Use of air-steroid-saline mixture as contrast medium in greyscale ultrasound imaging: Experimental study and practical applications in rheumatology

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Abstract

Objectives

To investigate experimentally the echogenicity of air, a steroid suspension and physiological saline mixed with water in order to find the best contrast medium for injections. To show the practical applications of an air-steroid-saline mixture as a contrast medium in rheumatology.

Methods

In vitro. *First, quality assurance measurements were conducted twice on the ultrasound (US) equipment. Subsequently air, a steroid suspension, or physiological saline mixed with water, first alone and then in different combinations, were examined with US using quantitative image analysis.*

Clinical. *The effectiveness of an air-steroid-saline mixture as contrast medium in ultrasonography was tested in joint, bursa and tendon sheath injections.*

Results

In vitro. *Based on the quality assurance measurements the physical performance of the US equipment was excellent. Verified visually and quantitatively the mixture of air, steroid and saline produced the best contrast on US. The importance of air bubbles producing contrast was obvious.*

Clinical application. *Firstly, visualisation of the contrast medium with US made it possible to follow in real-time the passage of a drug to the target area. Secondly, the use of the contrast method verified the presence of steroid in the synovial target intended after a blind injection. Thirdly, anatomical and pathologic anatomical connections could be visualized using this contrast medium in the wrist, shoulder, knee, ankle and foot joint areas.*

Conclusions

Verification of US system performance by quality assurance measurement is essential for US imaging. The air-steroid-saline contrast medium method of ultrasound scanning is a somewhat invasive, but inexpensive and rapid method. It can verify the existence or non-existence of an air-steroid-saline contrast medium in the desired place and in adjacent structures, thus showing possible pathologic anatomic connections. The method has a diagnostic and therapeutic value, and expands the interventional spectrum of sonographic imaging.

Key words

Clinical ultrasound, contrast medium, rheumatology, injection.

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Introduction

A needle guided with US can be inserted accurately into the body's soft tissues, such as joints, bursae and tendon sheaths if an acoustic window is available (1,2). When a steroid and air are injected into a synovial structure, the drug flow and air bubbles can be seen on the monitor in real-time (3). Thus an operator can verify accurately where the needle is and where the drug is going. Sometimes the injected suspension can be seen to go into an adjacent structure through an obvious pathologic anatomical route. These observations have raised the idea of using a steroid suspension as contrast medium. Hawe (1991) used air as a contrast medium in sonography ("Aero-Sonografie") to detect rotator cuff ruptures (4).

Quality control of all medical devices is essential to ensure an accurate interpretation of results when they are being used for diagnostics and research. As far as the authors know, quality control checks of clinical ultrasound devices have not been widely reported in scientific articles. In 1995 Kollmann reported the results of a quality control programme for B-mode ultrasound equipments used in clinical routine (5), concluding that a regular quality assurance of clinical ultrasound equipments is necessary to ensure an optimal image quality and a safe operation.

This study had two main aims. Firstly, to investigate the echogenicity of air, steroid suspension or physiological saline, and a mixture of these combined with water and, subsequently, to show practical applications of the contrast method in rheumatology. In order to ensure the accuracy and reliability of the ultrasound imaging, quality assurance measurements were conducted on the ultrasound equipment in the course of the study.

Materials and methods

The ultrasound equipment used in this study was Esaote Technos® (Esaote Biomedica, Genova, Italy) equipped with two probes: LA424 (frequency range 7.5-13 MHz) and LA523 (frequency range 5-10 MHz). The pre-defined protocol for LA424 was chosen and all settings (frequency, image size, overall gain, time gain compensation and dynamic range) were kept constant during the *in vitro* experiments.

In vitro study

Quality assurance measurements were conducted on the ultrasound equipment and both probes. A general purpose CIRS Model 40-phantom (CIRS Inc., Norfolk, VA, USA) was used and measurements were conducted twice at an interval of 18 months. Near-field resolution, axial resolution, lateral resolution, penetration depth and accuracy of the horizontal and vertical distance measurements were determined. All quality assurance measurements were conducted according to the AIUM recommendations (6).

