

Pain associated with fine-needle aspiration biopsy of thyroid nodules

Ból związany z biopsją cienkoigłową guzków tarczycy

Adam Stangierski¹, Marek Ruchała¹, Izabela Warmuz-Stangierska¹, Maria Danuta Głowacka²,
Joanna Zdanowska², Alicja Głowacka-Rębała², Renata Rasińska², Agata Czarnywojtek¹

¹Department of Endocrinology, Metabolism and Internal Diseases, Karol Marcinkowski University School of Medical Sciences, Poznan, Poland;

Head of Department: prof. dr hab. n. med. Jerzy Sowiński

²Faculty of Health Sciences, Karol Marcinkowski University School of Medical Sciences, Poznan, Poland;

Head of Faculty: prof. dr hab. n. med. Maria D. Głowacka

Przeгляд Menopauzalny 2012; 3: 233–238

Summary

Introduction: The importance of FNAB tool in the pre-surgical diagnosis.

Aim of the study: The aim of this study was to look for patients' comfort improvement and the best diagnostic conditions as we intended to obtain the real estimation of patient's pain intensity and the correlation between patient's hormonal status, age, sex, nodule type with the level of pain sensation.

Material and methods: The research was carried out in a group of 75 patients of the Clinic of Endocrinology, Metabolism and Internal Medicine. The inclusion criteria at a thyroid outpatient clinic were as follows: the thyroid nodules that required an US-FNAB were 10 mm or larger in the maximum diameter and the locations of the thyroid nodules were intraglandular and were relatively central in thyroid. The main study method was the pain scale measuring patient's pain intensity, based on a self-report.

Results: The obtained scores showed moderate pain as dominant in the study group and no statistically significant correlation between the intensity of pain, age, sex, density of the nodules (calcifications), initial diagnosis and hormonal status of the patient.

Conclusions: The use of different anesthetics during thyroid FNAB has already been reported as ineffective, thus alternative methods of decreasing pain during biopsy should be considered.

Key words: biopsy, thyroid nodules, pain, visual analogue scale, local anesthesia.

Streszczenie

Cel pracy: Celem niniejszej pracy była ocena nasilenia odczuć bólowych pacjenta podczas biopsji cienkoigłowej tarczycy, a także wykazanie korelacji pomiędzy stanem hormonalnym, wiekiem, płcią, strukturą guzka a nasileniem odczuwanego bólu.

Materiał i metody: Badanie zostało przeprowadzone na grupie 75 pacjentów w Klinice Endokrynologii, Przemiany Materii i Chorób Wewnętrznych Uniwersytetu Medycznego im. Karola Marcinkowskiego w Poznaniu. Doznania bólowe towarzyszące biopsji cienkoigłowej tarczycy porównywano w grupie pacjentów ze zmianami ogniskowymi o minimalnym wymiarze 10 mm, zlokalizowanymi w centrum gruczołu. Do pomiarów subiektywnych doznań bólowych użyto zmodyfikowanej wersji popularnej wizualnej skali analogowej (*visual analogue scale* – VAS).

Wyniki: Uzyskane wyniki wykazały umiarkowany ból jako dominujący w grupie badanej. Ponadto nie wykazano istotnej statystycznie korelacji pomiędzy nasileniem bólu a wiekiem, płcią, strukturą nakłuwanej zmiany i stanem hormonalnym pacjenta.

Wnioski: Uzyskane wyniki wskazują, że ewentualne zastosowanie środków znieczulających w trakcie biopsji cienkoigłowej znajduje uzasadnienie jedynie w wybranych grupach pacjentów, zwłaszcza w przypadku

Address for correspondence:

Joanna Zdanowska M.Sc., Poznan University of Medical Science, Faculty of Health Sciences, 11 Smoluchowskiego Str., 60-179 Poznan, Poland, tel. +48 61 861 22 50, +48 604 466 980, Email: jzdano@ump.edu.pl

nasilonych reakcji emocjonalnych. W niektórych przypadkach redukcja stresu, a nie doznań bólowych, może ograniczyć liczbę pacjentów unikających biopsji cienkoigłowej tarczycy.

