Cite as: Mlosek RK, Skrzypek E, Migda B, Migda M, Woźniak W: The efficacy of high-frequency ultrasound-guided injection lipolysis in reducing fat deposits located on the inside of the knees. J Ultrason 2020; 20: e273–e278. doi: 10.15557/JoU.2020.0048.

Submitted: 27.09.2020
Accepted: 26.11.2020
Published: 18.12.2020

The efficacy of high-frequency ultrasound-guided injection lipolysis in reducing fat deposits located on the inside of the knees

Robert Krzysztof Mlosek[1], Ewa Skrzypek[2], Bartosz Migda[1], Michał Migda[3], Witold Woźniak[4]

[1] *Ultrasound Diagnostic Department Faculty of Medical Sciences, Medical University of Warsaw, Warsaw, Poland*
[2] *Department of History of Medicine, Medical University of Warsaw, Poland*
[3] *Clinical Unit of Obstetrics, Women's Disease and Gynecological Oncology, United District Hospital, Collegium Medicum University of Nicolaus Copernicus in Toruń, Torun, Poland*
[4] *First Department of General and Vascular Surgery, Faculty of Medicine, Medical University of Warsaw, Poland*

Correspondence: Ewa Skrzypek, MD, PhD, Department of History of Medicine, Litewska 16, 00-575 Warsaw, Poland; tel. +48 604 075 561, e-mail: ewa.skrzypek@wum.edu.pl

DOI: 10.15557/JoU.2020.0048

Keywords
subcutaneous tissue, high-frequency ultrasound, injection lipolysis, Aqualyx

Abstract

Introduction: Many women consider local fat deposits unacceptable for aesthetic reasons as they have negative impact on appearance and thus, contribute to reduced self-esteem. Injection lipolysis (intralipotherapy) may be an alternative for conventional liposuction in reducing fat deposits. **Aim:** The aim of this paper was to assess the efficacy of high-frequency ultrasound-guided injection of deoxycholic acid (intralipotherapy) to remove fat deposits on the inner side of knees. **Materials and methods:** The procedure was performed in 7 women (14 inner sides of knees). The formulation was administered under high-frequency ultrasound guidance. The procedure was performed twice at 4-week intervals in each patient. High-frequency ultrasound guidance was used to monitor such parameters as the thickness of the dermis (DermaMed, Dramiński S.A.) or the subcutaneous tissue (Philips Epiq 5, USA). Ultrasound was performed both before and after treatment. Additionally, anthropometric measurements were taken, a questionnaire was performed, and a photographic documentation was recorded. **Results:** Reduction in knee circumference and subcutaneous tissue occurred in 71.42% of patients. **Conclusions:** Intralipolysis with deoxycholic acid formulation is an effective method for reducing fat deposits on the inner part of the knees. Ultrasonography proved to be a useful method to monitor the procedure (correct administration of the preparation) and to assess treatment outcomes. A small sample size was a limitation of our study; therefore further studies are needed.

Introduction

Contemporary women tend to use diets and lead an active lifestyle in order to achieve and maintain a slim figure. However, patients unable to eliminate local adipose tissue deposits despite normal body weight and physical activity report to dermatological and aesthetic medicine clinics. Such deposits may be located in many body regions, such as the chin, neck, upper limbs in the area of the triceps muscle, abdomen, hips, buttocks, lower limbs (thighs, knees), etc. For many years, surgical interventions and liposuction were the only methods for elimination of fat pads[1]. Although liposuction has proved to be a very effective method in removing large amounts of fat, it carries a high risk of complications, including edema, hematomas, scars, postoperative pain, and even deep vein thrombosis and pulmonary embolism[1,2], and it is usually associated with the need to discontinue activity for a few days after the procedure. Furthermore, surgical intervention associated with multiple complications is not justified in patients with local fat deposits. Considering the risk of complications and limitations of this method, it seems important to seek techniques that will allow for non-invasive reduction of the subcutaneous tissue. Injection lipolysis is an effective method for local fat pads[3,4]. Although it has been used for more than 30 years, it requires further research due to previous mistakes.

The aim of this study was to assess the efficacy of high-frequency ultrasound-guided injection of deoxycholic acid formulation (intralipotherapy) to remove fat pads on the inside of knees.

The study was performed in accordance with the Declaration of Helsinki. All patients signed an informed consent for the procedure.

