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Cover picture

THE SHAKERS AND MEDICINAL HERBS
(About 1830)

A religious group, the Shakers inaugurated the medical herb industry in the United States. Tons of pressed herbs and extracts were produced under the Shaker label, which became internationally known for quality and reliability.

One of a series: *A History of Pharmacy in Pictures*, presented by Parke, Davis & Company.

George A. Bender, Director Robert A. Thom, Artist

Managing menopausal symptoms

Summary

Until the mid 1990s, hormone therapy was seen as not only a safe means of relieving troublesome menopausal symptoms but as a way of preserving youth and vitality. Adverse findings from a number of studies in the 1990s cast doubt on some of the earlier claims, but it was the publication of the Women's Health Initiative study in 2002 that resulted in a complete reappraisal of the principles of menopause management.

Keywords: bioidentical hormones, hot flushes, libido, urogenital symptoms.

*(Aust Prescr 2010; **33**: 171-5)*

Introduction

Menopause, literally the 'end of menstruation', marks an important transition in a woman's life and occurs in Australia at an average age of 51 years. Menopausal symptoms, which may commence even before the last menstrual period, include vasomotor symptoms, urogenital problems, psychological changes, sleep disturbance and decreased libido. Managing patients with these symptoms can be a challenge.

Vasomotor symptoms

Vasomotor symptoms include hot flushes, night sweats and formication, which is a particularly unpleasant sensation that feels like ants crawling on the skin. It is estimated that up to 80% of women experience vasomotor symptoms around the time of menopause with an average duration of 5-6 years.[1] However, one in four women will still experience significant vasomotor symptoms well into their sixties and in 10% these will persist for life.

Lifestyle modification and natural therapies

Regardless of any other therapies, education and lifestyle advice are integral to effective menopause management. Since smoking has the added impact of increasing the severity of vasomotor symptoms and increasing the risk of osteoporosis,[2] menopause provides a good opportunity to discuss smoking cessation.

Dietary modification and the use of herbal supplements are avenues commonly explored by women seeking a more natural approach to menopause management. For some women with milder symptoms, avoidance of known vasomotor triggers such as alcohol, hot drinks and spicy foods may be the only intervention required. Although a diet rich in plant oestrogens such as those found in foods like soy, chickpeas, lentils and flaxseed is likely to be a more healthy option, there is unfortunately no clear evidence that they improve vasomotor symptoms for the majority of women.[3]

Red clover extract has been widely used for the relief of vasomotor symptoms, but there is no convincing evidence that it is any more effective than placebo.[4, 5] A number of small clinical trials investigating other herbal products – such as dong quai, *Ginkgo biloba*, wild yam and *Vitex agnus castus* – have also shown no benefit over placebo.

Black cohosh is a herbal compound which appears to have some serotonergic activity. Its use for menopausal symptoms remains controversial, with some studies indicating significant improvement while others have failed to demonstrate any benefit over placebo. Black cohosh preparations vary in dose and potency and this further complicates their evaluation as a treatment. Since at least some reviews indicate evidence for its effectiveness,[6] it may be worth trying in those women who are looking for a natural alternative to oestrogen therapy. In my experience it is relatively safe to use and is available as an over-the-counter product. The commonest adverse effect is gastrointestinal upset but there have been reports of idiosyncratic liver failure[7] and all black cohosh products marketed in Australia now carry a warning to this effect.

Hormone therapy

Women using systemic oestrogen therapy can expect a 75% reduction in the frequency of hot flushes and an 87% reduction in their severity.[8] However, there are risks associated with hormone therapy. Most of the contemporary evidence is derived from the

Women's Health Initiative trial data.[9] Although it is the oestrogen which controls menopausal symptoms, women with a uterus also require progestogen for at least 10 days per month to prevent endometrial hyperplasia (Table1). For such combined therapy there appears to be an increased risk of coronary artery disease, thromboembolism and stroke from the time of initiation. However, some argue that the risk of heart disease is less if therapy is commenced before the age of 60.[10,12]

*Table 1**

Progestogens used in combined therapy for menopausal symptoms

Cyclical therapy Use for at least 10 days per month until 12-18 months after last menses. Allows for scheduled monthly bleed.	Dydrogesterone 10 mg Medroxyprogesterone 5-10 mg Norethisterone/norethisterone acetate 0.7-2.5 mg
Continuous therapy Defer until 12-18 months after last menses. No scheduled bleed.	Dydrogesterone 5 mg Medroxyprogesterone 2.5-5 mg Norethisterone/norethisterone acetate 0.35-1 mg
Progestogen intrauterine device	Releases 20 microgram levonorgestrel daily

* adapted from 'Hormone replacement – oestrogen and progestin dosage schedule'. National Prescribing Service. 2009 Aug. www.nps.org.au/ppr_47_insert [cited 2010 Nov 16]

An increase in cases of breast cancer was also seen after 4-5 years of combined hormone therapy, with eight additional cases per 10 000 women years. Therapy with oestrogen alone appears to be associated with fewer risks, with an increased risk of stroke being the sole adverse finding after seven years.[13]

A variety of hormonal preparations and different delivery systems are available in Australia. As a general principle the lowest dose of oestrogen should be prescribed that adequately controls symptoms, with the appropriateness of continuing therapy assessed at 6-12 month intervals. Typical starting doses for oestrogen are shown in Table 2, but even at the six-month review it may be worthwhile attempting to reduce the dose further.

