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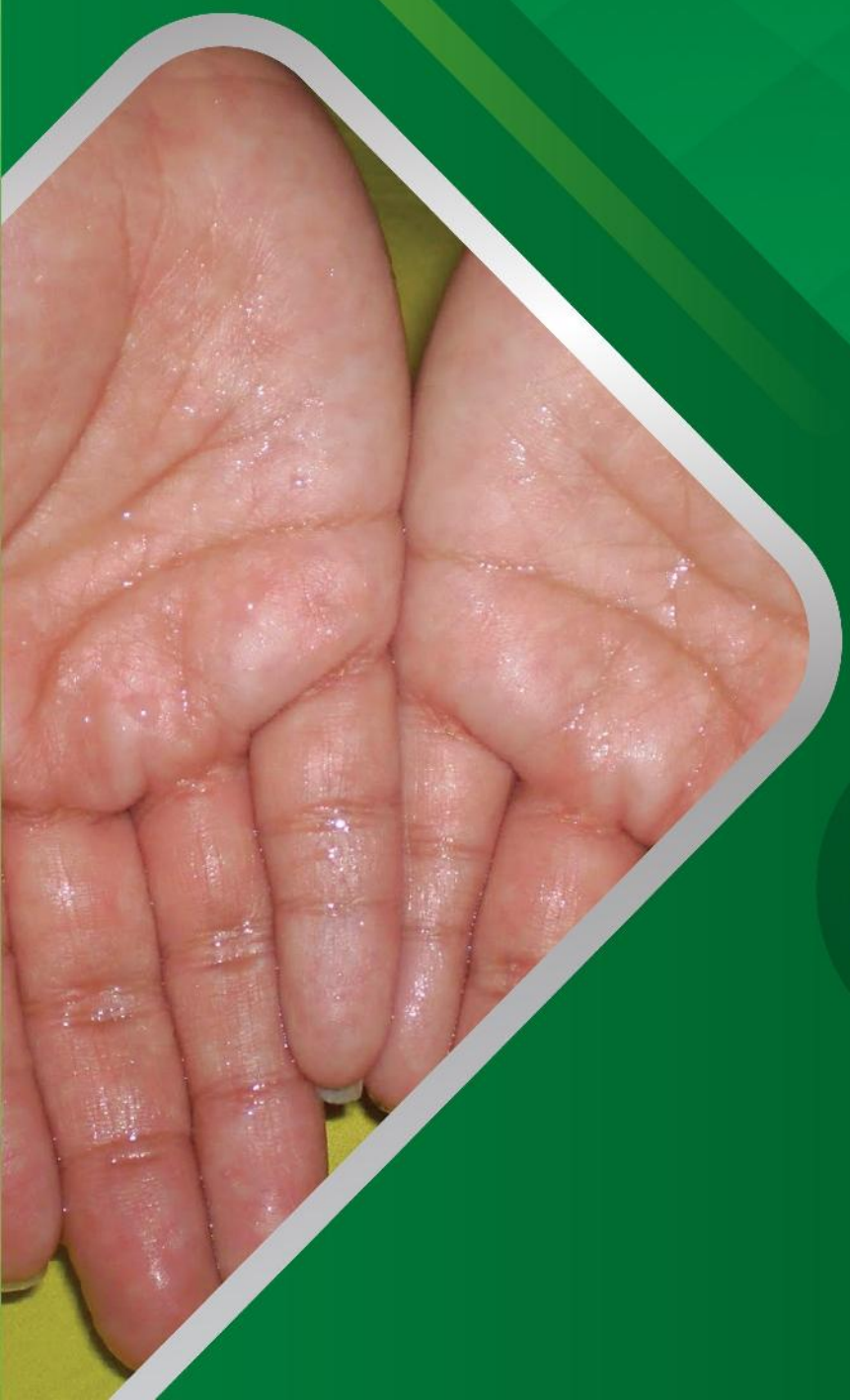
Info Medicus

The essence of medical practice



CONTENTS

Editorial Board

EDITORIAL

Dear Doctor,

As we enter the "Info Medicus" 16th Anniversary, it is a time for celebrating the newsletter's many accomplishments, recognizing the trust and respect that have been accorded by the readership as well as the hard work and diligence of the editorial board and the newsletter's authors. What started as a modest English language 4 pages quarterly publication; has now blossomed into 20 pages bilingual publications, that has had major impact on disseminating current medical information to our medical practitioners that in turn has help them in providing the best possible care to their patients.