Słowa kluczowe: biopsja, guzki tarczycy, ból, wizualna skala analogowa, znieczulenie miejscowe.

Introduction

In recent decades fine needle aspiration biopsy (FNAB) of thyroid lesions has become the most important and effective tool in pre-surgical diagnosis. The use of cytological aspiration seems to be one of the principal examinations in the whole endocrinology, especially in Europe, where the occurrence of thyroid gland nodular goiter is very high. In spite of its obvious benefits such as high efficacy (from 79% to 95%), sensitivity (85.7%), specificity (up to 100%), positive predictive value (up to 100%), negative predictive value (94.9%), accuracy (96.1%) [1], in our study we wanted to focus on side effects of this procedure which may influence parameters listed above. One of them, which affects each patient undergoing thyroid fine needle aspiration, is the sensation of pain. Some of our patients describe the sensation as a pinch, but others feel it much stronger. Sometimes the pain accompanying biopsy may interrupt the procedure [2]. There are no sufficient data about the pain type and its relation to parameters like needle size, number of passes, physician's expertise, technique used, although the influence of those parameters on the efficacy of the procedure is a very popular topic of publications.

Looking for the best conditions of medical examinations, influencing not only the procedure, but also results of treatment, it would be important not to avoid underestimated patient's sensations of pain. The goal of the study was to estimate the correlation between the patient's hormonal status, age, sex, nodule type with the level of pain sensation. We also intended to check whether the pain sensation is lower if the

patient undergoes repeated procedures during a follow-up period.

Material and methods

The study was designed for consecutive patients who met the inclusion criteria for study participants. A total of 75 patients of the Clinic of Endocrinology, Metabolism and Internal Medicine who agreed to participate in the study were included between January and November 2010. The inclusion criteria at a thyroid outpatient clinic were as follows: - first, the thyroid nodules that required an US-FNAB were 10 mm or larger in the maximum diameter, - second, locations of the thyroid nodules were intraglandular and were relatively central in thyroid. The exclusion criteria for study participants were as follows: patient's refusal (patient did not sign consent), participants who had a history of bleeding tendency and who had been taking anticoagulants, substernal or subclavicular localization of the lesion in the case of large goiter. The Poznan Medical University Institutional Review Board approved this study and all participants provided informed written consent.

Mean age of the study group is 55.0 ± 14.67 years, for women 55.2 ± 14.59 , for men 54.4 ± 15.24 years (Fig. 1).

The main study method was the pain scale measuring a patient's pain intensity based on a self-report. Just after the biopsy, each of the participants was asked to complete the scale in which he was supposed to estimate his individual degree of the pain sensation during the procedure. When responding to a question, respondents specified their level of pain severity by indicating a position along a continuous line between two end-points: from 1 (lowest pain), to 10 (unbearable pain). Our questionnaire was based upon a very popular psychometric scale VAS, which was previously confirmed to be very effective in subjective pain estimation among patients with various diagnoses [3, 4]. Different modifications of VAS were used in psychological assessment of a wide variety of health-related constructs including pain [5], quality-of-life [5], and mood [6]. In our research we divided the scale into 3 ranges: - lowest pain (1-3); - moderate pain (4-7); - severe pain (8-10). Fine needle aspiration biopsy was performed under the guidance of the US examination using a high-resolution ultrasound device (Aixplorer Multiwave by Supersonic Imagine) with a 12-15-MHz linear probe within a few days before, or just prior to the US-FNAB. An experienced endocrinologist performed all biopsies