*Table 2**

Typical starting doses of oestrogens for menopausal symptoms

Oral	Conjugated equine oestrogens 0.3-0.625 mg Oestradiol/oestradiol valerate 1-2 mg
Transdermal (over 24 hours)	Oestradiol 25-50 microgram Oestradiol gel 1 mg/g
Sub-dermal implant (usually reserved for women who have had a hysterectomy)	Oestradiol 50 mg

* adapted from 'Hormone replacement – oestrogen and progestin dosage schedule'. National Prescribing Service. 2009 Aug. www.nps.org.au/ppr_47_insert [cited 2010 Nov 16]

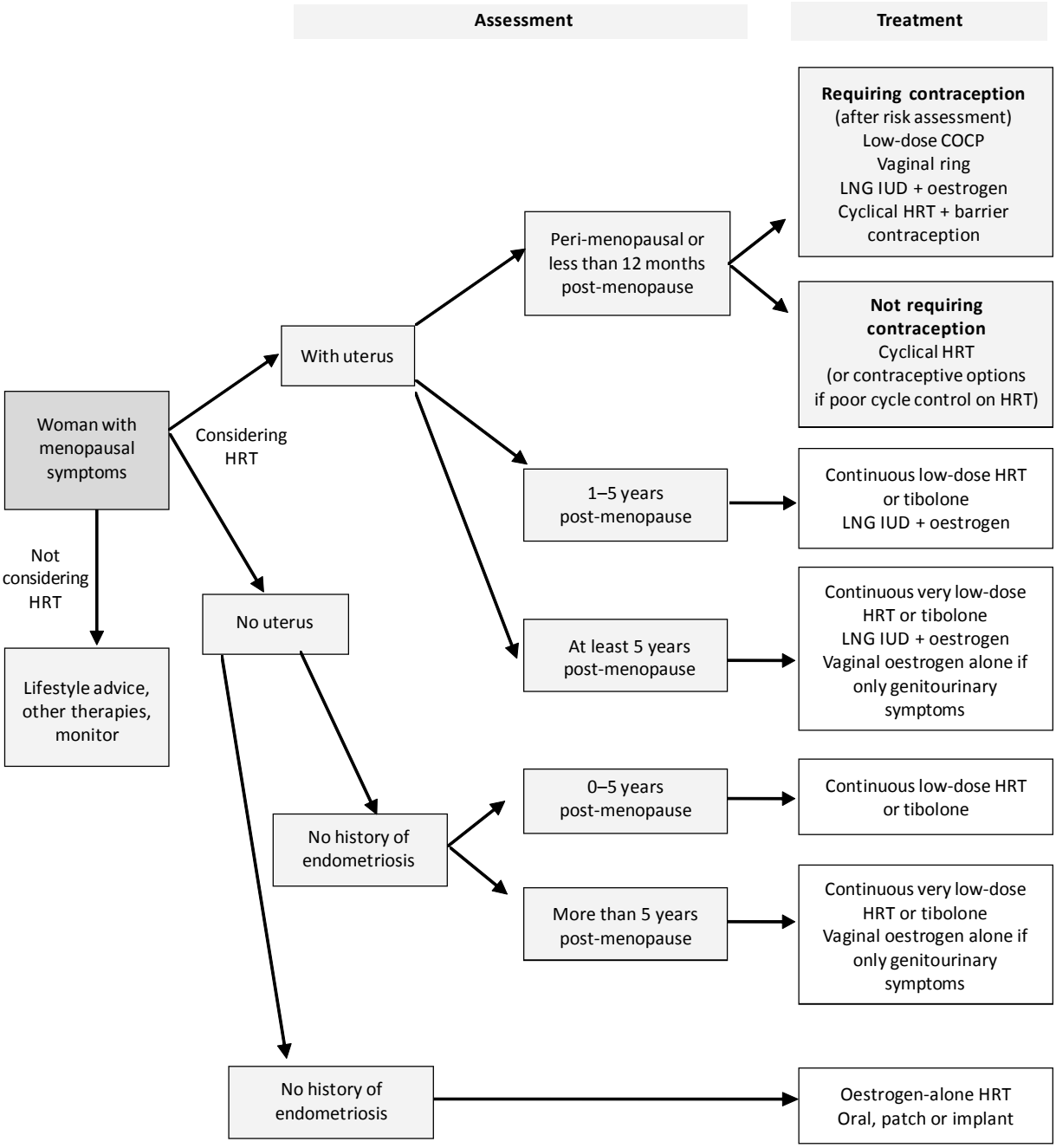
Within two months of commencing therapy approximately 80% of women will achieve adequate symptom relief.[14] With the remaining 20%, it may be useful to explore an alternative delivery system before increasing the dose. Older women who still require therapy may find their symptoms are controlled on half the standard starting dose.