Peritonsillar abscess is a very common and painful condition. We have focused on peritonsillar abscess as one of the topics in Patient handouts. Intraosseous access is used for situation in which adverse environmental condition makes it very difficult to obtain intravenous access. Therefore, we have selected insertion of an intraosseous needle in adults as our topic in Essential procedure.

We have highlighted "Hyperhidrosis" as our review article as it is a common and embarrassing situation and has also become a challenging area in medicine. We hope you will find interesting information from it and will be beneficial in your daily practice. Other sections are there as usual.

On behalf of the entire editorial board, we wish you all a healthy and successful life and looking forward to seeing your continued encouragement and support to propel Info Medicus to its glorious year.

Thanking you and warm regards

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Elevated liver enzymes

What are liver enzymes?

An enzyme is a chemical that accelerates chemical reactions within the body. There are several enzymes in the liver, including, alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP).

What does the liver do?

The liver performs many functions, including the following:

- Produces most of the proteins the body needs
- Prevents shortages of nutrients by storing certain vitamins, minerals and glucose
- Produces bile, which helps digest fat and absorb vitamins A, D, E and K
- Produces substances that help with blood clotting

What causes elevated ALT and AST levels?

There are many causes of mildly elevated ALT and AST levels. The most common causes are nonalcoholic fatty liver disease (NAFLD) and alcoholic liver disease. In NAFLD, the liver has more fatty tissue in it than normal. Regular or heavy alcohol use can also hurt the liver and increase liver enzymes. Other medical conditions can increase liver enzymes, like hepatitis B or C and a condition that runs in families called hemochromatosis. Using certain medicines and over-the-counter supplements can also increase liver enzymes.

How is it treated?

It depends on what is causing the liver enzymes to be elevated.

For NAFLD lifestyle should be changed. These changes include eating a healthier diet, exercising, losing weight and limiting alcohol and sugary foods and drinks.

Treatments for hepatitis depend on whether it is acute or chronic. In case of acute hepatitis, treatment may include bed rest, intake plenty of fluids and avoiding alcohol. In case of chronic hepatitis antiviral medication is indicated.

Cirrhosis is permanent liver damage, so it is not always treatable. However, the underlying cause of liver damage is usually responsive to treatment. Treatments such as a modified diet, weight loss and reduced alcohol consumption can all reduce the risk of further liver damage. The prompt diagnosis and treatment of conditions that affect the liver can help prevent cirrhosis.

References: 1. Am. Fam. Phy., 01 December 2017, Vol. 96(11)
2. www.medicalnewstoday.com
3. my.clevelandclinic.org

Peritonsillar abscess

What is a peritonsillar abscess?

Peritonsillar abscess is the most common deep infection of the head and neck, occurring primarily in young adults. The peritonsillar space lies between each tonsil and the wall of the throat. An infection can cause a pus filled swelling to develop in this space. Peritonsillar abscesses, also called quinsy, usually occur as a complication of tonsillitis. They most often are caused by "strep throat" bacteria (group A beta-hemolytic *streptococci*).

How to know if someone has peritonsillar abscess?

Patients with peritonsillar abscess appear ill and report malaise, fever, progressively worsening throat pain and dysphagia. The associated sore throat is markedly more severe on the affected side and is often referred to the ear on the ipsilateral side. Swallowing can be difficult and painful. The combination of odynophagia and dysphagia often leads to the pooling of saliva and subsequent drooling. Patients often speak in a muffled or "hot potato" voice.

How is it treated?

Generally, treatment of peritonsillar abscess involves intravenous antibiotics, surgical drainage, adequate hydration, analgesia and close clinical monitoring for complications. Parenteral antibiotics should be started as soon as the diagnosis is suspected. The choice of surgical drainage depends on various factors. Older cooperative children, who can tolerate local anesthesia, can undergo needle aspiration by a skilled otolaryngologist in an outpatient setting. In fact needle aspiration can be performed quickly, is relatively safe and can be both diagnostic and therapeutic. Those patients will require observation for complications of needle aspiration such as bleeding, aspiration of pus or blood. Prior to discharge, patients have to be able to take oral antibiotics and liquids and have their pain well controlled. In addition, patients should have a close medical follow up.