100 ml of 37°C tap water was poured into a clean pot. The liquid was left to stand for about 5 minutes so that all air bubbles disappeared and the water was fully anechoic on ultrasound (probe LA424). The imaging focus was directed into the middle of the liquid. Four ml of physiological saline (22°C), 1 ml of room air (22°C), and 1 ml of steroid suspension (22°C) or these components in different combinations in one syringe either shaken or not were added one at a time into the water. The steroid suspensions were methylprednisolone (Solomet®, Orion Pharma, Finland), triamcinolonehexacetonide (Lederspan© Pharmalink AB, Sverige) and betametasone (Celeston Chronodose©, Schering-Plough Oy, Finland). When these components had been added the liquid was stirred with the probe (two turns clockwise and two counter clockwise), and the liquid was scanned immediately and the monitor image was depicted.

The contrast medium's dissolving (dots disappearing) time was measured on 4 mixtures: air+Nacl, air+Nacl+methylprednisolone, air+Nacl+triamcinolonehexacetonide and air+nacl+betametasone. The scanning of the mixtures went on for 5 minutes and pictures were taken at 30-second intervals.

A quantitative analysis was conducted on the in vitro images using Paint Shop Pro 7.0 (Jasc Co., MN, USA) and Matlab 6.0 (The Mathworks Inc., Natick, MA, USA) programme. All the images

acquired were randomised before analysis. The images were first stored in a bitmap format (RGB scale) and later converted to the greyscale and normalized with the largest pixel value (i.e. in every image, the pixel value was always between 0 and 1). With this method an objective comparison between images was possible. The echogenicity (E_c) of the images was quantified as follows:

$$\mathrm{Ec} = \frac{N_{threshold}}{N_{total}} . 100,$$

in which the $N_{threshold}$ is the number of the pixels exceeding the specific threshold value and N_{total} is the total number of the pixels in the image. Analyses were first conducted with different threshold values and, finally, 15% of the largest pixel value was chosen as optimal for all images.

Clinical part

A. In 10 randomly patients with symptomatic rheumatoid arthritis the stability of the contrast medium was studied scanning with US the injected synovial structure for 5 minutes. The injections were done under the guidance of US. There were 5 cases of air+methylprednisolone+saline and 5 of air+triamcinolonehexacetonide+saline. The amount of the steroid was 0.5-1 ml and of saline 1-10 ml, depending the size of the synovial space. After adding these drugs into the syringe, non-sterile room air (0.5-1ml) was drawn and the syringe was then shaken. The sites examined were: the proximal interphalangeal joint of the hand, metatarsophalangeal joint, tibiotalar joint, intermetatarsal bursa, flexor tendon sheath of the hand, knee joint, two elbow joints and two wrist joints. Parts A and B were conducted by the rheumatologist (JK), who has 15 years experience of soft tissue injections in rheumatology giving 1200 injections per year.

B. In this part we report the observations done during the 15 years of US guided synovial space injections. The indication of a steroid injection has been the treatment of synovial inflammation in joints, bursae or tendon sheaths. The author (JK) has used a mixture of methylprednisolone or triamcinolonehexacetonide with physiological saline. Air bubbles appear always more or less at random in the mixture (0.5-1 ml). The amount of steroid and saline are specified in part A. After an injection of the mixture into the target under ultrasound guidance a proper extension and flexion exercise and massage of the site involved were done repeatedly for about 15 seconds. In the case of the ankle and foot, the patients can be asked to walk a few meters in the room. A scan of the target area was performed immediately after this procedure and monitor images were depicted and compared with those taken before the injection.

The study was approved by the local ethical committee and the patients gave their informed consent.

Results

In vitro part

In quality assurance measurements the near-field resolution, axial resolution and lateral resolution of the system were < 1.0 mm, < 0.5 mm and < 1.0 mm, respectively. The maximum penetration depth was 60 mm when working with the LA424 probe and 100 mm with the LA523 probe. The accuracy of the horizontal distance measurements was 1.0% at the depth of 2 cm from the surface (both probes) and 1.0% at the depth of 9 cm from the surface (probe LA523). The accuracy of the vertical distance measurements was between 1% and 5% depending of the probe, measured distance or depth. All the parameters measured were the same after 18 months.

It turned out that the injection of room air, physiological saline or a steroid alone produced relatively little contrast in water. When saline was added to the steroid or saline to the air the contrast increased to some extent but a remarkable increase of contrast occurred when all three components were mixed in one syringe. This finding was constant with all the steroids examined. It seemed obvious that the air was the principal producer of contrast; however, it did not produce a strong increase of echogenicity by itself, but together with saline and steroid. An air-methylprednisolone-saline mixture seemed to produce the strongest contrast (Fig. 1). In experimental *in vitro* conditions the contrast disappeared rapidly and the concentration was about 50% after 30 seconds. The air-methylprednisolone-saline mixture stayed at a level of 40% for 5 minutes but the concentration of other air-steroid-saline mixtures was lower in function of time (Fig. 2).