Tibolone is a steroid which has oestrogenic, progestogenic and androgenic activity. The standard dose is 2.5 mg although a half dose could be considered in older patients. Once a decision has been made to commence hormone therapy, the approach to treatment will be influenced by many factors (Fig. 1).

Transdermal progesterone cream has been used for the management of menopausal symptoms since the 1970s. It is minimally absorbed through the skin and there is no good evidence for its usefulness in relieving flushes, or in improving mood, libido or lipid profile.[15]

Fig. 1

Implementing hormone therapy for menopausal symptoms in women with no contraindications



HRT	hormone replacement therapy
COCP	combined oral contraceptive pill
LNG IUD	levonorgestrel-releasing intrauterine device

Other pharmacological therapies for vasomotor symptoms

When hormone therapy is contraindicated, or when women choose not to use it, low-dose selective serotonin or noradrenaline reuptake inhibitors may be considered. In short-term trials, they have been shown to reduce the number and severity of hot flushes by approximately 60%.[16,17] A quarter to a half of the antidepressant dose is recommended, and in fact higher doses have the potential to make vasomotor symptoms worse. However, adverse effects such as breast tenderness and sexual dysfunction may still limit the use of these drugs in some women even at such low doses. Venlafaxine and paroxetine appear to be the most effective of this class for this purpose. Paroxetine should be avoided in breast cancer survivors on tamoxifen since liver enzyme inhibition may render tamoxifen less effective.[18]

Clonidine and high-dose progestogens also seem to be effective at reducing troublesome vasomotor symptoms in some women, but adverse effects tend to limit their widespread use. A number of small trials[19] have indicated that gabapentin and pregabalin may also be effective in controlling hot flushes, but expense and limited clinical experience has meant that their use is usually restricted to those women with significant symptoms who have failed to respond to other therapies.

Bioidentical hormone therapy

Compounded bioidentical hormone therapy has been widely promoted in Australia. These preparations are said to have been derived only from natural products such as wild yam and soy and to deliver steroids identical to those made by the woman's own body. Advocates claim the ability to titrate the preparation to the woman's own individual hormonal needs, guided by salivary or blood tests.

Most compounded preparations deliver a combination of oestriol and oestradiol. Other hormones such as oestrone, progesterone, testosterone and dehydro-epiandrosterone may be added.

The hormone therapy is delivered by means of a dissolvable lozenge (troche) or a transdermal cream. There is no doubt that many women find these preparations effectively relieve their menopausal symptoms. The problem is that although bioidentical hormones are often perceived by women as a safer alternative to conventional hormone therapy, there is actually no evidence for this, particularly regarding long-term safety.[20] One emerging concern is that the natural progesterone used in many bioidentical regimens to protect the endometrium may not be particularly effective, especially with long-term use. There have been a number of reports recently of endometrial hyperplasia and endometrial cancer in users.[21]

Urogenital symptoms

Unlike vasomotor symptoms, urogenital symptoms such as vaginitis, dyspareunia, cystitis and incontinence tend to worsen as a woman grows older.

Oestrogen

Pooled data from several randomised controlled trials indicate that oestrogen improves genital symptoms regardless of the route of administration.[22] Vaginal oestrogen is the preferred delivery system for women whose symptoms are primarily urogenital. There is minimal systemic absorption and when vaginal oestrogen is used at the recommended dosages progestogen cover is not necessary in women with a uterus. Even this small absorbed dose may however compromise therapy in breast cancer survivors receiving aromatase inhibitors, such as anastrozole.

Vaginal oestrogen may also be useful in the 27% of women who still experience vaginal symptoms when using low-dose systemic hormone therapy.[23] Oestradiol is more potent than oestriol and will therefore provide a more rapid clinical effect when used topically. Vaginal tablets tend to be better tolerated than pessaries and creams since they result in less vaginal discharge. As a therapeutic option vaginal oestrogen remains very much underused, particularly in women troubled by recurrent urinary tract infections and incontinence.

Vaginal moisturisers and lubricants

For women who cannot, or do not wish to, use even low-dose vaginal oestrogen, polycarbophil vaginal

moisturisers have been shown to improve vaginal pH and normalise vaginal cytology.[24]

Lubricants can also be useful for augmenting natural lubrication during intercourse. Silicone lubricants offer particular advantages for the older couple since they do not absorb so easily into the skin.

