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A Second Ductoscopy Procedure in Patients with Recurrent and Persistent Pathological Nipple Discharge

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Breast disease · Ductoscopy · Minimally invasive surgery · Nipple discharge

Abstract

Background: Most patients suffering from pathological nipple discharge (PND) undergo local surgical procedures because standard radiological imaging often fails to reveal the cause. Ductoscopy is a minimally invasive endoscopic technique that enables direct intraductal visualization and can avoid unnecessary diagnostic surgical procedures. Hence, patients with recurrent or persistent PND after an unsuccessful ductoscopy procedure still undergo unnecessary surgery. This study describes the experience of a second ductoscopy procedure in patients with recurrent or persistent PND without suspicious radiological findings. ***Methods:*** Patients with recurrent or persistent PND who underwent two ductoscopy procedures between 2010 and 2017 were retrospectively analyzed. The second ductoscopy was performed when the first ductoscopic attempt was unsuccessful due to technical problems. The primary outcome was the number of preventable surgical procedures. ***Results:*** A total of 17 patients underwent two ductoscopy procedures. The first ductoscopy showed a polypoid lesion in 10 patients (58.8%), no abnormalities in 3 patients (17.6%), and in 4 patients (23.5%), it was not possible to visualize the ductal tree. Post-procedure, all patients suffered from PND. After two ductoscopic attempts, PND stopped in 10 patients (58.8%), and 7 patients (41.2%) still suffered from PND and were operated on. Pathology of the resection specimens showed no abnormalities in 1 patient, a papilloma in 5 patients, and ductal carcinoma in situ in 1 patient. ***Conclusion:*** A second ductoscopy procedure can be considered in the diagnostic work-up of patients suffering from persistent or recurrent PND after an unsuccessful first ductoscopic attempt to avoid unnecessary surgery in about 59% of the cases.

Introduction

Nipple discharge is the third most common breast-related complaint among women after breast pain and a palpable lump [1]. It is often associated with breast cancer and accounts for up to 5 percent of surgical breast clinic referrals [2–4]. Pathological nipple discharge (PND) is defined as spontaneous, persistent, unilateral, and serous or bloody discharge, usually from a single duct opening [5]. The most common causes of PND are benign, namely, an intraductal papilloma and duct ectasia [6–8]. In around 5–10% of the patients suffering from PND without radiological abnormalities, the cause of nipple discharge is an underlying malignancy (ductal carcinoma in situ [DCIS] or invasive carcinoma) [7–10].

Patients with PND usually undergo mammography and ultrasound to rule out cancer. However, when PND is the only complaint, mammography and ultrasound show

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limited sensitivity to detect malignancy (22% and 50% for mammography and ultrasound, respectively) [11]. Magnetic resonance imaging (MRI) has a higher sensitivity (83%), but its specificity is low (76%) [11]. A low specificity with a low prevalence of malignancy means that, despite the high sensitivity, the positive predictive value is low. This means that MRI in this group of PND patients often leads to additional (invasive) procedures such as core needle biopsy and diagnostic surgical excision [12–14]. Additionally, cytology of nipple discharge is used to determine malignancy. However, it is a poor indicator of malignancy, and the clinical relevance is contested [15, 16].

Ductoscopy is a minimally invasive micro-endoscopic approach for direct visualization and removal of intraductal lesions of the breast, performed under local anesthesia at the outpatient clinic. After mammography and ultrasound, ductoscopy can be performed in the diagnostic work-up in patients suffering from PND without radiological abnormalities. It is a safe and effective diagnostic and interventional procedure, with a specificity of 92% and a sensitivity of 58% [11, 17, 18].