Materials and methods

The study group included 7 women aged 26–55 years (mean age 40.43 years). Since each patient underwent bilateral knee injection lipolysis, 14 local fat pads on the inside of knees were assessed. Obesity was one of the inclusion criteria. The mean body mass index (BMI) in the study group was 23.39, indicating normal body weight. All patients were healthy and had no contraindications for the procedure.

Aqualyx™ (Marllor Biomedical, Italy), which is an aqueous solution containing agarose, buffer, 12alfa-dihydroxy-5beta-24-oico cholanic acid sodium salt (deoxycholic acid), water for injections and sodium chloride, was used for fat reduction. Two procedures at 4–5-week intervals were performed in each woman. The formulation was administered via injections (needle size 22G – 40 mm, 10 mL syringe). A dose of 8 mL (one ampule) was usually administered to one knee during a single session. In one patient, a dose of 12 mL was administered to one lateral side of the knee. No local anesthesia was used.

Ultrasound was performed in each patient twice: before the therapy and 4 weeks after the last procedure. We used a conventional scanner Philips Epiq 5 (Philips Healthcare, USA) with a linear 5–18 MHz transducer and high-resolution settings, as well as DermaMed scanner (Dramiński S.A, Poland) with a single-element 48 MHz mechanical transducer, which is intended for skin assessment. Philips Epiq 5 was used to assess the thickness and echogenicity of the subcutaneous tissue, whereas the thickness of the dermis was measured based on DermaMed images. Each procedure was ultrasound-guided so as to ensure precise administration of the formulation (Fig. 1).

Additionally, we performed knee circumference measurements and collected photographs using the Fotomedicus system (ELFO®, Poland). The patients were also asked to complete a questionnaire regarding satisfaction with the procedure.

Results

As a result of the therapy, changes were observed in all parameters assessed. Statistical analysis was performed

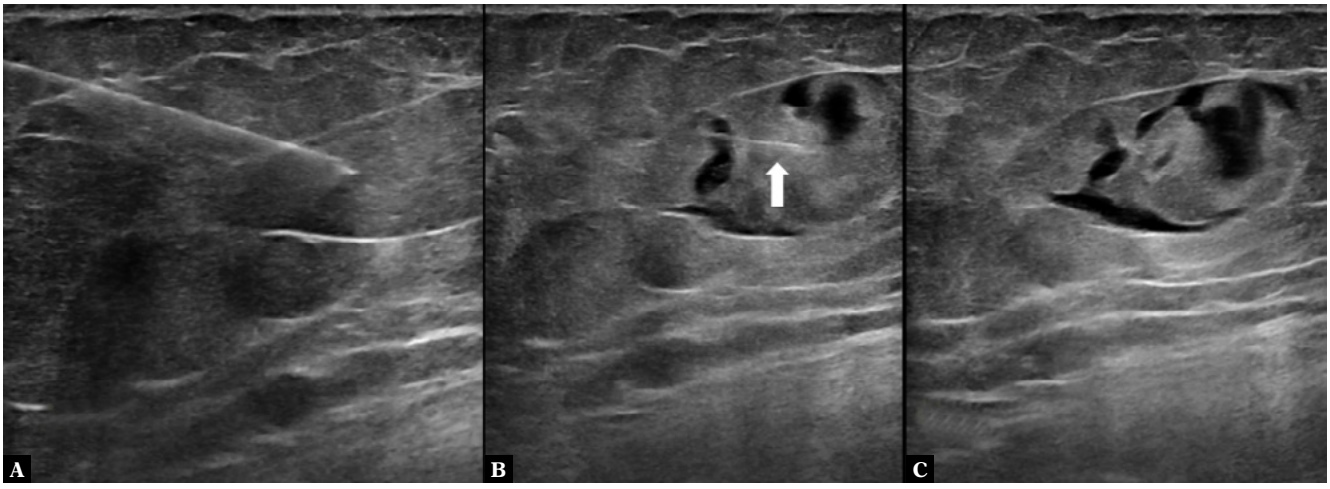

Fig. 1. *Elimination of local fat pads with sodium deoxycholate formulation – ultrasound monitoring.* **A.** *Introduction of the needle.* **B.** *Administration of the formulation.* **C.** *An image taken immediately after injection*

Tab. 1. *Pre- and post-interventional parameters*

No.	Parameter	*n*	Before intervention				After intervention				t- test	
			Mean	Min.	Max.	SD	Mean	Min.	Max.	SD	*t*	*p*
1	Knee circumference [cm]	14	38.79	32.00	44.00	3.72	37.46	30.50	42.50	3.57	**6.19**	<0.001
2	Dermis thickness [mm]	14	1.25	1.03	1.53	0.15	1.35	1.11	1.62	0.16	**–11.32**	<0.001
3	Subcutaneous tissue thickness [mm]	14	22.07	16.80	28.20	3.61	15.98	11.50	19.50	2.72	**4.88**	<0.001

N – sample size, SD – standard deviation, *p* – significance, *t* – t- test result
Statistically significant results are in bold.