Libido and desire

Painful sex is a potent inhibitor of desire and local oestrogen therapy may be all that is required in some women. A recent review of postmenopausal trials indicated that conventional oestrogen hormone therapy tended to increase sexual desire, arousal and satisfaction.[25]

A gradual decline in androgen levels from the mid-thirties may lead to symptoms such as decreased libido and a lack of energy in some women. Several small studies[26] suggest that the androgenic component of tibolone may improve both sexual interest and general well-being. However, the role of androgens in the treatment of postmenopausal loss of libido remains controversial. There are currently no preparations licensed for use in women across Australia, though a low-dose transdermal testosterone cream is available on prescription in Western Australia. Androgen therapy should never be used indiscriminately and only after discussion with the patient about potential adverse effects.

There is also no doubt that study after study has shown that sexual satisfaction is most closely correlated with satisfaction with the relationship. Any pharmacological therapy may be more effective if combined with couple counselling.

Conclusion

The promotion of a healthy lifestyle forms an integral part of an overall approach to menopause management. The findings of the 2002 Women's Health Initiative study profoundly affected long-held notions as to the benefits and safety of menopausal hormone therapy, though it remains a useful option for those with significant symptoms. Vaginal oestrogen therapy in particular provides excellent relief of genitourinary symptoms with very few associated risks. Although many women regard complementary therapies as a safer alternative to conventional medical treatment, there is conflicting evidence as to their effectiveness and long-term safety. The application of an evidence-based approach to decision-making should assist both clinician and patient to make the choices that are most appropriate to a woman's individual needs.

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Radiological investigations: risks involved and patient preparation

Introduction

Radiological imaging plays a vital role in patient management. Both diagnostic and interventional imaging is increasingly requested by clinicians. The threshold for requesting radiological imaging in clinical practice has lowered, resulting in an influx of requests to the radiology departments, increasing workload and financial burden. There are a number of risks associated with radiological imaging. The risks to the patient by radiological imaging seem to be often overlooked when requesting it. The risk to the patient should be balanced against the net benefit. This is widely discussed globally as cost-risk-benefit analysis for radiological investigations, mostly in terms of cost and radiation risk.

Once an investigation is justified, accurate and adequate preparation of the patient for the selected investigation is mandatory. It helps to achieve maximum information from the radiological investigation, as well as to minimize potential adverse effects and radiation harm to the patient. Optimum patient preparation also reduces the need for repeating radiological investigations, reducing unnecessary radiation exposure. Management of adverse events of imaging is not discussed in this article.

Risk associated with radiological investigations

These can be broadly classified as: a) risks caused by radiation, b) risks caused by the use of contrast media, and c) risks related to individual procedures or technique.

Radiation risk

Radiological imaging modalities may be divided into 2 groups based on radiation risk (Box 1).

Box 1

Investigations causing exposure to ionizing radiation

- Plain radiography (x-ray)
- Mammography
- Fluoroscopy
- Computed tomography (CT)
- Nuclear imaging studies including PET

Investigations which do not cause exposure to ionizing radiation

- Ultrasound scan (USS)
- Magnetic resonance imaging (MRI)

Ionizing radiation may cause damage to DNA and increase a person's lifetime risk of developing cancer. The lag period between radiation exposure and cancer diagnosis may be as long as one to two decades or longer. Radiation risk is more in the fetus, infants and children as they are more radiosensitive than adults, and longer life expectancy gives greater opportunity for the radiation damage to be expressed.

The radiation dose varies for different investigations. The effective dose is an approximate indicator of potential harm from ionizing radiation. This can be expressed as dose equivalents of chest x-ray for better understanding and comparison. An x-ray of lateral lumbar spine gives a radiation dose which is 80 times that of a chest x-ray, and an abdominal x-ray is equivalent to 33.3 chest x-rays. CT examinations exert high levels of radiation (Table 1). CT should be avoided in pregnant patients as pelvic and abdominal CT will expose the fetus to very high doses of ionizing radiation.

Box 2. Radiation dose of CT examinations of different regions of the body compared with chest x-ray

CT examination	Mean effective dose (mSv)	Equivalent number of PA chest radiograph (each 0.02 mSv)
Head	2	100
Neck	3	150
Calcium scoring	3	150
Pulmonary angiography	5.2	260
Spine	6	300
Chest	8	400
Coronary angiography	8.7	435
Abdomen	10	500
Pelvis	10	500
Virtual colonoscopy	10	500
Chest (pulmonary embolism protocol)	15	750

Contrast media related risk

Contrast media are used to enhance the visibility of radiological anatomy as well as to characterize pathology in imaging. Some commonly used types of contrast media and investigations using them are shown in Box 3. The risks of iodine-based contrast media, gadolinium-based contrast media (GBCM), and barium are discussed.

