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Evaluation on Adequacy and Diagnostic Comparability of Discarded Residual Materials of Fine-needle Aspirations Processed using Thinprep^{TM} for Lesions on Four Different Organs

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Abstract

Objective: The study was to evaluate the adequacy and diagnostic accuracy of discarded residual materials of fine-needle aspirations (FNA) processed using ThinPrep^{TM} on four different organs; breast, thyroid, lymph nodes and salivary glands.

Study Designs: Aspirated materials of these lesions were directly smeared on glass slides as routinely done. The needles used were then vigorously rinsed by drawing in the ThinPrep^{TM} medium in order to obtain the needle-residual materials. The direct smears [the gold standard] were reviewed by pathologists on rotation and each was given a diagnosis as per routine testing. The needle-residual material smears [test method] were reviewed separately by one pathologist who was blinded to the diagnoses made.

Results: A total of 118 cases comprising 47(39.8%) breasts, 42(35.6%) thyroid, 25(21.2%) lymph node and 4(3.4%) salivary glands lesions were included. The overall diagnostic accuracy of needle-residual materials was comparable to the direct smears materials with overall kappa score of 0.653. Lymph nodes, breast and salivary glands diagnostic accuracy show good agreement (kappa: 0.769, 0.636 and 0.617 respectively). Moderate agreement was seen in thyroid (kappa: 0.569).

Conclusion: Residual materials left in needles have sufficient materials for cytological assessment for future molecular studies if needed.

Keywords: Residual materials; Thyroid FNA; Breast FNA; Lymph node FNA; Salivary glands FNA

Introduction

Fine-needle aspiration (FNA) is a valuable diagnostic tool both for neoplastic and non-neoplastic diseases. The major indication in pathology is its use in neoplastic condition to differentiate between benign and malignant lesions [1]. Materials obtained from fine needle aspiration can be processed in several ways; direct smears, filtration (Milipore, ThinPrep), cyto-centrifugation-based preparations (Cytospin) and made into cell/tissue blocks. In order to produce high-quality diagnostic materials, the processing method used should cause minimal cell loss and can still preserve the morphologic details for accurate diagnosis to be made. Despite the availability of numerous cytological processing techniques, properly prepared direct smears are regarded as the best method [gold standard] of collecting the aspirated materials [2-4]. In direct smears preparation, air in syringe is used to expel the materials onto the glass slides. Commonly the needle is discarded afterwards. The cells which remain trapped within the discarded needle are known as needle-residual materials and are found to be useful for diagnostic purposes [5].

ThinPrep is an automated thin-layer cytological material processing device that has been accepted for non-gynecological specimen processing including fine-needle aspirations materials of various organs [6-10]. The cell yields are higher than direct smears. The cell loss during processing is also less when compared with cytocentrifuge. ThinPrep processing retains 3 times as many cells as processed using cytocentrifuge [11]. Several studies show the diagnostic accuracy of fine-needle aspirated materials is at least comparable or superior to direct smears [7,8,12,13].

Adequate diagnostic materials are crucial for making an accurate diagnosis. By maximizing the recovery of diagnostic materials, it is hoped that it could further increase the adequacy and accuracy of fine-needle aspirations [14]. The aim of this study was to determine the adequacy and diagnostic agreement of needle-residual materials processed by ThinPrep^{TM} when compared with conventional smear method [The gold standard] and the agreement of the diagnoses on four different organs.

Materials and Methods

This is a prospective study on breasts, thyroids, lymph nodes and salivary glands lesions over a specified period. The number included in the study reflects the workload of the department during that period. For each case, the aspirated materials were directly smeared on glass slides as done routinely. The needle used was then vigorously rinsed by drawing in the ThinPrep^{TM} medium in order to obtain the needle-residual materials. These materials were further processed into monolayered smears. Smears made from both methods were stained

with Papanicolaou (all cases) and May-Grunwald-Giemsa (MGG) (some cases) stains using standard staining techniques. The FNA direct smears [the gold standard] were reviewed by pathologists on rotation and each was given a diagnosis as per routine testing. The needle-residual material smears [test method] were reviewed separately by one pathologist (NHO; corresponding author) who was blinded to the diagnoses made on direct smears. The diagnostic categories are those used in routine cytology; Malignant, Suspicious of Malignancy, Atypical/Borderline, Benign and Non-diagnostic. The diagnoses made on both methods were compared.

