Guidelines for percutaneous ethanol injection therapy of the parathyroid glands in chronic dialysis patients

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Abstract
Percutaneous ethanol injection therapy (PEIT) of the parathyroid was originally introduced as an alternative to surgical parathyroidectomy. After the recent elucidation of the pathogenesis of parathyroid hyperplasia in uraemia, ‘selective PEIT of the parathyroid glands’ was developed, in which enlarged parathyroid glands with nodular hyperplasia are ‘selectively’ destroyed by ethanol injection, and other glands with diffuse hyperplasia are then managed by medical therapy. The ‘Guidelines for percutaneous ethanol injection therapy of the parathyroid glands in chronic dialysis patients’ proposed by the Japanese Society for Parathyroid Intervention are presented, including indications, techniques, and post-PEIT management. These guidelines also apply to direct injection therapy using drugs other than ethanol, such as calcitriol and 22-oxacalcitriol.

Keywords: secondary hyperparathyroidism; percutaneous ethanol injection therapy (PEIT); ultrasonography; nodular hyperplasia
Fig. 1. Parathyroid intervention. (A) Total parathyroidectomy with autotransplantation. (B) Selective PEIT. In total parathyroidectomy with autotransplantation, all glands are surgically removed and fragments from the smallest gland, hopefully with diffuse hyperplasia (white gland) are transplanted in the forearm muscle. In selective PEIT, an enlarged parathyroid gland with nodular hyperplasia (grey gland) was destroyed selectively by ethanol injection, and other glands with diffuse hyperplasia (white glands) are managed by medical therapy. Other modes of direct injection therapy are also based on the same principles.

Table 1. Guidelines for percutaneous ethanol injection therapy (PEIT) of the parathyroid glands in chronic dialysis patients

1. Indications for percutaneous ethanol injection therapy (PEIT) of the parathyroid glands. (a)
   (i) Intact parathyroid hormone (i-PTH) concentration \( \geq 400 \text{ pg/ml} \). (b)
   (ii) Verification of osteitis fibrosa or high-turnover bone using X-ray images and bone metabolism markers.
   (iii) Enlarged parathyroid glands detectable by ultrasonography. (c)
   (iv) Patients resistant to medical therapy. (d)
   (v) Patients who have given informed consent to undergo PEIT. (e)

Exclusion criteria
   (i) Enlarged parathyroid gland located where ultrasonographic-guided puncture is impossible.
   (ii) Paralysis of the recurrent laryngeal nerve on the opposite side. (f)
   (iii) Operation on the neck region for thyroid carcinoma, etc. is scheduled.
   (iv) Institutions without the equipment required or without skilled operators.

Footnotes
   (a) High-risk parathyroidectomy patients are regarded as good candidates for PEIT.
   (b) The serum calcium concentration should always be considered in the interpretation of PTH concentration. Lower PTH concentration may indicate hyperparathyroidism in the presence of hypercalcaemia.
   (c) The target parathyroid glands should be \( \geq 1 \text{ cm in length and } \geq 0.5 \text{ cm}^3 \) in estimated volume. If three or more glands are enlarged by this amount, PEIT will probably be ineffective in the long term.
   (d) For patients with enlarged parathyroid glands that are smaller than the specifications, intravenous vitamin D pulse therapy might be effective.
   (e) An explanation of the importance of regular check up, restricted diet and compliance after PEIT should be given to the patient before obtaining informed consent for the procedure.
   (f) Because the paralysis caused by ethanol results in diplegia of the recurrent laryngeal nerves, concurrent bilateral injection of ethanol should not be considered, even if there is no paralysis of either laryngeal nerve before PEIT.

2. PEIT equipment and techniques
   (i) Equipment: an electronic linear scan and mechanical sector scan system with a frequency \( \geq 7.5 \text{ MHz} \), spatial resolution \( \geq 0.5 \text{ mm} \), and colour Doppler function.
   (ii) Needles: approximately 22 g visible under ultrasonographic guidance (special needles for PEIT are commercially available).
   (iii) Technique: advance the needle visually, using ultrasonographic guidance to check the location of the tip.
   Flush with a minimum amount (0.02–0.1 ml) of ethanol, confirm jet echo within the gland, then inject the required amount of ethanol.
   Adjust the amount of ethanol for the initial injection to \( \leq 80\% \) of the estimated volume of the gland detected by ultrasonography.
   When an additional ethanol injection is needed, the minimum amount should be injected into sites where there is blood flow.
   (iv) Complications: PEIT can cause pain, haematomas or paralysis of the recurrent laryngeal nerve, so it should be performed with care.

3. Post-PEIT management
   (i) Following the procedure, administration of active vitamin D sterols (including intravenous pulse therapy) and control of serum phosphorus concentration must be started. Parathyroid hormone (PTH) estimation should be carried out on each patient; target value \( \sim 200 \text{ pg/ml} \) together with a determination of bone metabolism.
   (ii) Indications for additional PEIT: if the PTH concentration measured 2–4 weeks after PEIT does not decrease to the target concentration, PEIT should be repeated at a site with blood flow.
   (iii) Indications for further PEIT: if the PTH concentration increases again, ultrasonographic examination should be repeated.
   If increased blood flow is seen in glands that were treated with PEIT, additional ethanol injections should be planned even if criteria (i) and (ii) for initial PEIT are not satisfied. If hyperplasia of the intact glands is detected, the patient should undergo initial PEIT.
   (iv) If the target gland has been completely destroyed and the PTH concentration is still elevated, diagnostic imaging for ectopic glands should be carried out.
glands under ultrasonographic guidance [14,15]. As detailed in this supplement, these agents include calcitriol, 22-oxacalcitriol and acetic acid. We assume that these guidelines can also be applied to those new modalities of parathyroid intervention. Nevertheless, modifications may be needed for the other modes of parathyroid intervention by comparing their efficacy with that of PEIT. Furthermore, different indications for parathyroid intervention, including surgical parathyroidectomy, also need to be established from the accumulation of clinical experience in the near future [16].

Finally, we should all be conscious of the importance of preventing parathyroid hyperplasia from the early stages of dialysis therapy. Furthermore, early application of parathyroid intervention, including surgical parathyroidectomy, should also be considered for the prevention of irreversible bone diseases and metastatic calcification of blood vessels.

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References