The majority of patients suffering from PND still undergo local surgical procedures since standard radiological imaging often fails to reveal the cause. These surgical procedures may lead to undesirable side effects such as scar tissue, perioperative complications, decreased sensitivity of the nipple, and compromised breastfeeding in the future [18–23]. These side effects are especially important to consider since the most common cause of PND is benign. Ductoscopy can avoid unnecessary diagnostic surgical procedures in around 2 out of 3 patients with PND [24]. Hence, patients can still suffer from PND after ductoscopy. In most cases, these patients eventually undergo a surgical procedure because of recurrent or persistent PND [18, 25, 26].

Imaging is often used as a follow-up tool for PND. However, there are currently no studies describing the value of a second ductoscopy procedure in patients suffering from PND after an unsuccessful first attempt. Consequently, this study describes the experience with a second ductoscopy procedure in patients with recurrent and persistent PND without suspicious radiological findings.

Materials and Methods

Study Design and Population

This retrospective cohort study included patients with PND without radiological and/or pathological suspicion for malignancy who underwent two regular patient care-indicated ductoscopy procedures between 2010 and 2017 at the University Medical Center Utrecht (UMCU) in The Netherlands. PND was defined as persistent, unilateral, bloody, or serous nipple discharge during a non-lactational period, persisting for at least 3 months. The study population was a part of a previously conducted cohort study by the same research team [24].

Standard clinical variables were collected, including age at presentation, characteristics of the nipple discharge (laterality and spontaneous vs. expressed), physical exam findings (palpable breast mass and productive ducts), and follow-up period. In addition, diagnostic methods, findings from any imaging studies performed, operative procedures, and histopathological details were recorded for each case.

Before ductoscopy, a standard diagnostic evaluation was performed in all patients with PND in the UMCU or at the referring hospital. This included a medical history, physical examination, and recent radiological imaging (mammography, ultrasonography, and/or MRI and/or core needle biopsy and/or cytology of nipple fluid within 3 months). Patients were eligible for a ductoscopy procedure when radiological and pathological findings were negative.

Ductoscopy Procedure

Ductoscopy was performed by one of two specialized surgeons with experience in ductoscopy at the outpatient clinic under local anesthesia, as described before [24]. Patients without spontaneous PND on the day of the procedure received oxytocin nose spray 30 min before ductoscopy. First, the surgeon identified the affected duct by pressing the nipple. After disinfection with 70% ethanol, the nipple was locally anesthetized with lidocaine 1%. A salivary duct probe (size 0000 to 1; KARL STORZ, Tuttlingen, Germany) and an obturator (Polydiagnost, Pfaffenhofen, Germany) were used for dilatation of the lactiferous duct orifice in the nipple to a diameter of 1.2 mm. After widening, a port (SoLex nipple expander; Polydiagnost) was placed in the affected duct to introduce the ductoscope. Ductoscopy was performed with a 6,000-pixel, 0.55-mm optic (LaDuScope T-flex; Polydiagnost) and a polyshaft (1.15 mm outer diameter, PD-DS-1015; Polydiagnost). First, 4 mL of lidocaine was infused into the affected duct. Collaps of the ducts was prevented by continuous saline irrigation into the ductal tree through the polyshaft. The surgeon explored the major ducts until the ducts became too narrow to pass. When necessary, additional intraductal anesthesia (bupivacaine) was administered. In the presence of an intraductal polypoid lesion, a basket-shaped guidewire was used to extract the lesion, followed by a histologic examination for diagnosis.

Ductoscopy was regarded as successful when it was possible to visualize the ductal tree. Possible findings during ductoscopy were, e.g., normal duct morphology, ductitis, polypoid lesions, epithelial lesions/damage.

Follow-Up

All patients were followed for at least 2 weeks and 3 months after ductoscopy to evaluate the effect of treatment on symptoms. Patients were offered a second ductoscopy procedure when persistent or recurrence of PND occurred in patients in whom complete removal of the intraductal lesion was not possible during the first attempt (due to technical errors such as duct perforation or basket failure). Patients underwent surgery (or not), depending on the findings at second ductoscopy (persistent or recurrent PND, suspicious findings, patients' preference).