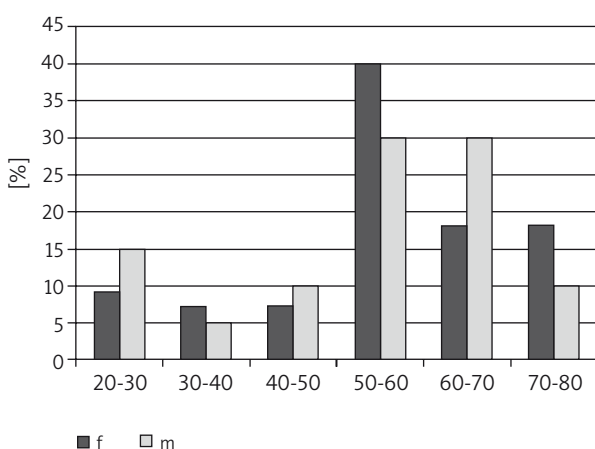


Fig. 1. Age structure of study group

using a 5-ml plastic syringe attached to a conventional 25-gauge needle (0.5 mm x 40 mm by KDM) under the US guidance. Patients were placed in the supine position with their neck a little extended and after they confirmed to feel comfortable, the procedure was started. First, skin was sterilized with a conventional alcohol solution. The target nodule was placed in the center of the image by adjusting the US probe after appropriate positioning. The needle was then vertically inserted into the target nodule in the center of the transverse US image. If the target part of the nodule was properly punctured, the needle was moved up and down for a few seconds only by movement of the operator's wrist, without aspiration with a syringe. After the hub of the needle became filled with the material, the syringe needle unit could be rapidly withdrawn and the puncture site on the skin was compressed for several minutes [7]. Just after the procedure (within maximum 5 minutes), each patient was transferred to another room, where a nurse instructed him how to complete a pain survey, and then he estimated his pain sensation by marking the number. We also asked if the pain accompanying recent biopsy was stronger comparing to the same procedure performed in the past.

Spearman rank correlation test was performed to determine whether there was a significant correlation between pain scores, type of the nodule (with/or without calcifications), age, sex, hormonal status (TSH level), and subjective pain sensation during previous biopsies.

Collected data were tabelarized and SPSS 17 for Windows was used for statistical analysis. In all correlation cases, more than 20% of cells have number expected less than 5, so a chi square test cannot be applied. In all cases statistical significance was above 0.05, which implies that those are non-significant statistics and we can only calculate the correlation for the sample. Correlations were measured using Spearman factor for qualitative variables and for quantitative variables, phi Youles factor for even tables and V-Cramer for odd tables.

Results

Results of the study confirmed increased intensity of pain sensation only in a few of examined patients. The obtained scores showed no statistically significant correlation between the intensity of pain, age, sex, the density of the nodules (calcifications), initial diagnosis, and hormonal status of the patient.

Mean pain sensation for the whole study group was 3.6 ± 1.40 .

1. Calcifications

There was no statistically significant correlation between pain and presence of calcifications in nodules, although mean pain sensation in patients with calcifications in nodules was estimated as 4.6 ± 1.81 , while average pain in patients with soft lesions was 3.5 ± 1.29 .

(Tab. I). There were some discreet differences in pain sensation between the patients representing those two groups: 55.5% of the patients with calcified nodules quantified pain as 5 or more, meanwhile 81.8% of the patients from the second group estimated it as 3 points or less. It revealed a quite obvious tendency that the operating endocrinologist had to use more power to combat the stiffness of tissue to get into the nodule while aspirating the material. The lack of positive correlation might be a result of quite a small group of patients with calcifications in the study group (Tab. I).

2. Sex differences

There was no correlation between men and women in subjective estimation of pain intensity during FNAB. 85% of women valued the impact of pain as 4 and less, in the men population it was 75%. It can be supposed that lack of differences might be a result of a small number of men involved in the study, as in the general population most of thyroid patients are women (Tab. II).

3. Initial diagnosis

There was no correlation found between the type of goiter and the pain sensation. Only 17.7% of patients with solitary nodule declared their pain as 5 and more, while toxic goiter and non-toxic goiter patients were a bit more susceptible, more of them (25%) described pain as 5 or more (Tab. III).