The FNA was done by the medical officer who was on roster as per routine testing while the left over residual materials in the needles were processed by the first author [NZ].

Data were entered and analyzed using SPSS version 21.0. Kappa agreement was used to calculate the agreement between the direct smears (gold standard) and the needle residuals (test method). The range of kappa value are as follows: <0.0: poor agreement, 0.01 – 0.20: slight agreement, 0.21-0.40: fair agreement, 0.41-0.60: moderate agreement, 0.61-0.80: substantial agreement and 0.81-0.99: almost perfect agreement. Significant value was taken as p-value less than 0.05.

Results

A total of 118 lesions of which 47 (39.8%) were breasts, 42 (35.6%) thyroid, 25 (21.2%) lymph nodes and 4 cases of salivary glands (3.4%) lesions. The mean number of needle passes per each lesion was 1.77 times. Adequate needle-residual cellular material processed in Thinprep medium was present in 81/118 of the cases (68.6%) compared to 98/118 cases (83.1%) for the direct smear method. The agreement between direct smears [the gold standard] and the needle-residual material smears [test method] in various diagnostic categories for all lesions are shown in Table 1. The overall agreement of diagnosis of these 2 methods was moderate (Kappa value: 0.653; value: <0.001) (Table 1).

Diagnostic category for needle-residual materials [Test method]	**Diagnostic category for direct FNA smear materials [Gold Standard]**				
	Malignant	Suspicious for malignancy	Atypical/ borderline	Benign	Non-diagnostic
Malignant	15	0	0	0	0
Suspicious for malignancy	1	3	0	0	0
Atypical	0	0	1	0	0
Benign	0	0	0	58	3
Non-diagnostic	0	0	0	20	17
Kappa value: 0.653; value: <0.001					

Table 1: Agreement in cytological diagnoses made from needle-residual materials and direct FNA smear materials by various diagnostic categories for all lesions [n=118].

For individual organ, the findings were; significant substantial agreement for breasts, (Kappa value: 0.617; P value:<0.001) and lymph nodes (kappa=0.769, p<0.001) (Tables 2 and 3), significant fair agreement for thyroid (kappa=0.569, p<0.001) (Table 4) and significant moderate agreement for salivary lesions (kappa=0.636, p=-0.046) (Table 5).

Diagnostic category for needle residual materials for breast lesions [Test Method]	**Diagnostic category for direct FNA smear materials for breast lesions [Gold Standard]**				
	Malignant	Suspicious for malignancy	Atypical/ Borderline	Benign	Non diagnostic
Malignant	6	0	0	0	0
Suspicious for malignancy	0	0	0	0	0
Atypical/Borderline	0	0	1	0	0
Benign	0	0	0	24	2
Non diagnostic	0	0	0	8	6
Kappa value: 0.617; P value: <0.001					

Table 2: Agreement between diagnostic categories for needle residual materials and direct FNA smear materials for breast lesions [n=47].

Discussion

Fine-needle aspirations cytology is primary routine investigation for palpable and impalpable lesions. Direct smear materials have been shown to have good accuracy and are widely accepted in evaluating aspirated materials. We conducted the study with the assumption that there are still retained diagnostic materials within the needles after completion of the smearing process. We then examined the agreement of the diagnoses made in four organs; breasts, thyroids, lymph nodes and salivary glands. This is a prospective study and the number of

cases for each organ included in the study reflects the workload of the department over the same period of time. We found that the residual materials left in the needles have sufficient materials for cytological assessment in majority of cases. The overall diagnostic agreement between needle-residual materials and FNA direct smear materials was significant. The needle-residual materials were adequate to correctly diagnose more than half of the cases recruited (67.8%). For the rest of the cases, there were due to; no residual cellular materials obtained and these cases also did not have adequate cellular materials on direct smears (the gold standard); the needles contained scanty materials while the direct smears were good and the needles yielded cellular materials while the direct smears were inadequate.