Statistical Analysis

SPSS (v25.0.0.2, Chicago, IL) was used to analyze the data for this study. For the normally distributed continuous data, the values were described using mean with standard deviation. If continuous data were not normally distributed, a median with an interquartile range of frequency was used.

Table 1. Clinical data of 17 patients with pathological nipple discharge (PND) undergoing two ductoscopy procedures

Age, mean ± SD, years	50.8±16.3
Follow-up, mean ± SD, months	10.2±10
Affected breast, *N* (%)	
Left	6 (35.3)
Right	10 (58.8)
Both	1 (5.9)
Ultrasound findings, *N* (%)	
BI-RADS 1	4 (23.5)
BI-RADS 2	6 (35.3)
BI-RADS 3	5 (29.4)
BI-RADS 4a	2 (11.8)
Mammography findings, *N* (%)	
BI-RADS 1	2 (11.8)
BI-RADS 2	6 (35.3)
BI-RADS 3	5 (29.4)
BI-RADS 4a	2 (11.8)
Not performed	2 (11.8)
MRI findings, *N* (%)	
BI-RADS 1	1 (5.9)
BI-RADS 2	0 (0)
BI-RADS 3	2 (11.8)
BI-RADS 4a	1 (5.9)
Not performed	13 (76.4)
Pathology before ductoscopy, *N* (%)	
No abnormalities	2 (11.8)
Papilloma	3 (17.6)
Benign	3 (17.6)
Not performed	9 (52.9)
Cytology PND, *N* (%)	
Normal/benign	7 (41.2)
Papilloma	2 (11.8)
Atypical cells	1 (5.9)
Other	1 (5.9)
Not performed	6 (35.3)

SD, standard deviation; PND, pathological nipple discharge; MRI, magnetic resonance imaging.

Results

Baseline Characteristics

From 2010 to 2017, a total of 244 patients with PND underwent a ductoscopy procedure. Seventeen patients underwent a second ductoscopy procedure. This patient population had a mean age of 50.8 ± 16.3 years (range: 21–75 years) and a mean follow-up period of 10.2 ± 10 months. Clinical data of the patients are summarized in Table 1. Work-up began with a detailed history and physical examination. In 94% of the cases, the discharge was unilateral, and in 82%, it was spontaneous. The majority of patients suffered from single-duct PND (82%), two patients from two ducts (12%), and one from four ducts (6%). A palpable abnormality was found in 1 patient (6%).

Ultrasound was performed as part of the standard evaluation in all patients. The ultrasound was normal or showed a benign lesion with a low suspicion of malignancy. Most patients had mammography performed (15 of 17 cases) but 2 patients did not due to their young age. The mammogram was normal or showed a benign lesion in 13 cases (76.5%) and a lesion with low suspicion for malignancy in 2 cases (11.8%). MRI was performed in 4 cases and was normal or showed a benign lesion in 3 cases and a lesion suspected of malignancy in 1 patient. Eight of the 17 patients had a biopsy before ductoscopy. Histology revealed that 3 cases had a papilloma, 3 cases had benign tissue, and two showed no abnormalities. Cytology of the nipple discharge before ductoscopy was performed in 11 patients. In most cases (63.6%), cytology showed no abnormalities or was benign.

Multiple Ductoscopy Procedures

Table 2 shows the results of the ductoscopy procedures. At first ductoscopy, it was possible to visualize the ductal tree in 14 patients (82.4%). The second ductoscopy procedure was successful in 13 patients (76.5%). The first ductoscopy showed a polypoid lesion in 10 patients (58.8%) and no abnormalities in 3 patients (17.6%). In 4 patients, it was not possible to visualize the ductal tree; in 3 patients, it was because of perforation of the duct and in one, it was because of narrow ducts. Nine basket extractions were suitable for histopathological examination. In 8 patients (47.1%), these lesions were papillomas without atypia, and in 1 patient, normal tissue was found. After successful ductoscopy, PND stopped in 10 patients (58.8%) for a short period. After weeks to months, these patients suffered again from PND (recurrent symptoms). Seven patients (41.2%) suffered from persistent symptoms.