Iodine-based contrast media

Ionic compounds were the first water soluble iodine-based contrast agents to be used. These are hyperosmolar (HOCM), and less popular due to their higher risk of side-effects. Non-ionic compounds do not dissociate into component molecules and are low or isosmolar (LOCM, IOCM), and cause side-effects in less than 1% of patients. Side-effects caused by intravascular LOCM vary from minor physiological disturbances to rare life-threatening situations (Box 4). The incidence of severe or very severe non-ionic contrast reaction is 0.044%. Nearly all life-threatening allergic-like reactions occur within the first 20 minutes from contrast injection. Patients taking metformin may develop lactic acidosis if acute kidney injury occurs following iodinated contrast media.

Box 3. Different types of commonly used contrast media and radiological investigations

Investigation		Route of administration	Type of contrast media
Radiography	Intravenous urogram (IVU)	I.V	Water soluble, non-ionic, (iodine based) *omnipaque (iohexol)*
Fluoroscopy	Digitally subtracted angiography (DSA)	Intra-arterial	Water soluble, non-ionic, (iodine based) *omnipaque (iohexol)*
	Urinary tract: MCUG	Per urethra	
	Billiary tract: percutaneous transhepatic cholangiogram	Percutaneously in to the biliary tract	
	Subarachnoid space: myelogram,	Intrathecal	
	Genital tract: hysterosalphingogram	Intrauterine	
	Other: fistulous tracts, joints	Tracts, joint space	
	GI luminal contrast studies (e.g. Upper GI contrast studies)	Oral Rectal	Water soluble, ionic iodine based *Diatrizoate (urograffin)*
	GI luminal contrast studies (e.g. Barium enema)	Oral Rectal	Barium (non-water soluble)
Contrast enhanced CT (CECT)		I.V	Water soluble, non-ionic, (iodine based) *omnipaque (iohexol)*
MRI		I.V Oral (e.g. for MRCP)	Gadolinium based

Box 4

Adverse effects resulting from iodine-based contrast media: intravascular use (LOCM)

- acute reactions (mild, moderate, severe)
  - physiological reactions (e.g. vasovagal reactions etc)
  - allergic-like reactions
- delayed reactions
  - contrast induced nephropathy (CIN) and post-contrast acute kidney injury (PC-AKI)
  - metformin induced lactic acidosis

Gadolinium-based contrast media (GBCM)

Gadolinium (Gd)-based contrast agents are the traditionally used contrast agents in MRI. Gd is a heavy metal ion which is toxic to tissue in its free state. It is tightly bound to an organic ligand and safely used in MR imaging. MR contrasts agents continue to evolve becoming more organ and system specific. Currently there are non-gadolinium based agents such as iron oxide and manganese-based agents which are already popular in liver imaging. GBCM is generally considered safe. Adverse events caused by GBCM are rare (0.07% to 2.4%) at the routinely used clinial doses of 0.1-0.2 mmol/kg. These can be acute or delayed. (Box 4) Acute events are mostly mild physiologic reactions. Allergic reactions are extremely rare (0.004% to 0.7 %). The incidence of allergic reactions caused by GBCM is less than with iodine-based contrast media. Severe life-threatening anaphylactic reactions with GBCM are extremely rare.

Box 5

Adverse events caused by intravascular (GBCM)

- acute reactions (mild, moderate , severe)
  - physiological reactions (e.g. warmth at the injection site, nausea etc)
  - allergic-like reactions
- delayed reactions
  - nephrogenic systemic fibrosis (NSF)

Gadolinium does not cause significant renal impairment when used at standard doses. However, its use is a concern in patients with renal impairment. More recently, deposition of gadolinium in the brain after iv use has been shown but its clinical consequences are uncertain. GBCM should be used with caution, preceded by sound risk-benefit analysis, in pregnancy. MR contrast media are considered safe during lactation, for the mother and the baby.

Barium-based contrast agents

Barium is made into a slurry with water and administered directly into the gastrointestinal tract via the rectal or oral route, where it provides fine delineation of mucosal detail. Barium is irritant to both the peritoneum and the mediastinum, and can cause peritonitis or mediastinitis if leaked from the gut. Using barium is contraindicated in suspected bowel perforation and in patients at risk for aspiration, as it can cause penumonitis.

USS contrast media

USS uses microbubbles of gas coated in a thin shell of albumin or lipid, and are well tolerated. Serious adverse effects and allergic reactions are rare.

Procedure related risk

Both invasive and non-invasive radiological examinations are associated risks specific to the procedure eg. aspiration during barium swallow, haematoma formation following catheter angiogram. These are not discussed in this article.

