 83.1±2.02% in the 6 studies where it was studied in the test group and 54.3±1.96% in the 24 studies where it was used in the control group. The difference between the two groups was statistically significant (p < 0.01).

4. Between-group comparison: Most of studies provided demographic and general medical information of their patient groups, including the mean age, degree of hearing loss and duration of disease, comparison between test and control groups, were ambiguous. None of the 234 articles described statistical approaches for between-group comparison.

5. Other issues: Placebo control was used in none of the studies reviewed here. As only 6 studies reported side-effects. All 234 papers lacked follow-up data.

Discussion

From analyzing the 234 articles, it becomes clear that besides the large number of studies on SD and their resultant achievements, there are obvious problems that affect the quality of these studies. Only a small portion of studies(28.5%) between 2000 and 2002 were RCTs, which is seriously compromising their value in guiding clinical practice. Evidence-based medicine requires that clinical decision be based on reliable study evidence, such as obtained from properly designed clinical research and rigorous literature study. RCT is the preferred design for clinical research (Ruan et al, 1999), which minimizes interference from the relative factors between different researchers to ensure that findings are reliable.

The majority(90%) of the 126 articles on SD treatment published between 2000 and 2002 reported superior treatment results in the test group over the control, although contradictory conclusions were reported between studies. For example, the average effective rate with prescription Dan-shen is 83.1% when studied in the test group and 54.3% when used in the control, and the difference is statistically significant. Vickers et al. (Vickers et al, 1998) pointed out that publication bias
existed in certain countries including China. Unusually high proportions of positive results have been reported in clinical research works published in Chinese academic journals. While diagnosis and therapy standards for SD have been recommended since 1996, only 20.6% of the SD related papers published between 2000 and 2002 based their diagnostic criteria on the standards, although this improved significantly in papers published between 2003 and 2004, of which all noting compliance with the "1996 Standards". Other factors that may potentially affect treatment results including age, duration of disease, disease incidence, severity of symptoms and comorbidities. These factors need to be taken into consideration when studying the etiology and treatment effect in SD. When "etiology unknown" is used as an inclusion criterion, it needs to be clearly defined to avoid confusion in subject inclusion and difficulties in cross-comparing studies.

The majority of reports on SD treatment focused on pharmacological therapies. Treatment agents were selected based on their pharmacological action and clinical indications. For agents used to produce vasodilation, microcirculation improvement and/or reduction in blood viscosity, pre- and post-treatment laboratory tests are important in both the test and control groups to verify treatment effects and to help understand the relationship between the drugs and therapeutic effects. For antiviral medications, the relationship between the onset of disease and viral symptoms should be established. If the agent is used to affect blood supply to the cochlea, a good understanding of factors that can change cochlear blood supply is critical and the factors should be included in the analysis. It is well known that prognosis in SD can be influenced by multiple factors. Some SD patients may recover spontaneously without medical intervention. All these can potentially complicate studies aimed at evaluating treatment effects in SD. Other factors that can compromise the value of the 234 studies are lack of use of placebo control and lack of statistical analysis between groups in all 234 papers.

In a clinical study that involved medication trials, it is important to report any side-effect or complications from the treatment, in addition to reporting treatment results. While short-term results were reported in most of the studied reports, few included long-term results. None of the 234 papers included follow-up data. Evidence based medicine warns against conclusions based on partial, temporary or superficial results. Results from large sample size, long-term follow-up, and randomized controlled trials are encouraged for meaningful interpretation (Kirk, 2001).

Considering the current state of clinical studies on SD and the many challenges of SD poses to clinical researchers regarding its etiology, prognosis and possibility of spontaneous recovery, the authors make the following recommendations for future studies on the diagnosis and treatment of SD: 1. Multi-centric, prospective, randomized and blind controlled clinical trials should be considered in study design. 2. Pathophysiological mechanisms should be taken into account when formulating treatment plans. Appropriate management of blood pressure and cholesterol levels, completed with pre- and post-treatment rheological tests, should be considered for patient with hypertension and hyperlipidemia. Blood rheological study, in addition to audiometric evaluation, should be an important part of treatment effects evaluation. Liu chan(Liu, 1997) believes that treatments of diseases caused by viral infection and circulatory disorders should be different. Selection of treatment agents should therefore be the result of a thorough study of potential etiologies. 3. Now may be the time to revise the 10 years old of "1996 Standards", which may have been too simple and general to provide much meaningful guidance in SD study. Its diagnostic criteria and the guidelines for reporting treatment results are difficult to follow. Application of the standards in SD study should not be affected by the concerns at the time of their compilation regarding limited resources at primary care facilities. The focal points in revision of the "standards" may include quantitative measurement of hearing loss, detailed diagnosis and therapy standards, and guidelines for treatment indications and protocols. The goal should be to increase their value in guiding clinical practice and research.

References