The interval between both ductoscopy procedures was 6.3 ± 7.9 months. The second ductoscopy showed a polypoid lesion in 9 patients (52.9%) and no abnormalities in 4 patients. In 5 patients (29.4%), it was possible to perform basket extraction. These lesions turned out to be papillomas on pathology. In 3 of these 5 patients, it was not possible to remove the lesion completely. The 7 patients (41.2%) that still suffered from PND after 2 ductoscopic procedures were operated on.

After the first ductoscopy procedure, 2 of the 17 patients experienced post-procedural pain lasting longer than 1 day and 2 patients had minor complaints of pain. The remaining 13 patients (76.4%) did not experience post-procedural pain. There were no other complications reported after the first ductoscopy procedure. After the second ductoscopy procedure, 2 patients reported mild post-procedural pain. Other complications after the second ductoscopy were a retracted nipple in 1 patient and less sensitivity of the nipple in 1 patient. Both complications were self-limiting and improved after weeks.

Table 2. Evaluation of two ductoscopy procedures in patients with persistent and recurrent pathological nipple discharge (PND)

Findings at ductoscopy	*N* = 17
Interval between ductoscopy procedures, months (SD)	6.3 (7.9)
Succeeded first ductoscopy, *N* (%)	
Successful ductoscopy	14 (82.4)
Unsuccessful ductoscopy	3 (17.6)
First ductoscopic diagnosis, *N* (%)	
Polypoid lesion	10 (58.8)
Normal	3 (17.6)
No diagnosis, perforation	3 (17.6)
No diagnosis, narrow ducts	1 (5.9)
Pathology after extraction during first ductoscopy, *N* (%)	
Papilloma	8 (47.1)
Normal	1 (5.9)
No extraction (possible)	8 (47.1)
Reason for second ductoscopy	
Recurrent symptoms	10 (58.8)
Persistent symptoms	7 (41.2)
Succeeded second ductoscopy, *N* (%)	
Successful ductoscopy	13 (76.5)
Unsuccessful ductoscopy	4 (23.5)
Second ductoscopic diagnosis, *N* (%)	
Polypoid lesion	9 (52.9)
Normal	4 (23.5)
No diagnosis, perforation	2 (11.8)
No diagnosis, narrow ducts	2 (11.8)
Pathology after extraction during second ductoscopy, *N* (%)	
Papilloma	5 (29.4)
No extraction (possible)	12 (70.6)
Operated, *N* (%)	
Not operated	10 (58.8)
Operated	7 (41.2)

Surgery after Ductoscopy

Radiologic, ductoscopic, and pathological findings of 7 patients who underwent surgery after two ductoscopy procedures are shown in Table 3. It was not possible to visualize the ductal tree during both ductoscopy procedures in 2 patients.

Four patients were operated on because of recurrent PND and three because of persistent PND. Three patients underwent a major duct excision, two a microdochectomy, and two a lumpectomy. Pathology after surgery showed a papilloma in 5 patients and no abnormalities in 1 patient. One of 17 patients (5.9%) with PND and no suspicious radiological findings was diagnosed with DCIS after surgery. During both ductoscopy procedures, it was not possible to visualize the ductal tree in this patient.

Discussion

Here, we present the yield of a second ductoscopy procedure in patients with persistent or recurrent PND in whom the first ductoscopic attempt was not successful. The results of this study, based on a cohort of 17 patients, indicate that a second ductoscopy procedure can successfully be performed in the vast majority after an unsuccessful first attempt due to technical problems, avoiding surgery in more than half of the cases.