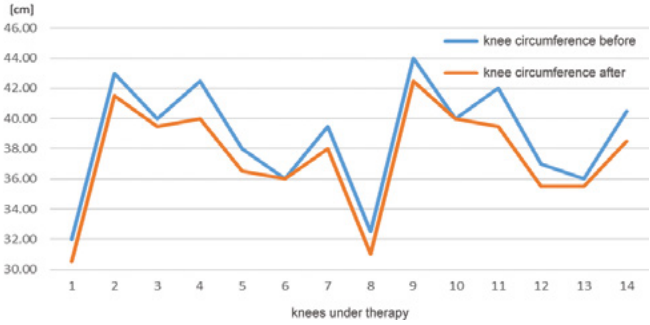

Fig. 2. *A change in knee circumference as a result of therapy to eliminate fat pads on the inner side of the knee*

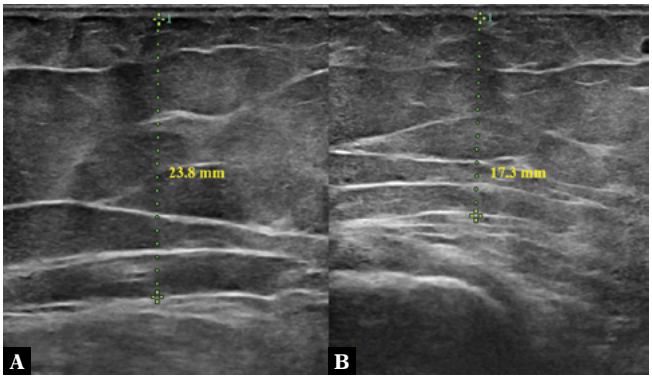

Fig. 3. *Ultrasonographic assessment of the subcutaneous tissue using conventional ultrasonography.* **A.** *Before treatment.* **B.** *After treatment (evident thickness reduction)*

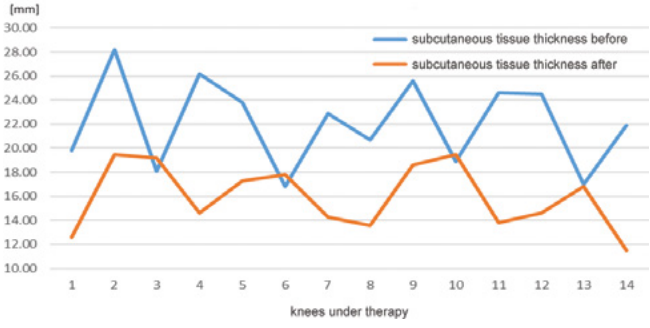

Fig. 4. *A change in the thickness of the subcutaneous tissue as a result of procedure to reduce fat pads on the inner side of the knee*

with Statistica 13.3. In the first stage, the distribution of variables was verified and, once it was considered normal, the t-test for dependent groups was used to compare pre- and post-interventional findings. Statistically significant level was set at $\alpha = 0.05$.

The mean pre-interventional knee circumference was 38.79 cm compared to 37.46 cm after the procedure. The observed difference was statistically significant (Tab. 1, Fig. 2).

Reduced thickness of the subcutaneous tissue was also observed after the second procedure (Fig. 3). After the therapy, the adipose tissue was reduced on average by 6.09 mm, which was statistically significant (Tab. 1, Fig. 4). Thickness measurement of the dermis showed that it was thinner before vs after the procedure (Fig. 5). The pre-interventional thickness of the dermis was 1.25 mm compared to 1.35 mm after the procedure (Tab. 1, Fig. 6). The difference was statistically significant. A qualitative analysis of ultrasound scans obtained with conventional scanner showed increased echogenicity of the subcutaneous tissue in all patients who completed the therapy. According to the questionnaire, 57.14% patients were satisfied with the therapeutic outcomes, 28.57% of respondents expected better results, and 14.29% of patients considered that the outcomes were poor. Photographic documentation confirmed the changes seen on ultrasound (Fig. 7).

