Hormone replacement therapy for chronic tinnitus in menopausal women: Our experience with 13 cases

Dear editor,

Tinnitus is a common complaint among patients visiting an ENT clinic. It can cause severe annoyance and distress to some patients. Many treatment modalities are available for the management of tinnitus, with different degrees of effectiveness\(^1\). Owing to the heterogeneity of tinnitus, it is very unlikely that an omnipotent therapy will cure all forms of tinnitus\(^2\). Therefore, treatment should be individualised and targeted at the possible cause. In our tinnitus special clinic, we encountered a special group of subjects: women in their menopausal period or in the immediate post-menopausal period, whose tinnitus responded exceptionally well to hormone replacement therapy (HRT). The effects of HRT on migraine-related vertigo have been previously reported, but no reports have documented its effects on chronic tinnitus\(^3\). In this study, we report our experience in treating this specific group of patients and provide another perspective to clinicians who treat tinnitus.

1. METHODS

The study was a retrospective review of medical records and was approved by the institutional review board of the hospital. Between August 2015 and August 2016, we encountered in our tinnitus clinic 13 women in their menopausal period or immediate post-menopausal period who complained of experiencing chronic tinnitus for more than 1 year. Sequential patients were invited to enrol, and those reported here self-selected to try low-dose HRT as their tinnitus therapy after thorough discussion with our gynaecologist. Their age ranged from 48 to 62 years (average age, 55.6 years). With their consent and in collaboration with our colleagues in the gynaecology department, we started to give them low-dose HRT (conjugated oestrogen [0.625 mg, one tablet once a day to every other day] plus medroxyprogesterone [5 mg, one tablet at bedtime]) to treat their tinnitus and other menopause-associated symptoms such as insomnia, flushing, night sweating and emotional problems. The

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demographic data of these patients and their pre-treatment follicle-stimulating hormone (FSH) levels are shown in Table 1. They underwent complete otological and audiological assessments, and ear diseases such as chronic otitis media, acoustic neuroma and Meniere’s disease were ruled out. The severity and loudness of their tinnitus were evaluated using the Tinnitus Handicap Inventory (THI) and a visual analogue scale (VAS). The THI and VAS scores were evaluated between 3 weeks and 1 month, during their first follow-up visit. Each patient also received a session of counselling and education after all assessments. No regular counselling, cognitive behaviour therapy or tinnitus retraining therapy sessions were offered to this group. All patients were requested to report any side-effects to our treatment team.

2 | RESULTS

The pre-treatment and post-treatment THI and VAS scores of the 13 patients are shown in Table 1. The average pre-treatment THI score was 58.5, and the post-treatment score was 12.6. The difference was statistically significant (paired t test, \( P < .001 \)). The average pre-treatment VAS score was 8.2, and the post-treatment score was 2.5. The difference was also significant (paired t test, \( P < .001 \)) (Figure 1). Nine of the 13 (69%) patients had THI scores below 10 after treatment, and five patients even had a THI score of 0, indicating almost complete disappearance of tinnitus. All patients also reported an improvement in other menopause-related symptoms, especially the sleep quality. In the THI questionnaire, the question number 7 and question number 20 are related to tinnitus and sleep. The added scores of these two questions were shown in Table 1 and Figure 1. Marked improvement was found after HRT.

The averaged hearing thresholds before and after HRT are also shown in Table 1. No significant changes in hearing were observed during the follow-up period in any of the patients. None of them reported any major side-effects of HRT during follow-up. Six patients complained of occasional breast fullness and vaginal spotting. These were considered minor adverse effects and easily treated by our gynaecological teammates. In the first five patients, we tried discontinuing their hormone supplement after 1-3 months. However, all of them reported a tinnitus recurrence. Therefore, all patients continued the HRT during their follow-up period of 8-18 months. The exact duration needed or endpoint of treatment is unknown and

