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ORIGINAL ARTICLE

Conventional smears versus liquid-based preparations for thyroid fine-needle aspirates: a systematic review and meta-analysis

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Introduction Thyroid fine-needle aspiration has traditionally been prepared using conventional smears (CS). Liquid-based preparations (LBP) have grown in popularity and yet, there is a lack of consensus about which method is superior. This review compared CS and LBP as an intervention in the management of thyroid nodules.
Materials and methods Medline, EMBASE, Scopus and ClinicalTrials.gov were searched to locate relevant studies. Observational studies comparing CS and LBP of consecutive thyroid fine-needle aspirations were included. Two reviewers independently screened, extracted, and entered data. Double data extraction included the following outcomes: (1) the proportion of inadequate smears and (2) the proportion of indeterminate smears. Studies were also assessed for risk of bias and heterogeneity.
Results From 599 unique studies, title/abstract screening identified 136 studies, and full text screening identified 13 studies. The 13 studies included 24,307 fine-needle aspirations from 19,433 patients and had high clinical, methodological, and statistical heterogeneity with low risk of bias. For CS and LBP, a meta-analysis of 12 studies showed no difference in the proportion of inadequate smears (risk difference: −0.00; 95% confidence interval [CI]: −0.04-0.04); 13 studies showed no difference in the proportion of indeterminate smears (risk difference: −0.02; 95% CI: −0.05-0.01). Sensitivity analysis of studies with low risk of bias had similar results.

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Conclusions There is no difference between CS and LBP in the proportion of inadequate and indeterminate smears. Recommendations of one method over the other should be based on cost, feasibility, and accuracy, all of which require further study.

Introduction

Fine-needle aspiration (FNA) cytology of the thyroid is the mainstay for initial evaluation of thyroid nodules with a negative predictive value of >95% for benign readings and a positive-predictive value of >99% for malignant readings.[1-3] Additional measures and techniques such as ultrasonography guidance[4] and on-site evaluation of adequacy[5] have been employed to improve the diagnostic yield of FNA procedures. Furthermore, the standard classification introduced by the Bethesda System for Reporting Thyroid Cytopathology[6] has created more precise guidelines for cytologic reporting.

Despite these improvements, thyroid FNA is limited by variable adequacy rates, a high indeterminacy rate, and a reliance on morphologic evaluation that is inherently subjective.[7] These problems are unlikely to resolve without substantial new improvements and, changing the method of preparation of cytologic specimens is among the proposed strategies that may improve quality. Currently, thyroid FNA is usually prepared using conventional smear (CS). Preparation by CS method involves coating the aspirated material evenly onto multiple microscope slides. The other commonly used method is liquid-based preparation (LBP). This method employs advanced concentration techniques to yield a single slide that contains most or all of the FNA material. LBP is becoming popular for thyroid specimens primarily due to logistical advantages: LBP does not require manual smearing skills of whomever performs the FNA; the LBP preservative, concentration devices, and staining reagents are commercially produced according to stringent quality guidelines; there is reduced blood; the resulting FNA material is fixed and stained with more consistency than is possible in CS-prepared material; and, a single LBP slide is cheaper for the laboratory to screen and archive. Although these logistical advantages for LBP are significant, there is little available evidence comparing LBP and CS with regard to adequacy and indeterminacy rates. Furthermore, most of the published literature to date has arisen from laboratories that have converted to LBP and reported their experience only after conversion, thus not providing a direct comparison of the 2 techniques. For these reasons, we performed a systematic review and meta-analysis combining the available evidence, and herein we aim to compare the proportion of inadequate and indeterminate smears in CS and LBP preparations of thyroid FNA.

Material and methods

The protocol used for this study has been previously published in the PROSPERO International Prospective Register of Systematic Reviews.[8]

Search methods for identification of studies

A complete outline of the search strategy, dates, and number of citations retrieved is detailed in Supplementary Appendix A. In short, Medline, EMBASE (Excerpta Medica database), and Scopus were searched to identify studies. The Clinicaltrials.gov and ICTRP (International Clinical Trials Registry Platform) databases were searched to locate studies in progress. The search criteria were sufficiently broad to include any retrospective or prospective observational study that compared CS and LBP preparations of thyroid FNA. Searches were not restricted based on language, study population, publication date, or type of institution. No restriction was made with regard to patient sex, ethnicity, comorbidities, or severity of disease. Studies were excluded if they had not included all consecutive cases of thyroid FNA within the specified time frame. After these database searches were performed, the citations of the studies that were identified via these primary search methods were in turn searched to identify any additional studies that may not have been identified in the primary searches.

Outcome measures

The meta-analysis studied 2 primary outcomes: (1) the proportion of cases that were inadequate and (2) the proportion of cases that were indeterminate. The indeterminate diagnostic category included atypia of undetermined significance, suspicious for follicular neoplasm, and suspicious for Hürthle cell neoplasm.

Data collection and analysis

After duplicates were removed, the unique studies were reviewed by screening the title and abstract. The inclusion of each study was based on predefined eligibility criteria. Following this, the full text was reviewed. Two reviewers independently screened the data presented in these papers to determine whether the data included in them was sufficiently comprehensive for inclusion in the meta-analysis. When the two reviewers disagreed on inclusion of a study, a consensus was reached after discussion.