The population of this study was based on a selected population consisting of patients with persistent or recurrent PND who underwent a second ductoscopy procedure after an unsuccessful first attempt. We performed a second ductoscopy on these patients because we considered an additional intervention might be effective to remove the (remaining) lesion that was visible during the radiological screening or first ductoscopy. Our results showed a positive effect of a second intervention in these patients. Hence, since the study population is a sub-selection of patients, the results were not representative of the entire patient population with PND in the outpatient clinic. In patients suffering from persistent or recurrent PND after ductoscopy, careful consideration has to be done whether another ductoscopic intervention can yet have an additional effect on treatment.

Currently, patients suffering from persistent or recurrent PND after a ductoscopy procedure are usually offered radiological follow-up or undergo a surgical procedure for further diagnosis and treatment [18, 25, 26]. The focus of this study was to evaluate if unnecessary surgery for these patients in whom the first ductoscopic attempt was unsuccessful for diagnosis and/or treatment can be prevented by a second ductoscopy.

Table 3. Overview of seven patients with pathological nipple discharge (PND) who were operated on after two ductoscopy procedures

Patient	Age	Radiology	Ductoscopic findings 1	Ductoscopic findings 2	Reason for operation	Type of operation	Pathology after surgery
1	49	US + MMG: BI-RADS 4a	Perforation, no visualization. No PA	Polypoid lesion visible, no successful PA	Persistent symptoms	Lumpectomy	Papilloma
2	24	US + MRI: BI-RADS 1	Polypoid lesion visible, no successful PA	Polypoid lesion visible, PA: papilloma	Recurrent symptoms	Microdochectomy	Papilloma
3	50	US + MMG: BI-RADS 2 MRI: BI-RADS 4a	Normal, no PA	Normal, no PA	Recurrent symptoms	Microdochectomy	Papilloma
4	68	US + MMG: BI-RADS 2	Perforation, no visualization. No PA	Perforation, no visualization. No PA	Persistent symptoms	Lumpectomy	DCIS grade 1
5	65	US + MMG: BI-RADS 2	Polypoid lesion visible, normal PA	Polypoid lesion, PA: papilloma	Recurrent symptoms	Conus excision	Papilloma
6	38	US + MMG: BI-RADS 3	Perforation, no visualization. No PA	No successful cannulation. No PA	Persistent symptoms	Conus excision	Benign
7	41	US + MMG: BI-RADS 3	Polypoid lesion visible, no successful PA	Polypoid lesion visible, no successful PA	Recurrent symptoms	Conus excision	Papilloma

US, ultrasound; MMG, mammography; MRI, magnetic resonance imaging; PA, extraction and pathological diagnosis.

After the second ductoscopic attempts, PND stopped in 10 patients (58.8%), and seven patients (41.2%) still suffered from PND and were eventually operated on. Thereby, a second ductoscopy procedure prevented surgery in 58.8% (10/17 patients). To the best of our knowledge, there are no other published studies on multiple ductoscopy procedures to compare our results with. In 2 of these 7 operated patients, it was not possible to visualize the ducts during both ductoscopy procedures. In 4 of the 7 operated patients, it was not possible to completely remove the benign intraductal lesion. Furthermore, in 2 patients in whom ductoscopy was not successful, surgery was not performed because PND disappeared. According to a previous study, in cases in which no obvious lesions were observed on ductoscopy, there was a 90% probability that the PND would disappear [27]. This indicates a self-limiting disease or a therapeutic effect of ductoscopic saline flushing alone.

On the operated patients, pathology showed a benign lesion in 6 of 7 patients after surgery. One patient was diagnosed with DCIS after surgery, leading to a malignancy rate in the study population of 5.9%. This is in line with previous studies in which the malignancy rate in patients with PND without radiological suspicion for malignancy was between 5 and 10% [7–10]. This means that the vast majority of the patients who suffered from PND were operated on because of a benign lesion.