| Case No. | Age | Tinnitus laterality | Tinnitus duration (years) | Pre-treatment PTA (dB) | Post-treatment PTA (dB) | FSH level (ng/mL) | THI Pre-treatment | THI Post-treatment | VAS Pre-treatment | VAS Post-treatment | Q7+Q20 Pre-treatment | Q7+Q20 Post-treatment |
|---------|-----|---------------------|---------------------------|------------------------|------------------------|-------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| 1       | 56  | R                   | 8                         | 20                     | 20                     | 45.1              | 24               | 8                | 5                | 1                | 2                | 2                |
| 2       | 52  | B                   | 1.5                       | 25                     | 25                     | 48.3              | 50               | 30               | 10               | 1                | 6                | 4                |
| 3       | 52  | B                   | 5.5                       | 12                     | 20                     | 44.6              | 78               | 32               | 8                | 5                | 6                | 4                |
| 4       | 52  | B                   | 3                         | 23                     | 23                     | 88.1              | 100              | 0                | 10               | 1                | 8                | 0                |
| 5       | 62  | B                   | 2.5                       | 17                     | 20                     | 82.8              | 36               | 0                | 6                | 1                | 6                | 0                |
| 6       | 51  | B                   | 4                         | 8                      | 10                     | 91.7              | 34               | 0                | 7                | 1                | 2                | 0                |
| 7       | 61  | L                   | 1                         | 45                     | 37                     | 69.3              | 52               | 2                | 10               | 1                | 8                | 0                |
| 8       | 59  | R                   | 4                         | 10                     | 15                     | 77.5              | 76               | 38               | 10               | 4                | 8                | 4                |
| 9       | 56  | R                   | 1.5                       | 10                     | 12                     | 99.1              | 44               | 8                | 9                | 7                | 8                | 2                |
| 10      | 57  | R                   | 2                         | 8                      | 12                     | 45.2              | 42               | 0                | 5                | 0                | 4                | 0                |
| 11      | 56  | B                   | 3.5                       | 8                      | 8                      | 79.7              | 88               | 36               | 10               | 7                | 4                | 0                |
| 12      | 60  | B                   | 1                         | 17                     | 17                     | 49.1              | 68               | 0                | 8                | 1                | 8                | 0                |
| 13      | 48  | B                   | 1                         | 55                     | 52                     | 43.8              | 68               | 10               | 8                | 2                | 6                | 0                |
| Average |     |                     |                           | 58.46                  | 12.62                  | 8.15              | 2.46             | 5.85             | 1.23             |

Laterality, B, bilateral; L, left; R, right.
PTA, pure tone average, averaged threshold of 500, 1000 and 2000 Hz.
THI, Tinnitus Handicap Inventory; VAS, visual analogue score.
Q7+Q10: the added score of Question 7 and Question 20 of THI. These two questions are related to tinnitus and sleep.

Keypoints
- Tinnitus can be a distressing complaint for menopausal women.
- Low-dose HRT can be considered as a therapy to reduce the tinnitus handicap and loudness in certain patients.
- Continuous HRT is needed for 8-18 months to prevent the recurrence of chronic tinnitus in our series, and no major side-effects were reported.
may vary case by case. It is obvious that longer observation and analysis from more subjects are required.

Although this case report did not include any prospectively randomised control cases, the improvement in the patient’s conditions was dramatic and fast. In our clinic and according to the literature, treatment of tinnitus due to other or unknown causes requires much more time and counselling sessions to produce an improvement.

3 | DISCUSSION

This is a preliminary retrospective report of our experience in a selected patient group. It is not a systematic, randomised, controlled clinical trial. The counselling and education that we performed may have helped relieve the patients’ chronic tinnitus, but we believe the dramatic, rapid and substantial improvement should be attributed to the HRT. Of course, without proper controls, potential bias existed behind such a remarkable result. For example, with respect to case selection, patients who were willing to accept HRT may have better compliance and tended to be more cooperative with the therapists. Therefore, they could have had better outcomes. For performance and attrition bias assessment, all patients reported their tinnitus handicap and loudness the same way as all of our patients with tinnitus, and no one withdrew from HRT in this group. The “lack of side-effects” may be because our follow-up period was relatively short. While we do not intend to advocate this therapy to every patient with tinnitus, we would like to point out this treatment option to all clinicians who may encounter a similar situation.