Clinical part

A. Injected into a large synovial space such as the glenohumeral joint or Ba-

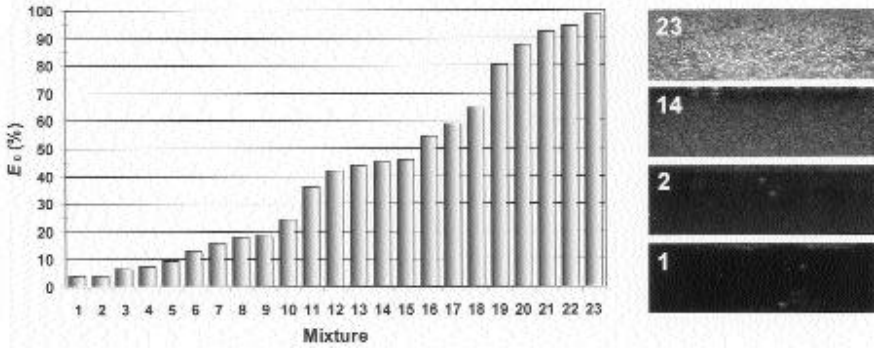

Fig. 1. The echogenicity (E_c) of air, physiologic saline and steroid suspensions alone and in different combinations mixed with tap water and depicted with ultrasound. Corresponding US images of air, Nacl, methylprednisolone and mixture of these on the right. 1=air, 2=Nacl, 3=triamcinolonehexacetonide, 4=betametasone, 5=Nacl+air, 6=triamcinolonehexacetonide shaken, 7= betametasone shaken, 8= betametasone+Nacl, 9=Nacl+air shaken, 10=Nacl shaken for 10 seconds, 11= triamcinolonehexacetonide+Nacl, 12= betametasone+Nacl+air, 13= betametasone+Nacl shaken, 14=methylprednisolone, 15=methylprednisolone shaken, 16=methylprednisolone+Nacl, 17= triamcinolonehexacetonide+Nacl shaken, 18=methylprednisolone+Nacl shaken, 19= betametasone+Nacl+air shaken, 20= triamcinolonehexacetonide+Nacl+air, 21=methylprednisolone+Nacl+air shaken, 22= triamcinolonehexacetonide+Nacl+air shaken and 23=methylprednisolone+Nacl+air.

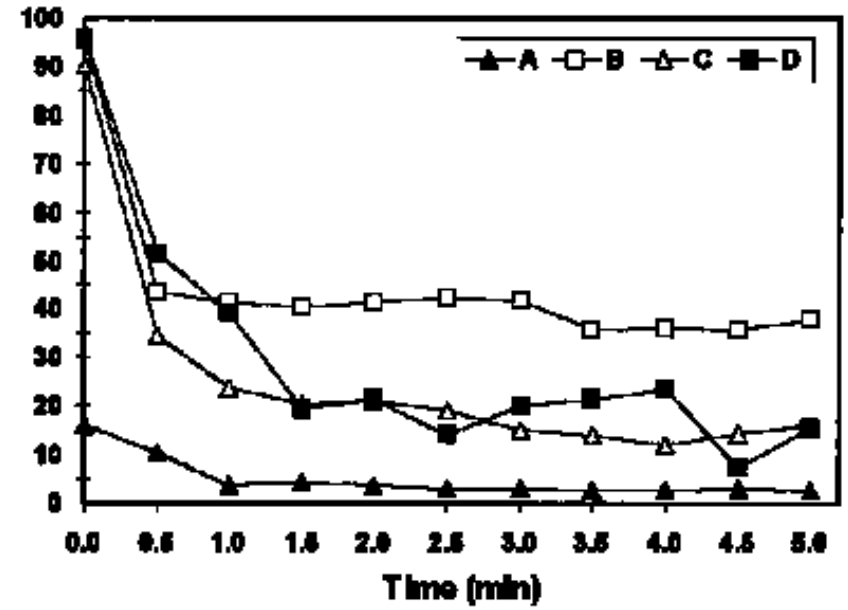

Fig. 2. The echogenicity (E_c) curves of different mixtures. A: Nacl+air, B: methylprednisolone+Nacl + air, C: triamcinolonehexacetonide+Nacl+air and D: betametasone+ Nacl+air.