Besides the diagnostic nature, ductoscopy offers therapeutic options for patients with intraductal benign lesions like papillomas [28–30]. Hence, when in the first ductoscopy procedure a benign lesion is diagnosed but not (fully) removed by endobasket extraction leading to remaining or recurrent PND, a second ductoscopy procedure to attempt to remove the remainder of the lesion may be successful.

Limitations

To our knowledge, this is the first study to report on yield of a second ductoscopy procedure in patients with PND. The major limitation of this study is the small sample group size of included patients. Also, because of the retrospective nature of this study, we were unable to collect some baseline factors and long-term follow-up data in our center. A future prospective study can address the above limitations.

Conclusions

A second ductoscopy procedure in selected patients with remaining or recurrent PND after a first unsuccessful ductoscopy attempt can be useful to diagnose and/or treat the cause of PND, preventing about 59% of the patients from undergoing unnecessary surgery.

Statement of Ethics

This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Written informed consent from participants was not required in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

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Author Contributions

S. Makineli, M.D. Filipe, P.J. van Diest, M.R. Vriens, and A.J. Witkamp contributed to the study conception and design. Material preparation, data collection, and analysis were performed by S. Makineli and M.D. Filipe. The first draft of the manuscript was written by S. Makineli, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Hussain AN, Policarpio C, Vincent MT. Evaluating nipple discharge. Obstet Gynecol Surv. 2006;61(4):278–83.
2 Seltzer MH. Breast complaints, biopsies, and cancer correlated with age in 10,000 consecutive new surgical referrals. Breast J. 2004;10(2):111–7.
3 Santen RJ, Mansel R. Benign breast disorders. N Engl J Med. 2005;353(3):275–85.
4 King T, Carter K, Bolton J, Fuhrman G. A simple approach to nipple discharge. Am Surg. 2000;66(10):960–5; discussion 965–6, 2000.
5 Onstad M, Stuckey A. Benign breast disorders. Obstet Gynecol Clin North Am. 2013;40(3):459–73.
6 Morrogh M, Park A, Elkin EB, King TA. Lessons learned from 416 cases of nipple discharge of the breast. Am J Surg. 2010;200(1):73–80.
7 Lustig DB, Warburton R, Dingee CK, Kuusk U, Pao JS, McKevitt EC. Is microductectomy still necessary to diagnose breast cancer: a 10-year study on the effectiveness of duct excision and galactography. Breast Cancer Res Treat. 2019;174(3):703–9.
8 RE Foulkes, G Heard, T Boyce, R Skyrme, PA Holland, CA Gateley. "Duct excision is still necessary to rule out breast cancer in patients presenting with spontaneous bloodstained nipple discharge,". Int J Breast Cancer. 2011;2011:495315–6.
9 Wong Chung JERE, Jeuriens-Van De Ven SAH, Van Helmond N, Wauters CAP, Duijm LEM, Strobbe LJA. Does nipple discharge color predict (pre-) malignant breast pathology? Breast J. 2016;22(2):202–8.
10 Ohlinger R, Stomps A, Paepke S, Blohmer JU, Grunwald S, Hahndorf W, et al. Ductoscopic detection of intraductal lesions in cases of pathologic nipple discharge in comparison with standard diagnostics: the German multicenter study. Oncol Res Treat. 2014;37(11):628–32.
11 Filipe MD, Patuleia SIS, de Jong VMT, Vriens MR, van Diest PJ, Witkamp AJ. Network meta-analysis for the diagnostic approach to pathologic nipple discharge. Clin Breast Cancer. 2020;20(6):e723–48.