The interventions caused no serious complications. Pain and pressure sensation were experienced during injection by 85.7% of patients. Minor pain persisted for about 7 days after the procedure in 5 (71.43%) out of 7 patients. Three (42.85%) patients developed minor edema after the first and the second intervention, which resolved spontaneously within 1–2 days.

Discussion

The number of patients reporting for local fat pad removal for aesthetic reasons has increased recently. The use of surgical techniques, which always carry a higher risk of complications, seems unreasonable as these deposits occupy relatively small areas[1]. Therefore, minimally invasive procedures, including injection intralipolysis, have become an alternative. This method has been used for many years, and it dates back to the turn of the 19th and 20th centuries[5]; however, it was not until the last 30 years that scientific studies on this subject were published. Although many formulations to reduce adipose tissue were developed during this period, they all originate from the so-called Natterman formula, which is based on phosphatidylcholine (PC)[5]. At the beginning of the 21st century, several studies

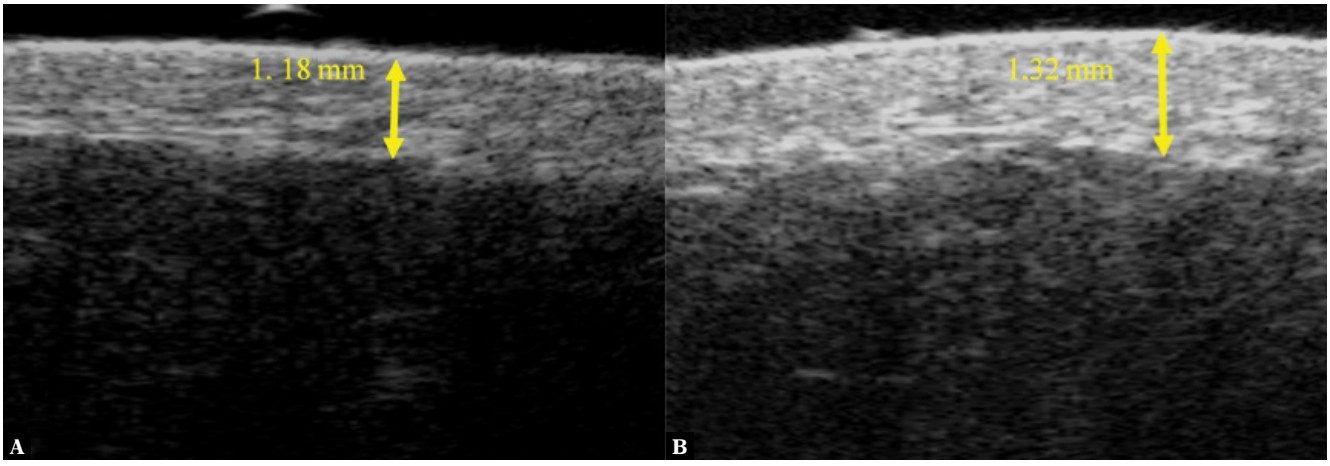

Fig. 5. *High-frequency ultrasonographic assessment of skin thickness using a mechanical transducer.* **A.** *Before treatment.* **B.** *After treatment (evident increase in thickness)*

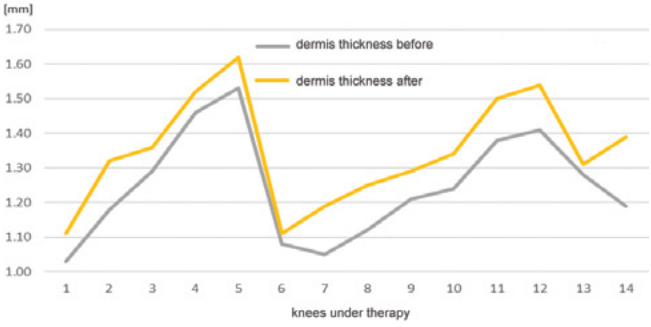

Fig. 6. *A change in the thickness of the dermis as a result of procedure to reduce fat pads on the inner side of the knee*

demonstrated effective PC elimination of fat deposits in the lower eyelid of the eye, as well as in a buffalo hump and other areas[6–8]. It was wrongly believed at that time that PC is responsible for cellular lysis. Further studies showed that sodium deoxycholate (DC) rather than PC causes cellular lysis and is effective[9–12]. This resulted in the development of second-generation preparations, with DC used as the basic component. Sodium deoxycholate is a detergent substance causing adipocyte lysis and it has been used since 2004, i.e. since it was isolated from PC[9].