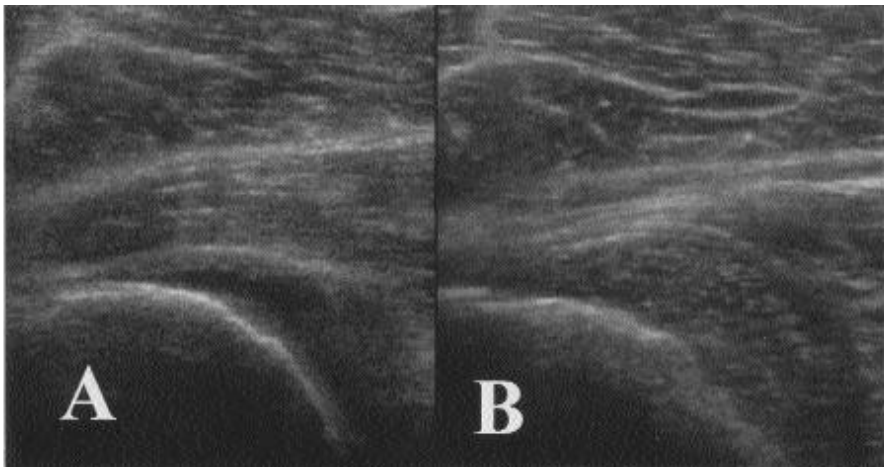

Fig. 3. Pathologic communication between the subacromial-subdeltoid bursa and the glonohumeral joint verifying full thickness rotator cuff tear. A posterior transverse oblique scan of the joint before the procedure showing some fluid (**A**). After the US guided air-steroid-Nacl injection into the bursa and exercise and massage numerous hyperechoic dots can be found in the joint space (**B**).

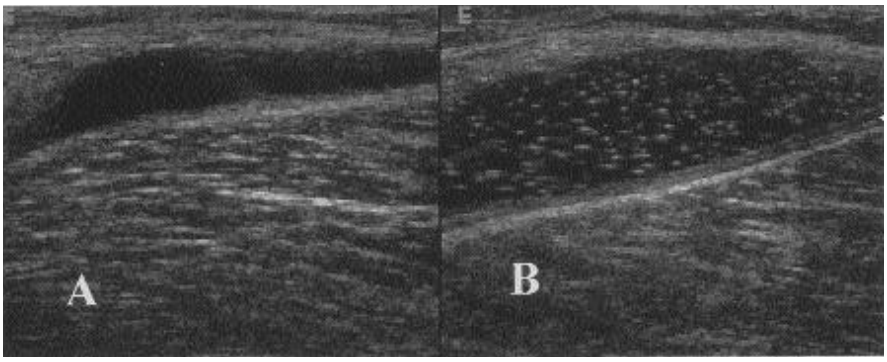

Fig. 4. Baker's cyst depicted before an intra-articular knee air-steroid-Nacl injection (**A**) and after the injection and exercise of the joint (**B**).

ker's cyst the air-steroid-saline contrast medium looks the same as in experimental conditions (Figs. 3b, 4b) but it can be found in the target also as minor dots, a white line (Fig. 5b) or in patches (because of synovial proliferation). Passive or active extension and flexion movements of the joint are essential in searching for the contrast medium in the target space. The dissolving time of this contrast medium *in vivo* is remarkably longer than *in vitro* and contrast medium could clearly be found in small and large joints, bursae or tendon sheaths for at least 5 minutes in all the ten cases studied.

B. The author (JK) has noted pathologic anatomical connections between different wrist compartments on US imaging: radiocarpal joint to midcarpal joint, radiocarpal joint to flexor carpi ulnaris tendon sheath, radiocarpal joint to carpal tunnel and radiocarpal joint to distal ulnaradial joint (Figs. 6 and 7). In the shoulder area a pathologic connection between the subacromial-subdeltoid bursa and the glenohumeral joint has been noted (Fig. 3). A connection between Baker's cyst and the knee joint was observed (Fig. 4), as well as a communication between the tibiotalar and subtalar joints. A communication was noted between the tibiotalar joint and the tibialis posterior tendon sheath and between the metatarsophalangeal joint and the intermetatarsal bursa.