The exact mechanism through which HRT reduced the chronic tinnitus is unknown. The effects of hormones and HRT on hearing have been widely studied8. In general, oestrogen tends to be beneficial to hearing and has neuromodulatory and neuroprotective effects. Tinnitus may be affected by alterations in the hearing and central auditory tract. However, HRT has been known to negatively affect hearing in aged women in a large clinical trial9. Smith and Hoare reported a more plausible physiological mechanism suggesting that changes in circulating levels of oestrogen and progesterone affect the chemical composition of the endolymph/perilymph and transported between these chambers of the cochlea. These processes regulate the electrochemical impulses generated by the hair cells in the cochlea; therefore, hair cell activity and, hence, tinnitus could be affected by their alteration8.

We think the other possible mechanism involves sleep improvement. All patients reported poor sleep before treatment and much better sleep after treatment. Sleep disturbance is one of the most significant complaints of patients with tinnitus, and evidence shows that insomnia is associated with more distressing tinnitus7. A recent study summarised the role of hormones in the mechanism of chronic pain, which is often used as an analogue of tinnitus8. This field of research definitely warrants further investigation in the future.

The use of HRT for menopausal syndrome is still controversial. However, emerging evidence shows that low-dose HRT does not increase the incidence to malignancies and can instead reduce composite deafness and heart failure9. It can also improve the sleep quality and prevent osteoporosis10. We emphasise here that, for this particular group of patients, their consent, close collaboration with gynaecologists and careful monitoring are all very important.

In conclusion, our preliminary 13 case series showed that menopausal women with chronic tinnitus could benefit by HRT. The treatment produces rapid, effective and safe results. However, HRT is not recommended as a standard treatment for chronic tinnitus now. Further rigorous controlled trials and investigations on the underlying mechanism are needed to confirm our findings.

CONFLICT OF INTEREST

None to declare.
Intraoperative and postoperative hyperkalaemia after total parathyroidectomy following exposure to cinacalcet in sixteen patients for renal hyperparathyroidism

1 | INTRODUCTION

This study arose from observations of patients on cinacalcet for renal hyperparathyroidism, (cinacalcet, phosphate binders, calcitriol and calcium) and subsequently underwent total parathyroidectomy, developed more severe hyperkalaemia in the intraoperative and immediate postoperative periods compared to patients on standard medical therapy, (phosphate binders, calcitriol and calcium) for renal hyperparathyroidism and had parathyroidectomy. The study researched hospital records to focus this difference by examining the pre-, intra- and postoperative serum potassium measurements.

2 | METHODS

The use of this patient group for research maintains full patient confidentiality and has undergone approval process by the Research and Ethics Committee of this institution. Hospital records between 1993 and 2014 were reviewed of chronic renal failure patients on long-term haemodialysis and with renal induced hyperparathyroidsim who underwent four-gland parathyroidectomy successfully at the first operation.

A hospital record was excluded if the patient had the following:

1. Primary hyperparathyroidism;
2. Subtotal parathyroidectomy;
3. Previous parathyroid surgery;
4. Histopathological diagnosis other than parathyroid hyperplasia;
5. Functioning renal transplant and was not on dialysis

A total of 104 patients were included in the study; 16 of these patients had been treated with cinacalcet prior to surgery. Other patients had been treated by standard medical therapy for the control of renal hyperparathyroidism. Subtotal parathyroidectomy cases were excluded to remove confounding effects of functioning parathyroid gland and serum calcium to compare postoperative hypocalcaemia. Additionally, it was excluded to demonstrate any possible association between hypocalcaemia and hyperkalaemia.

3 | RESULTS

The patient characteristics are given in Table 1.

Patient preparation prior to surgery included cardiovascular optimisation and volume control, and haemodialysis up to 24 hours prior to parathyroidectomy. Patients were operated by the same surgeon (author 1), using standard surgical equipment.