The formulation used in our study (AqualyxTM) also contains DC. The reason for choosing this preparation was the fact that it is the only available agent registered in the European Union as a class III medical device and having a CE certificate. As mentioned above, it contains DC, but also agarose, and probably the combination of these ingredients makes this preparation less aggressive compared to DC alone[13]. The choice of this medical device was also supported by its great popularity in aesthetic medicine clinics and its widespread use. It should also be noted that there were some ambiguities in the case of this preparation. These were associated with differences between the manufacturer's recommendations and those provided by its distributors. According to the patient information leaflet, the product is intended for the treatment of hypertrophy and hyperplasia of the subcutaneous tissue and HIV-associated lipodystrophy, and its role is to enhance the efficacy of external ultrasounds during microcavitation, which are

Fig. 7. *Treatment outcomes.* **A.** *Before treatment.* **B.** *After treatment (evident reduction in fat pad size)*

emitted by Sonolyx or Sonolyx2. Unfortunately, the distributor of the formulation provided no information regarding the need to use ultrasound[14] and, to our knowledge, external ultrasounds are not used in any of our befriended offices. This problem was also raised by Rauso *et al*.[13], who asked the manufacturer to account for the situation. The manufacturer explained that ultrasound plays a superior role, while the preparation only supports its effects. Our experience and the findings presented by Rauso *et al*.[13,15] support the efficacy of Aqualyx™, which is used without ultrasounds, in the elimination of local fat pads. Amore *et al*.[5], who are currently the authors of the largest study on the use of Aqualyx™, also used no ultrasound, although they indicate that they believe in a synergy between the action of the preparation and external ultrasound.

The method of administration is another important element affecting therapeutic efficacy. The manufacturer assumed administration of the preparation directly into the subcutaneous tissue with the lowest possible number of punctures. This method of administration is referred to as intralipotherapy. The needle should be long, so that once the puncture has been made, it can be moved and the largest possible amount of preparation can be administered over a large area without the need for a new puncture. It is recommended to perform a maximum of 2–3 punctures and use a special 10 cm needle for intralipotherapy; it is also possible to use a cannula[5,16]. In our study, we used 22G × 90 mm needles for lumbar puncture and a single puncture was made to administer the preparation. Puncture accuracy and the administration process were monitored using a classic ultrasound scanner with a linear probe. This allowed to precisely determine the location of the needle and to avoid injecting the preparation into the dermis, vessel, muscle or ligament, thus minimizing the risk of complications. We found no studies using ultrasonography for the monitoring of the procedure. Ultrasonography was used only to monitor postoperative edema[5], as well as to present treatment outcomes after the use of PC-based preparation compared to two cases of Madelung's disease[17].

Our study showed that Aqualyx™ effectively reduced fat deposits on the inner side of the knees. The achieved efficacy of 71.42% correlates with the one obtained by Amore *et al*.[5] (76.7%) in a group of 1,344 patients. It should be noted, however, that this was cumulative efficacy estimated for different body parts subject to interventions; however, the authors classified the inner side of the knee as susceptible to the preparation. Patients' satisfaction with treatment outcomes also corresponded with Amore *et al*.[5] A characteristic feature is that the patients assessed the therapeutic outcomes poorer than indicated by the performed measurements. The use of high-frequency ultrasound to assess changes occurring as a result of intralipotherapy, which enabled an objective measurement of the individual parameters, was an innovative solution in our study. We found no report in which individual parameters were assessed using ultrasound despite the fact that its usefulness in skin evaluation has been repeatedly confirmed[18,19]. The thickness of the subcutaneous tissue should be considered the most useful ultrasonographic parameter. As already mentioned, a comparison of pre- and post-interventional ultrasound images showed an increase in the echogenicity of the entire subcutaneous tissue. This may indicate persisting inflammation, which would require longer follow-up. Furthermore, echogenicity was assessed in this case based on a qualitative analysis (an evaluation of the image by the researcher), which may be biased. In further studies, echogenicity should be assessed quantitatively, based on the measurement of the number of pixels in a given range of brightness. The result for the thickness of the dermis, which was assessed with a high-frequency scanner, is also interesting as the thickness of this structure increased significantly after treatment completion. In our opinion, this may be due to the persistent inflammation in the dermis, which increases skin thickness. However, this requires further observations. In light of our results, the poor therapeutic outcomes in the case of two women are also puzzling.

No data that would provide clear explanation were collected in this study; however, this could have resulted from an insufficient amount of the preparation administered during the procedure and an insufficient number of treatments.