12 Bahl M, Baker JA, Greenup RA, Ghate SV. Evaluation of pathologic nipple discharge: what is the added diagnostic value of MRI? Ann Surg Oncol. 2015;22(Suppl 3):435–41.
13 de Paula IB, Campos AM. Breast imaging in patients with nipple discharge. Radiol Bras. 2017;50(6):383–8.
14 Expert Panel on Breast Imaging; Lee SJ, Trikha S, Moy L, Baron P, diFlorio RM, et al. ACR appropriateness Criteria® evaluation of nipple discharge. J Am Coll Radiol. 2017;14(5S):S138–53.
15 Kooistra BW, Wauters C, van de Ven S, Strobbe L. The diagnostic value of nipple discharge cytology in 618 consecutive patients. Eur J Surg Oncol. 2009;35(6):573–7.
16 Dolan RT, Butler JS, Kell MR, Gorey TF, Stokes MA. Nipple discharge and the efficacy of duct cytology in evaluating breast cancer risk. Surgeon. 2010;8(5):252–8.
17 Yang X, Li H, Gou J, Tan Q, Wang L, Lin X, et al. The role of breast ductoscopy in evaluation of nipple discharge: a Chinese experience of 419 patients. Breast J. 2014;20(4):388–93.
18 Waaijer L, van Diest PJ, Verkooijen HM, Dijkstra NE, van der Pol CC, Borel Rinkes IHM, et al. Interventional ductoscopy in patients with pathological nipple discharge. Br J Surg. 2015;102(13):1639–48.
19 Montroni I, Santini D, Zucchini G, Fiacchi M, Zanotti S, Ugolini G, et al. Nipple discharge: is its significance as a risk factor for breast cancer fully understood? Observational study including 915 consecutive patients who underwent selective duct excision. Breast Cancer Res Treat. 2010;123(3):895–900.
20 Dillon MF, Mohd Nazri SR, Nasir S, McDermott EW, Evoy D, Crotty TB, et al. The role of major duct excision and microdochectomy in the detection of breast carcinoma. BMC Cancer. 2006;6(–8):164.
21 Kocdor MA, Sevinc AI, Canda T, Balci P, Saydam S, Cavdaroglu O, et al. Pathologic nipple discharge in patients with radiologically invisible mass: review of 28 consecutive subareolar explorations. Breast J. 2009;15(3):230–5.
22 Cabioglu N, Hunt KK, Singletary SE, Stephens TW, Marcy S, Meric F, et al. Surgical decision making and factors determining a diagnosis of breast carcinoma in women presenting with nipple discharge. J Am Coll Surg. 2003;196(3):354–64.
23 H Gulay, S Bora, S Kilicturgay, E Hamaloglu, H Goksel. "Management of nipple discharge,". J Am Coll Surg. 1994 May;178(5):471–4.
24 Filipe MD, Waaijer L, van der Pol C, van Diest PJ, Witkamp AJ. Interventional ductoscopy as an alternative for major duct excision or microdochectomy in women suffering pathologic nipple discharge: a single-center experience. Clin Breast Cancer. 2020;20(3):e334–43.
25 Zhang C, Li J, Jiang H, Li M. Use of fiberoductoscopy for the management of pathological nipple discharge: ten years follow up of a single center in China. Gland Surg. 2020;9(6):2035–43.
26 Çetin K. The effect of ductoscopy in the surgical selection of women with pathological nipple discharge. South Clin Istanb Eurasia. 2018;30(1):8–13.
27 Makita M, Akiyama F, Gomi N, Iwase T. Mammary ductoscopy and watchful follow-up substitute microdochectomy in patients with bloody nipple discharge. Breast Cancer. 2016;23(2):242–51.
28 Chang YK, Chen CTH, Wang M, Yang Y, Mark B, Zheng AQ, et al. Could ductoscopy alleviate the need of microdochectomy in pathological nipple discharge? Breast Cancer. 2020;27(4):607–12.
29 Balci FL, Feldman SM. Interventional ductoscopy for pathological nipple discharge. Ann Surg Oncol. 2013;20(10):3352–4.
30 Bender Ö, Balci FL, Yüney E, Akbulut H. Scarless endoscopic papillomectomy of the breast. Onkologie. 2009;32(3):94–8.