Discussion

Reporting on the quality assurance results of the devices used in research is not common in scientific papers but, in the author's opinion, it should be routine. In Finland, quality assurance measurements of ultrasound equipments are routine only in a few hospitals. In Germany Kollmann reported on the results of quality assurance surveys on five ultrasound scanners with 19 probes periodically measured within 18 months. The results indicated that 13 of the probes did not operate correctly and only 6 probes retained their normal functions. This is alarming since diagnostic ultrasound studies are some of the most popular clinical imaging modalities. Furthermore, the quality assurance of ultrasound equipment is quick

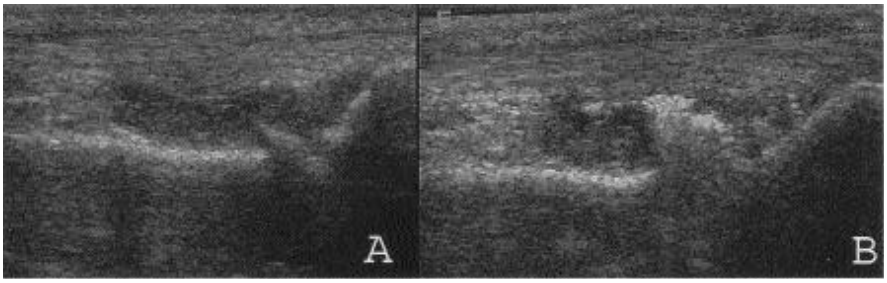

Fig. 5. Metatarsophalangeal joint arthritis before a blind intra-articular injection of the air-steroid-Nacl contrast medium. (**A**) After the injection air and the steroid can be found in the joint space as a sign of a successful injection (**B**).

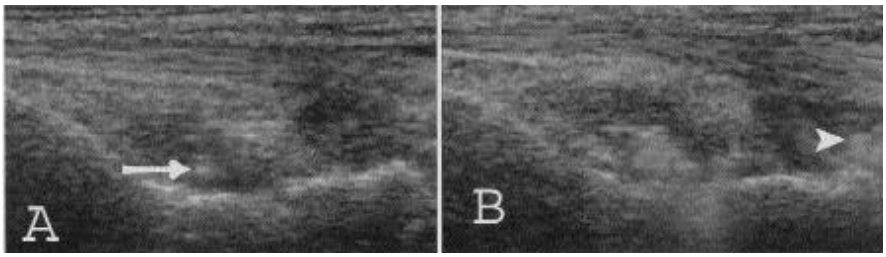

Fig. 6. A pathologic anatomic connection between midcarpal and radiocarpal joints. The tip of the needle in the midcarpal joint in the beginning of the procedure (arrow). (**A**) After an injection of an air-steroid-Nacl mixture into the midcarpal joint contrast medium can be found in the midcarpal joint as well as in the radiocarpal joint (arrow head) (**B**).

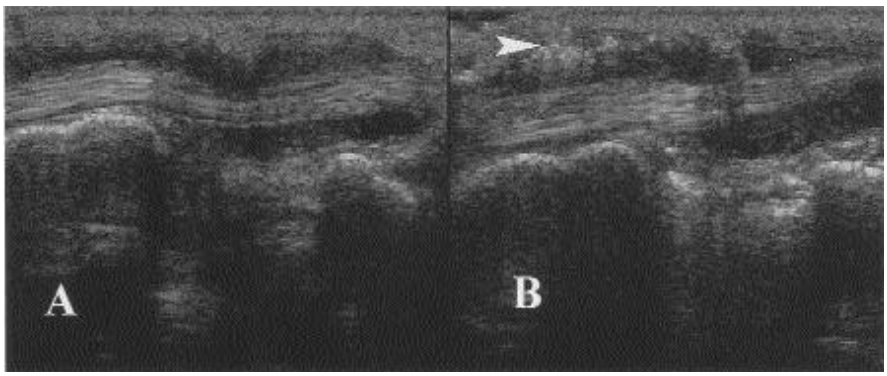

Fig. 7. The connection of the radiocarpal joint and the flexor carpi ulnaris tendon sheath. Tendon sheath tenosynovitis shown before an air-steroid-Nacl contrast medium injection performed into the radiocarpal joint (**A**). After the injection there is more fluid in the tendon sheath and air can be found in the sheath (arrow head) (**B**).

and straightforward to carry out.

As a conclusion and based on the quality assurance measurements conducted in this study, the physical performance of the ultrasound equipment was excellent in both the measurements conducted initially and those after 18 months.