A small number of postoperative complications is another advantage of the preparation. The only complications observed in our study included mild edema and tenderness, as well as mild pain at the site of administration. Probably the form and composition of the preparation minimize the risk of complications that occurred after PC or in preparations with higher amounts of DC, where the risk of complications increases with increasing concentration[20]. However, it should be noted that if administered incorrectly, Aqualyx™ may cause serious complications; therefore, the treatment should be performed by trained doctors.

Conclusions

The obtained results indicate that intralipotherapy with the use of Aqualyx™ is an effective method of eliminating local fat deposits located on the inside of the knees. However, these results need to be confirmed due to the small sample size. It also seems important to identify the reasons for the failure to reduce knee circumference in some patients. In our opinion, it would be worth considering further procedures and extending follow-up. High-frequency ultrasonography proved highly useful in planning, monitoring and treatment outcome assessment. It is likely that ultrasound guidance during the procedures contributed to reduced number of complications.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

References

1. Mordon S, Plot E: Laser lipolysis versus traditional liposuction for fat removal. Expert Rev Med Devices 2009; 6: 677–688.
2. Alderman AK, Collins D, Streu R, Grotting JC, Sulkin AL., Neligan P *et al*.: Benchmarking outcome sin plastic surgery: national complication rates for abdominoplasty and breast augmentation. Plast Reconstr Surg 2009; 124: 2127–2133.
3. Kutlubay Z: Evaluation of mesotherapeutic injections of three different combinations of lipolytic agents for body contouring. J Cosmet Laser Ther 2011; 13: 142–153.
4. Park SH, Kim DW, Lee MA, Yoo SC, Rhee SC, Koo SH *et al*.: Effectiveness of mesotherapy on body contouring. Plast Reconstr Surg 2008; 121: 179e–185e.
5. Amore R, Pinto H, Gritzalas K, Hernández C, Skwara-Guzikowska, Amuso D *et al*.: Intralipotherapy, the state of the art. Plast Reconstr Surg Glob Open 2016; 4: e1085.
6. Rittes PG: The use of phosphatidylcholine for correction of lower lid bulging due to prominent fat pads. Dermatol Surg 2001; 27: 319–312.
7. Young VL: Lipostabil: the effect of phosphatidylcholine on subcutaneous fat. Aesthet Surg J 2003; 23: 413–417.
8. Baumann LS: Phosphatidylcholine. Skin Allergy News 2003; 34: 24.
9. Rotunda AM, Suzuki H, Moy RL, Kolodney MS: Detergent effects of sodium deoxycholate are a major feature of an injectable phosphatidylcholine formulation used for localized fat dissolution. Dermatol Surg 2004; 30: 1001–1008.
10. Motolese P: Phospholipids do not have lipolytic activity. A critical review. J Cosmet Laser Ther 2008; 10: 114–118.
11. Salti G, Ghersetich I, Tantussi F, Bovani B, Lotti T: Phosphatidylcholine and sodium deoxycholate in the treatment of localized fat: a double-blind, randomized study. Dermatol Surg 2008; 34: 60–66.
12. Rose PT, Morgan M: Histological changes associated with mesotherapy for fat dissolution. J Cosmet Laser Ther 2005; 7: 17–19.
13. Rauso R, Salti G: A CE-marked drug used for localized adiposity reduction: a 4-year experience. Aesthet Surg J 2015; 35: 850–857.
14. Aqualyx [online]: http://aqualyx.com.pl/images/upload/file/ulotka_aqualyx_2.pdf, dostęp: 29.10.2020.
15. Rauso R, Rusciani A, Curinga G: An adipocitolitic aqueous micro-gelatinous solution for buffalo hump deformity reduction. J Drugs Dermatol 2014; 13: 1282–1284.
16. Pinto H, Hernandez C, Turra C, Manzano M, Salvador L, Tejero P: Evaluation of a new adipocytolytic solution: adverse effects and their relationship with the number of vials injected. J Drugs Dermatol 2014; 13: 1451–1455.
17. Scevola S, Nicoletti G, Neri A, Faga A: Long term assessment of intralipotherapy in Madelung's disease. Indian J Plast Surg 2014; 47: 427–431.
18. Bhatta AK, Keyal U, Liu Y: Application of high frequency ultrasound in dermatology. Discov Med 2018; 26: 237–242.
19. Schmid-Wendtner MH, Dill-Müller D: Ultrasound technology in dermatology. Semin Cutan Med Surg 2008; 27: 44–51.
20. Rotunda A: Lipomas treated with subcutaneous deoxycholate injection. J Am Acad Dermatol 2005; 53: 973–968.