Preparation for radiological investigations

Patient preparation for radiological investigations starts with informed consent. Possibility of pregnancy needs to be considered for all investigations of females. Preparation for USS, CT, MRI and x-ray/fluoroscopic investigations are discussed.

Preparation for USS. Why fasting or full bladder?

Ultrasound examinations use high frequency sound waves in the range of MHz and is considered a generally safe procedure [11]. Some US examinations need important preparations in the form of fasting and a full bladder (Box 6).

Box 6

Patient preparation for USS

- No special preparation USS of small parts: e.g. thyroid, breast, scrotum, musculoskeletal USS
- Fasting to image the gall bladder and upper abdominal structures: USS abdomen
- Full bladder to visualize the pelvis structures
- Empty bladder for transvaginal USS, transrectal USS

Ultrasound waves propagate well through a liquid medium. This basic principle makes fluid distended structures such as the fasting gall bladder and full urinary bladder USS friendly (Figure 1). Fasting for 8-12 hours is advocated in some radiological departments. However, newer studies have failed to show significant effect with fasting.

Ultrasound waves are reflected back at interfaces meeting air and gas, making the visibility of gas containing structures limited on USS e.g. normal bowel loops. Furthermore, due poor sound beam penetration through gas filled structures, detail that lies deep to them may be obscured, limiting the yield of information. In transabdominal pelvic assessment the full bladder raises the gaseous bowel loops out of the pelvis and creates a fluid filled window through which the US beam can reach the deeper structures (Figure 2). Transrectal and transvaginal scans do not have this limitation and bladder is emptied just before these scans to avoid discomfort to the patient

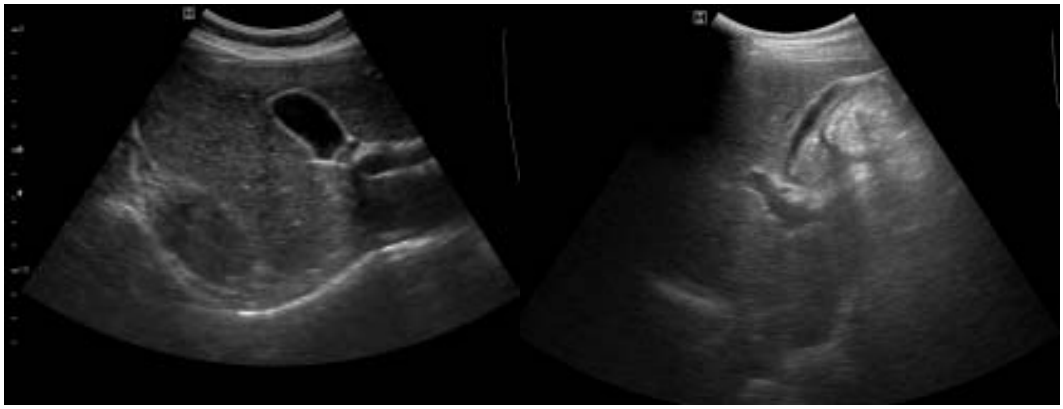

Figure 1. *USS of the gall bladder, A) distended gall bladder in the fasting state and B) contracted gall bladder in a patient who is not fasting.*

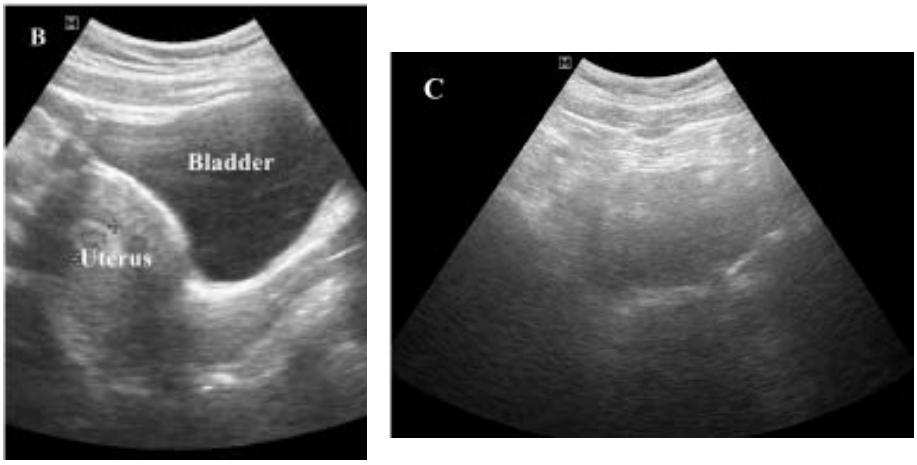

Figure 2. *B) Details of the uterus clearly seen when imaging with full bladder, and C) same patient after emptying bladder (uterine details are obscured by overlapping bowel gas).*

Preparation for CT

Patient preparation for CT depends on the region examined, the pathology that is suspected and the preexisting patient conditions. Relevant history should be provided to the radiologist to plan out the protocol. Both non-contrast CT (NCCT) and contrast CT (CECT) can be done on an outpatient basis depending on local hospital protocols. NCCT does not need special preparation other than taking off removable metal objects and ornaments lying in the area of interest.