The most common and important benefit of visualizing an air-steroid-saline mixture in rheumatology is guiding injections into synovial structures. The operator can follow on the monitor in real-time how the drug goes into the right place (Fig.8). Verifying the correct positioning of the needle is useful but not obligatory. The spreading of drug can also be depicted using Doppler ultrasound. The second use of this method could be verifying that the drug has found in the target after a blind injection (Fig. 5). This is the most common way of giving rheumatological injections (7). The verifying of the steroid in the synovial target intended after a blind injection serves a clinical purpose but it could also be used in medical teaching. A third use of the US-contrast medium method described is to show pathologic anatomical connections of adjacent structures in the same way as the x-ray is used in arthro- or bursography (8, 9).

In the light of the experimental studies it seems obvious that a tiny amount of air in the mixture is the essential part that produces the best contrast when combined with a steroid and saline. Saline is needed to increase the volume of the mixture which is important when the post injection images are compared with the images taken before the procedure. Saline is also needed as carrier of the steroid and the air bubbles. The steroid suspensions contain crystals and are less echogenic by themselves but combined with saline and air they produce the best contrast. Probably crystals destroy the air bubbles to come smaller and make the mixture more homogenous ? Methylprednisolone seems to have the best echogenic properties for use as a contrast medium in vitro. In the experimental conditions described the air bubbles dissolve rapidly but they stay for at least 5 minutes in synovial spaces because of the different physicochemical surroundings.

The method of using air-steroid-saline as a contrast agent might have a diagnostic value. For example ultrasound diagnostics of rotator cuff ruptures are not always an easy thing to verify and different figures concerning diagnostic accuracy can be found (10). The contrast method could add diagnostic accuracy to ultrasound scanning of rotator cuff tears. The accuracy of the method in the shoulder needs further research. The diagnostic use of steroid suspension as well as the use of air raises an ethical question. Intrasynovial steroid is contraindicated in suspicion of septic situation and caution is taken in patients with diabetes. However, the amount of air in the method described is not more than 1 ml and an injection of steroid suspension is inevitably harmless to a healthy person. Hawe used as much as 20 ml of air in “Aero-Sonografie” of the shoulder for verifying rotator cuff tears (4).

The US contrast method can also make a sense in terms of treatment. If there is a synovial inflammation in two or more adjacent sites in one anatomic region it

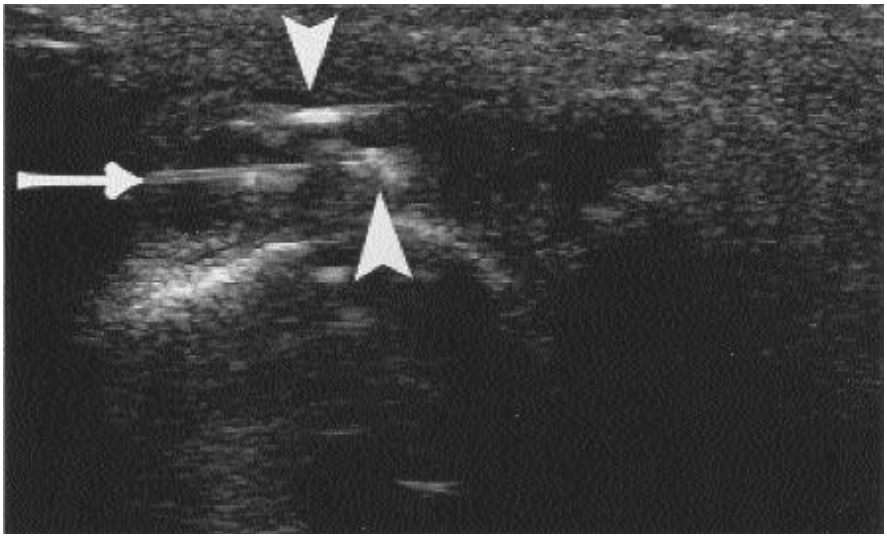

Fig. 8. Real-time observation of the air-steroid-Nacl injection into the metacarpophalangeal joint (arrow shows the needle and arrow heads show air+steroid gushing out of the needle).

might be enough to give a single steroid injection if the operator could show the existence of connections and the spreading of the drug into other sites too.

The air-steroid-saline contrast medium method of ultrasound scanning is a somewhat invasive but cheap and fast procedure. The method can show the existence or non-existence of the contrast medium in the desired structure and also in an adjacent structure. It expands the interventional spectrum of sonographic imaging. The usability and validity of the method need further controlled trials.

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