Diagnostic category for needle residual materials of lymph node lesions	**Diagnostic category for direct smear materials**				
	Malignant	Suspicious for malignancy	Atypical/ Borderline	Benign	Non-diagnostic
Malignant	6	0	0	0	0
Suspicious for malignancy	1	1	0	0	0
Atypical/Borderline	0	0	0	0	0
Benign	0	0	0	9	0
Non diagnostic	0	0	0	3	5
Kappa value: 0.769; p <0.001					

Table 3: Agreement between diagnostic categories for needle residual materials and direct FNA smear materials for lymph node lesions [n=25].

Diagnostic category for needle residual materials for thyroid lesions					
	Malignant	Suspicious for malignancy	Atypical/ Borderline	Benign	Non diagnostic
Malignant	2	0	0	0	0
Suspicious for malignancy	0	1	0	0	0
Atypical/Borderline	0	0	0	0	0
Benign	0	0	0	24	1
Non diagnostic	0	0	0	8	6
Kappa value: 0.569; p <0.001					

Table 4: Agreement between diagnostic categories for needle residual materials and direct smear materials of Thyroid Lesions [n=42].

Diagnostic category for needle residual materials	**Diagnostic category for direct smear materials**		
	Malignant	Benign	Non diagnostic
Malignant	1	0	0
Benign	0	1	0
Non diagnostic	0	1	1
Kappa value: 0.636; p=0.046			

Table 5: Agreement between diagnostic categories for needle residual materials and direct smear materials of salivary glands [n=4].

The diagnostic accuracy was better with atypical/suspicious/ malignant cases than benign lesions. In 3 cases, needle-residual materials yielded diagnostic materials where direct smear materials did not show. All the 3 cases were 'Benign' [2 breast and one thyroid]. Direct smears of these cases were 'Inadequate'. The cells of these benign cases might have attached to the inner surface of the needles thus could only be dislodged with rigorous rinsing in ThinPrep™ medium.

ThinPrep™ might have induced artifacts and cellular morphologic alterations, which influenced diagnostic accuracy. The interpretation requires familiarity with cytological appearance to avoid misdiagnosis [15]. For thyroid lesions the colloid is seen as droplets rather than a diffuse pattern [7]. The cells have better nuclear detail but the cytoplasm is often disrupted.

The proportion of lesions included in the study reflects our laboratory workload. We have very few salivary gland lesions. This is the first study which compared findings in different organs as seen routinely in a pathology laboratory. We observed the diagnostic agreement is best with lymphnode [kappa 0.769] and least with thyroid [kappa 0.569] lesions.

The percentage of cases with adequate needle-residual materials for diagnostic purposes in this study was similar to that of the previous study [16] however unlike ours in that study the FNA materials were converted into tissue blocks. Residual materials could also facilitate molecular testing for certain mutational genes in limited cytologic specimens [17] including microganisms such as tuberculosis [18]. Others argue that routine use of ThinPrep™ as an adjunct preparatory method to FNA material is not justified [19].

The FNA for all our cases were done by direct palpation in targeting the masses. It has been observed that higher percentage of needle-residual materials is obtained under image-guided deep-seated lesions [5,20]. This understandably is the results of more targeted aspirations. The limitation of our study is we made comparison on unequal number for each of the four organs due to reasons mentioned above.

In summary, residual materials left in needles have sufficient materials for cytological assessment. We suggest not discarding FNA needles after the procedure as the residual materials could be later use either to aid the direct smears or for future molecular studies if needed.

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