Preventing allergic-like reactions

Past history of allergic-like reaction to iodinated contrast media increases risk of a subsequent reaction five-fold, and history of atopy two-fold. Any allergic history is associated with increased risk, but no predictive relationship is proven between the incidence of reactions and the type of allergy. History of bronchial asthma should also be excluded as it may increase the risk of reactions (Box 7).

Box 7

Patient preparation for CECT

Preventing allergic-like reactions

- Identifying 'high risk' groups to develop allergic-like reactions. History of:
  - allergy to contrast media
  - allergy to food, drugs
  - atopy, bronchial asthma
- Premedication (if positive allergic history or bronchial asthma)

Premedication with corticosteroids is indicated in patients at 'high risk'. Recognized regimens of the American College of Radiology (ACR) for elective premedication are shown in Box 8. Oral prednisolone 10 mg 8 hourly for 3 days, a popular regimen practiced in Sri Lanka, is not included in ACR manual for prophylaxis. In situations where imaging is indicated urgently, emergency premedication can be done. (Box 9).

Box 8

Regimens for elective premedication

1. Oral prednisone 50 mg at 13 hours, 7 hours and 1 hour before contrast*
2. Oral methylprednisolone 32 mg 12 hours and 2 hours before contrast*
3. IV hydrocortisone 200 mg* (if the patient is unable to take orally)

(*Combined with diphenhydramine 50 mg iv, im or orally administered 1 hour before contrast injection)

Box 9

Regimens for emergency premedication

In decreasing order of preference

1. IV methylprednisolone 40 mg every 4 hours*
2. IV hydrocortisone 200 mg every 4 hours*
3. IV dexamethasone 7.5 mg (in patent with allergy to methylprednisolone) every 4 hours*
4. IV betamethasone 6.0 mg every 4 hours (in patients with allergy to methylprednisolone)*

(*Combined with diphenhydramine 50 mg iv, im or orally administered 1 hour before contrast injection)

For children, prednisolone 0.5 mg - 0.7mg /kg (up to 50 mg) should be given 13, 7, and 1 hour before injection of contrast. Weight calculated dose of antihistamine should be given 1 hour before contrast injection. Effective action of iv steroids takes 4-6 hours. If the radiological examination cannot be delayed corticosteroids should be omitted, and only iv H1 blockers given before contrast injection.

Preventing CIN and PC-AKI

Prevention is by identification of high risk groups, followed by either avoiding iv contrast or iv contrast administration after patient preparation (Box 10).

Box 10

Patient preparation for CECT
Steps to prevent CIN and PC-AKI

1. Identifying high risk patients by assessment of renal function in selected groups (Box 11)
2. Risk vs. benefit guided decision for avoiding iv contrast and considering alternative modalities or non-contrast studies in identified high risk patients
3. Seeking nephrology opinion
4. Volume expansion

Box 11

Patients who need assessment of serum creatinine (±eGFR) before iv contrast injection

- History of renal disease: dialysis, kidney transplant, single kidney, renal cancer, renal surgery
- Age > 60 years
- Hypertension requiring treatment
- Diabetes mellitus
- Patients on metformin

For patients with eGFR <30 mL / min/1.73m^2 risk for developing CIN is high. The decision to avoid iv contrast is essentially clinical, based on risk-benefit analysis. If baseline eGFR is more than >44ml/ min/ 1.73m^2, nephrotoxicity is unlikely.

Patient preparation is mainly iv volume expansion by hydration of the patient preferably with isotonic fluids such as lactated Ringer's or 0.9% normal saline. 0.9% saline infused at 100 ml/hour starting 6 to 12 hours before contrast, continuing up to 12 hours post-contrast is a recognized regimen for adults.

Preventing metformin induced lactic acidosis

The ACR Committee recommends that metformin is discontinued in selected categories of patients at the time of or prior to iv contrast injection (Box 12). It can be restarted if renal functions are found to be normal 48 hours after the procedure.

Box 12

Patient preparation for CECT
ACR recommendations for patients on metformin

1. No need to discontinue metformin if no evidence of AKI, eGFR ≥30 mL / min/1.73m^2
2. Need to discontinue metformin if stage IV or Stage V AKI, eGFR< 30, patients undergoing arterial catheter studies that might result in emboli to the renal arteries

Other adverse effects

Caution is needed when administering iodine-based contrast agents to patients with multiple myeloma, cardiac failure, pheochromocytoma and hyper-thyroidism (Box 13).

