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How Are Thyroid Function Tests Altered by Thyroid Replacement Medications?

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treated with Endoloop-assisted polypectomy.[4] This series demonstrated 2 bleeding complications in the Endoclip group (1 [3.0%] immediate and 1 [3.0%] delayed). Both of these bleeds occurred in the presence of histologic cancer and during the training phase of the technique. No episodes of bleeding occurred in the historical control group. In contrast to their own control group, the authors identified 3 prior RCTs where the rate of all bleeding complications in large polyps (occurring at any time) without any preventive intervention ranged from 10% to 15%.[4]

Colonoscopic polypectomy is considered a high-risk procedure for patients being anticoagulated. A retrospective case series of 41 snare polypectomies (mean polyp size 5 mm, range 3–10 mm; morphology not provided) in 21 patients used prophylactic Endoclip application with warfarin discontinued 36 hours prior to procedure rather than the standard 5 days. The mean pre-procedure INR was 2.3 (range 1.4–4.9), and warfarin was resumed immediately after the procedure. No episodes of postpolypectomy bleeding (95% CI, 0%–15%) occurred with the use of prophylactic Endoclips.[5]

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"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research."
—Sackett DL et al. Evidence based medicine: what it is and what it isn't. *BMJ* 1996; 312:71–72.

How are thyroid function tests altered by thyroid replacement medications?

Evidence-Based Answer

Small changes in the dosing of levothyroxine (±25 mcg) are associated with large changes in serum thyroid-stimulating hormone (TSH) and free thyroxine (FT_4) concentrations, but not with measurable changes in hypothyroid symptoms, well-being, or quality of life. (SOR: **B**, based on a single RCT.) Taking levothyroxine while fasting is associated with a higher serum FT_4 and lower serum TSH compared with administration after a meal, but these differences are small. (SOR: **C**, based on a single RCT using disease-oriented outcomes.)

A double-blind RCT with 52 hypothyroid patients (with baseline serum TSH between 0.1 and 4.8 mIU/L) assessed whether adjusting the dose of levothyroxine would result in improved well-being or decreased symptoms. The study utilized 3 dose levels: low (25 mcg below the patient's current dose), middle (patient's current dose), and high (25 mcg above the patient's current dose). Outcome measures were determined through the General Health Questionnaire 28 (GHQ-28), Short Form 36 (SF-36), and Thyroid Symptom Questionnaire (TSQ).[1]

Serum TSH concentrations after 8 weeks were 2.8 ± 0.4 mIU/L for the low dose, 1.1 ± 0.17 mIU/L for the middle dose, and 0.32 ± 0.08 mIU/L for the high dose ($P<.001$ for all 2-way comparisons). Moreover, serum FT_4 concentrations after 8 weeks were 14 ± 0.3 pmol/L for the low dose, 16 ± 0.3 pmol/L for the middle dose, and 18 ± 0.4 pmol/L for the high dose ($P<.001$ for all 2-way comparisons).[1]

Quality of life as measured by SF-36, psychiatric health as measured by GHQ-28, and hypothyroid symptoms as measured by TSQ did not differ significantly among the treatment groups. Moreover, 32% of patients preferred the low dose, 26% preferred the middle dose, 20% preferred the high dose, and 22% had no preference. The authors concluded that despite the significant changes in serum TSH and FT_4 concentration, no measurable effects on well-being, hypothyroid symptoms, or quality of life were noted. This study was limited by small sample size.[1]

An RCT with 42 primary hypothyroid patients (with baseline serum TSH between 0.5 and 4.5 mIU/L) and 23 thyroid cancer patients (with baseline serum

TSH between 0.01 and 0.5 mIU/L) evaluated changes in TSH and FT_4 when changing oral levothyroxine administration in relationship to meals. Patients completed 3 different 8-week timing regimens in a 3-period crossover design, acting as their own controls. The timing regimens entailed the following: thyroxine taken after an overnight fast and at least 1 hour before breakfast (fasting protocol), thyroxine taken within 20 minutes after breakfast (breakfast protocol), and thyroxine taken at bedtime at least 2 hours after the individual's last meal (bedtime protocol).[2]

Over a 24-week period, the mean serum TSH concentrations were 2.9 mIU for the breakfast protocol, 2.2 mIU/L for the bedtime protocol, and 1.1 mIU/L for the fasting protocol ($P<.001$ for all 2-way comparisons). The serum FT_4 was lowest with the breakfast protocol (FT_4 1.2 ng/dL; 95% CI, 1.2–1.3) and highest in the fasting protocol (1.4 ng/dL; 95% CI, 1.3–1.4). No significant differences were detected with the serum FT_3 concentrations against baseline. The authors concluded that nonfasting levothyroxine administration resulted in higher serum TSH concentration and lower serum FT_4 concentration. This study was limited by small sample size.[2]

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What is the upper limit of normal for an amniotic fluid index for a 41-week fetus?

Evidence-Based Answer

The upper limit of normal (95th percentile) for the amniotic fluid index (AFI) at 41 weeks ranges between 13 and 24 cm depending on the patient population studied. (SOR: **B**, based on cohort studies.)

A prospective cross-sectional study examined 2,868 low-risk pregnant Brazilian women at 20 to 42 weeks' gestation to generate population-based normative values for the AFI. The 90th percentile AFI at 41 weeks was 17.9 cm. The AFI at the 95th percentile was not given.[1]

A 2-year, prospective longitudinal study evaluated 117 Vietnamese women with normal singleton pregnancies at 28 to 42 weeks' gestation to generate population-based normative upper and lower AFI boundaries. A normal AFI was defined as any value between the 5th and 95th percentiles. The upper limit of normal for the AFI at 41 weeks in this study was 13.7 cm.[2]

Another prospective cross-sectional study was undertaken to analyze AFI values among 517 Indian women with a normal pregnancy at 16 to 42 weeks' gestation. The median, 5th, and 95th percentile values were calculated for each gestational week. The upper limit of normal AFI at 41 weeks was 15 cm.[3]

Another prospective cross-sectional study involved 750 Bulgarian women with uncomplicated singleton pregnancies at 16 to 43 weeks' gestation. The means and the 90%, 95%, and 98% confidence limits for the entire population and subgroups (preterm, term, and postterm) were calculated. The 95th percentile for AFI at 41 weeks was 24 cm.[4]

A prospective cross-sectional study investigated gestational age-specific boundaries of normal AFI in 791 urban Californian women with normal singleton pregnancies at 16 to 44 weeks' gestation. The boundaries for normal at each gestational week were established at the 5th and 95th percentiles. The upper limit of normal at 41 weeks was 19.4 cm.[5] EBP

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