4. Hormonal status

Half of the whole study group (53%) evaluated the pain accompanying biopsy as the lowest. Almost the same number of patients (42.7%) declared their pain

Tab. I. Pain score vs. calcifications

Pain score intensity	Calcifications		
	n	y	
low	37 56.1%	3 33.3%	40 53.3%
severe	2 3.0%	1 11.1%	3 4.0%
moderate	27 40.9%	5 55.6%	32 42.7%
	66 100.0%	9 100.0%	75 100.0%

Tab. II. Pain score vs. sex

Pain score	Sex		
	f	m	
low	27 49.1%	13 65.0%	40 53.3%
severe	3 5.5%	0 0%	3 4.0%
moderate	25 45.5%	7 35.0%	32 42.7%
	55 100.0%	20 100.0%	75 100.0%

Tab. III. Pain score vs. initial diagnosis

Pain score	Initial diagnosis			
	solitary nodule	solitary nodule (Hashimoto disease)	non-toxic nodular goiter	toxic nodular goiter
low	10 58.8%	1 50.0%	24 54.5%	5 41.7%
severe	1 5.9%	0 0%	1 2.3%	1 8.3%
moderate	6 35.3%	1 50.0%	19 43.2%	5 50.0%
	17 100.0%	2 100.0%	44 100.0%	12 100.0%

ensation as moderate. Only 4% of the study group estimated the pain as severe. A similar distribution of pain intensity was noticed in 2 groups with different TSH: euthyroid and hyperthyroid patients. A different distribution of pain intensity was identified in hypothyroid patients, where moderate sensations were noticed as more frequent than the lowest pain. The majority of hyperthyroid patients described their pain sensation as lowest and avoided the estimation as severe (Tab. IV).

The difference in pain estimation between patients with a different level of TSH was not statistically significant.

Discussion

USFNABs of thyroid nodules have been routinely performed for approximately the past 20 years at the UMP hospital in Poznan, without reporting any significant complications. We have been using one to five needle punctures and no local anesthesia. In consequence of using very thin needles (0.5 mm), which are thinner than those used during injections, patients seem to easily tolerate the pain or discomfort related to the procedure. But we also noticed many of patients complaining about the pain sensations and trying to avoid the next biopsy.

It has also already been reported that in some cases pain and discomfort might contribute to an inadequate cytological result, due to inexact operator's puncture [8]. It seems to be a consequence of different reasons: patient's instable position during the procedure, tensioning of neck muscles, emotional reactions affecting the operator's activity or probably other – awareness of the disease. Trying to meet patients' expectations, trying to prevent complications related to pain, and having in mind patients' rights we tried to find a way of improving their comfort during the procedure. The first and necessary step in this algorithm should be identification of pain intensity and reasons of its increased perception. The next step is modification of the procedure if necessary and then maybe preparation of anesthesia. There were some reports of using different anesthetics proving that it may be eligible for reducing the pain accompanying thyroid FNAB [9, 10], however some other reports lead to opposite conclusions [11-13].

It was supposed that anesthetic procedures might be necessary in some situations, for example when FNAB was performed on deep-seated nodules, with presence of calcifications or when vigorous aspiration was required. There were only a few situations like subacute thyroiditis, intrathyroidal hemorrhage, infarction or cyst leakage when using local anesthesia could be justifiable [14]. Another study denied the usefulness of local anesthesia administration before the procedure, if the patient underwent only one puncture [9]. The investigators found higher pain sensitivity in this group comparing to the group without any pre-biopsy anesthesia. As mentioned above, in our study we performed mostly only one needle puncture per patient so we obtained comparable results.

Thinking about anesthesia we intended to document the real intensity of pain. In spite of prior anxious declarations, most of the patients in the study described the pain as moderate. The average pain level among the patients was 3.6 on a scale of 1 to 10. High sensation of pain concerned only a small study group so we may treat it as a serious side effect and a problem to be solved without anesthesia. The fact that we did not reveal any correlation between the pain level and initial