Box 13

Special groups at risk of developing adverse effects form iodinated iv contrast media

1. Patients with history of paraprotenimia (increased risk of CIN with HOCM)
2. Patients with cardiac failure (problems with handling the osmotic load)
3. Patients with pheochromocytoma (can lead to an increase in serum catecholamine levels with HOCM)
4. Patients with hyperthyroidism (risk of developing delayed hyperthyroidism provoked by iodine).

Pregnancy is not a contraindication for iv LOCM administration, so pregnancy screening is not necessary before iodinated contrast studies. Breast-feeding can be continued normally after iodinated contrast administration to the mother.

Preparation for MRI

Preparation for MRI includes patient screening for objects and devices, and taking caution with MR contrast media (Box 14). It is important to explain about the constricted space inside the machine and the loud noises that may occur, as patients could feel claustrophobic or scared. Sedation or anesthesia may be necessary if the patient is unable to keep absolutely still during imaging, which may take 30 min to 1 hour. Small children may need general anesthesia. Pregnancy is not a contraindication for MRI with magnetic field strength of 3.0 tesla or less during second and third trimesters. MR imaging during the first trimester is best restricted for strong justification after risk benefit analysis.

Box 14

Preparation for MRI

1. Avoiding risks related to strong magnetic field. Patient screening before MRI for absolute or potential contraindications: aneurysmal clip, pacemaker, ocular metallic implant, electrically active implant, cochlear implant, coils, stents, filters etc.
2. Caution with contrast media

Patient screening before MRI

MRI uses a strong magnetic field that may cause both internal and external metallic and magnetic devices to dislodge, and electronic chips to malfunction. Tissue heating and burns can occur around metallic devices due to changing gradient fields and radiofrequency fields, so patients should be screened for such objects. If the MR compatibility of an internal or fixed object cannot be positively confirmed, such devices should be considered unsafe, and the patient should not enter the MRI room. Verification may need screening for devices using x-ray or CT and contacting the manufacturer of the device.

Caution with contrast media (Box 15)

Taking a history of allergic-like reactions. The main risk factor is a previous history of allergic-like reaction to the same contrast media which increases the frequency of a subsequent reaction by about eight times. However, in most instances contrast-enhanced MRI can be done after premedication with cortico-steroids (premedication is similar to iodinated contrast media). If possible, a different type of GBCM should be used for imaging specially in case of moderate to severe previous reactions. Allergy to iodinated contrast media does not increase the risk. Asthma and other allergic history may be a small increase in risk.

Testing serum creatinine and eGFR. Routine testing is not necessary in all patients. Serum creatinine with calculation of eGFR should be assessed in patients with specific risk factors.

Nephrogenic systemic fibrosis. In patients with end stage kidney disease on chronic dialysis and in CKD stage 4 and 5 gadolinium should not be used. The potential for NSF in patients with GFR >30ml/min/1.73m is very rare but ACR committee recommends a cutoff point of >40 ml/min/1.73m^2. No special precautions are needed for patients>eGFR 40 /min/1.73m^2.

Box 15

Caution with GBCM

- excluding history of
  - allergy to GBCM
  - asthma or other allergic history
- avoidance or premedication if positive history
- assessment of serum creatinine and eGFR if
  - > 60 years of age
  - existing kidney disease
  - diabetes mellitus
- avoiding gadolinium in patients with potential for NSF

Preparation of a patient for an x-ray or fluoroscopic examination

No preparation is needed for most routine x-rays other than removing metallic objects.

For x-ray KUB, fasting for solids for a period of 5 hours is recommended. Routine bowel preparation depends on departmental protocols, but a low fibre diet and bisacodyl 3 tables are commonly given for three days. IVP studies include x-ray KUB and IV contrast, so bowel preparation is needed, as well as precautions that should be taken before IV contrast

administration. HSG studies contrast is administered to delineate the uterus and fallopian tubes. As a precaution to avoid underlying pregnancy, the patient is asked to abstain from intercourse between booking and examination, and the examination is done between the 4th and 10th day of the menstrual cycle.

Contrast fluoroscopic examinations

Fluoroscopic studies are dynamic x-ray investigations. Upper gastrointestinal (GI) contrast studies such as barium swallow, barium meal, small bowel enema, need fasting for 6 hours before the examination. Lower GI contrast studies need preparation of bowel with low fibre diet for three days.

Summary

The clinicians requesting radiological investigations as well as radiologists need to be well aware of adverse effects, which can be potentially life-threatening. If the risk from the investigation outweighs the benefit for patient management, alternative investigations should be considered. If the benefit outweighs the risk, the procedure can be carried out with optimum patient preparation. Communication between the referring clinician and the radiologist, and individualized approach to risk-benefit assessment are necessary to ensure maximum benefit to the patient.

Further reading

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