Tab. IV. Pain score vs. TSH

Pain score		TSH			
		euthyrosis (TSH 0.29-4.0)	hyperthyrosis (TSH < 0.29)	hypothyrosis (TSH > 4)	
Pain score	low	31 57.4%	2 66.7%	7 38.9%	40 53.3%
	severe	2 3.7%	0 0%	1 5.6%	3 4.0%
	moderate	21 38.9%	1 33.3%	10 55.6%	32 42.7%
		54 100.0%	3 100.0%	18 100.0%	75 100.0%

diagnosis, hormonal status, sex or age also probably proves the accuracy of our findings. The performer of all biopsies was an experienced and well-trained specialist, so it excluded lack of expertise and vigorous handling of the needle which might also increase the severity of pain. Comparable impressions of pain among examined men and women did not confirm the results of other studies [14], but it might be a result of a small number of males in the group.

There were many publications indicating uselessness of anesthesia during thyroid FNAB. Pitman et al. reported that only if the sonography reveals deep-seated, non-palpable nodules, which require more time and probing to be reached, lidocaine can help the patient to decrease the pain [14]. In our study, only shallow-seated, mostly palpable lesions were examined. Amadee et al. proved that it also may be beneficial in children [15], although in the general population a small number of children undergo thyroid FNAB.

Taking this information and obtained results of the study into account, the only credible reason for using local anesthesia in thyroid nodule biopsy seems to be the patients' affected mental status increasing pain perception. Basing on our experience we noticed that anxious, non-cooperative, pain-phobic or needle-phobic patients might represent a small group with higher pain sensations. Some investigators confirmed this opinion in their studies [16]. A positive relationship between anxiety and pain was a common experience in clinical settings [17, 18]. Some authors reported that accurate preparatory information during medical invasive procedures alleviated pain by disengaging the hippocampus. It supports the proposal that during anxiety, the hippocampal formation amplifies aversive events to prime behavioral responses that are adaptive to the worst possible outcome [19]. Considering previous researches revealing the ineffectiveness of exploitation of local anesthesia during this procedure and our study results, we propose finding different methods of decreasing the pain during thyroid FNAB. The patient's mental status and attitude may be essential, thus we suppose that a proper psychological approach before every single procedure could help in fighting anxiety, tension and overreaction related to thyroid puncture. This may be helpful in decreasing the number of ineffective biopsies, but it could also encourage the patient to undergo repeated examinations. Such psychological support may be also helpful for the patient to agree for the biopsy. For such agreement to be effective it is necessary to inform the patient about biopsy side effects including accompanying pain and its meaning, which can involve fear and anxiety. In cases of painful methods of treatment, the patient should be also informed about possible types of anesthesia. This information must include both disadvantages and advantages of the specified method and it may

be applied after obtaining the patient's consent, but the rules of proper communications play a key role. A proper psychological approach, involving effective patient-physician communication before this invasive procedure seems to be one of many factors improving the quality of thyroid biopsy. We also have to consider using alternative FNAB methods such as core needle biopsy, which is performed with needles comparable in diameter, although the technique is different [20]. There are some studies suggesting that core needle biopsy could be more beneficial than classical FNAB due to its lower non-diagnostic rate [21], but others suggest lower accuracy [22].

In our opinion, core needle thyroid biopsy needs further investigations, not only as regards its accuracy. Due to a different technique of the procedure, which does not demand repeating of the needle movements in the nodule, it seems to provide less pain for the patient. There are still no studies investigating this problem.

Conclusions

1. A moderate level of pain accompanying thyroid biopsy appeared to be dominant in the study group.
2. There were no statistically significant correlations between the intensity of pain, age, sex, the density of the nodules (calcifications), initial diagnosis, and hormonal status of the patient.
3. The only reasonable cause of using anesthesia during thyroid biopsy seemed to be affected emotional status of the patient. Therefore, we should consider reducing anxiety, and not pain, as the best method of decreasing the number of patients avoiding biopsies.

References

1. Kim DW, Lee EJ, Kim SH, et al. Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules: comparison in efficacy according to nodule size. *Thyroid* 2009; 19: 27-31.
2. Newkirk KA, Ringel MD, Jelinek J, et al. Ultrasound-guided fine-needle aspiration and thyroid disease. *Otolaryngol Head Neck Surg* 2000; 123: 700-5.
3. Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. *J Pain* 2003; 4: 407-14.
4. Williams VS, Morlock RJ, Feltner D. Psychometric evaluation of a visual analog scale for the assessment of anxiety. *Health Qual Life Outcomes* 2010; 8: 57.
5. de Boer AG, van Lanschot JJ, Stalmeier PF, et al. Is a single-item visual analogue scale as valid, reliable and responsive as multi-item scales in measuring quality of life? *Qual Life Res* 2004; 13: 311-20.
6. Lingjaerde O, Førelund AR. Direct assessment of improvement in winter depression with a visual analogue scale: high reliability and validity. *Psychiatry Res* 1998; 81: 387-92.
7. Crockett JC. The thyroid nodule: fine-needle aspiration biopsy technique. *J Ultrasound Med* 2011; 30: 685-694.
8. Leung AM, Farwell AP. Unsatisfactory consequences from fine-needle aspiration biopsy of thyroid nodules. *Thyroid* 2008; 18: 491-2.
9. GURSOY A, ERTUGRUL DT, SAHIN M, et al. Needle-free delivery of lidocaine for reducing the pain associated with the fine-needle aspiration biopsy of thyroid nodules: time-saving and efficacious procedure. *Thyroid* 2007;

- 17: 317-21.
10. Gursoy A, Ertugrul DT, Sahin M, et al. The analgesic efficacy of lidocaine/prilocaine (EMLA) cream during fine-needle aspiration biopsy of thyroid nodules. *Clin Endocrinol* 2007; 66: 691-4.
 11. Rausch P, Nowels K, Jeffrey RB Jr. Ultrasonographically guided thyroid biopsy: a review with emphasis on technique. *J Ultrasound Med* 2001; 20: 79-85.
 12. O'Malley ME, Weir MM, Hahn PF, et al. US-guided fine-needle aspiration biopsy of thyroid nodules: adequacy of cytologic material and procedure time with and without immediate cytologic analysis. *Radiology* 2002; 222: 383-7.
 13. Demirci H, Erdamar H, Karakoc A, Arslan M. Thyroid fine needle aspiration biopsy: is topical local anaesthesia beneficial? *Int J Clin Pract* 2010; 64: 25-8.
 14. Pitman MB, Abele J, Ali SZ, et al. Techniques for thyroid FNA: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. *Diagn Cytopathol* 2008; 36: 407-24.
 15. Amedee RG, Dhurandhar NR. Fine-needle aspiration biopsy. *Laryngoscope* 2001; 111: 1551-7.
 16. Degirmenci B, Haktanir A, Albayrak R, et al. Sonographically guided fine-needle biopsy of thyroid nodules: the effects of nodule characteristics, sampling technique, and needle size on the adequacy of cytological material. *Clin Radiol* 2007; 62: 798-803.
 17. Melzack R. *The puzzle of pain*. Basic Books, New York 1979.
 18. Grachev ID, Fredrickson BE, Apkarian AV. Dissociating anxiety from pain: mapping the neuronal marker N-acetyl aspartate to perception distinguishes closely interrelated characteristics of chronic pain. *Mol Psychiatry* 2001; 6: 256-8.
 19. Ploghaus A, Narain C, Beckmann CF, et al. Exacerbation of pain by anxiety is associated with activity in a hippocampal network. *J Neurosci* 2001; 21: 9896-903.
 20. Pisani T, Bononi M, Nagar C, et al. Fine needle aspiration and core needle biopsy techniques in the diagnosis of nodular thyroid pathologies. *Anticancer Res* 2000; 20: 3843-7.
 21. Harvey JN, Parker D, De P, et al. Sonographically guided core biopsy in the assessment of thyroid nodules. *J Clin Ultrasound* 2005; 33: 57-62.
 22. Liu Q, Castelli M, Gattuso P, Prinz RA. Simultaneous fine-needle aspiration and core-needle biopsy of thyroid nodules. *Am Surg* 1995; 61: 628-32.