What are the complications?

- Airway obstruction
- Aspiration pneumonitis or lung abscess secondary to peritonsillar abscess rupture
- Extension of infection into the deep tissues of the neck or superior mediastinum

References: 1. Am. Fam. Phys., 15 April 2017, Vol. 95(8)
2. www.cancertherapyadvisor.com
3. www.drugs.com

Multiple renal arteries

A 9 year old girl with a single dysplastic kidney and chronic kidney disease presented to the hospital to undergo transplantation of a kidney from a deceased donor. During preparation of the kidney for transplantation, the donor kidney was found to have five renal arteries. During fetal development, multiple mesonephric arteries supply blood to the kidney. Typically, one mesonephric artery persists to become the renal artery; the persistence of multiple mesonephric arteries can lead to multiple renal arteries. Although two renal arteries is a common anatomical variant, three or more arteries in a single kidney is less common. Kidneys with multiple arteries are more technically challenging to transplant and are associated with an increased risk of vascular complications. The risks of such complications may be greater in children, who have smaller blood vessels. For these reasons, transplantation was deferred in the young patient, and the donor kidney was transplanted into a 35 year old man. At 3 years after transplantation, the adult recipient of the kidney was clinically well, with a serum creatinine level of 1.0 mg per deciliter (reference range, 0.7 to 1.2 mg per deciliter). The child underwent live donor kidney transplantation 18 months after the originally scheduled date. At the 2 year follow up, she was also clinically well, with a serum creatinine level of 0.9 mg per deciliter (pediatric reference range for age, 0.4 to 0.8 mg per deciliter).

Reference: N. Engl. J. Med., 29 August 2019, Vol.381(9)

Insertion of an intraosseous needle

Overview

Obtaining rapid vascular access is an essential step in the resuscitation of critically ill patients. Peripheral or central intravenous access may be difficult to obtain in a timely manner in such patients, especially in children and neonates but also in adult patients, in whom the vessels may be constricted. Obtaining peripheral intravenous access is especially challenging when environmental conditions are unfavorable. 1 to 3 central intravenous access carries the risk of pneumothorax and arterial injury and requires a high level of expertise; in most instances, it is not possible to perform the procedure in a prehospital setting. The insertion of an intraosseous needle provides an alternative route for vascular access in these circumstances; it is also used after other approaches have failed. Although intraosseous needle insertion was originally performed in the resuscitation of pediatric patients, it has gained acceptance for use in adults, especially since the advent of mechanical insertion devices. The most recent guidelines from the Advanced Cardiac Life Support Certification Institute, published in 2010, recommend the intraosseous route over the endotracheal route for the administration of fluids and medications in adult patients in whom intravascular access is not available. The primary advantages of the intraosseous route are speed of access and reliability.

Indications

Vascular access is vital for drug and fluid administration but may be difficult to achieve in certain patients. Peripheral venous access is the preferred route for fluid and drug administration, but only if it can be achieved in a short period of time (2 minutes or less). In such cases, the intraosseous access can be the alternate method to establishing a route for fluids and medications in adult and pediatric patients.

Infusions

Intraosseous access is indicated for patients in whom there is an urgent need for vascular access in order to provide fluid resuscitation or medication delivery and in whom conventional venous access is not readily available.

- Crystalloids
- Colloids
- Blood products
- Resuscitation drugs
- Vasopressor infusions

Laboratory testing

In addition, in the critically ill patient, a sample can be drawn from the intraosseous space for laboratory testing.

- Blood typing
- Measurement of hemoglobin level
- Serum chemical analysis
- Blood gas analysis

Anatomy

The medullary cavity is a highly vascular structure that functions as a noncollapsible vein capable of accepting a large volume of fluid and medications and rapidly delivering them to the central circulation. The medullary venous sinusoids drain into a central venous channel, which exits the bone in the form of emissary and nutrient veins. The rate of infusion is limited by the size of the medullary cavity and the diameter of the intraosseous needle.

Site selection

A number of sites can be used for intraosseous needle insertion in an adult, such as the proximal tibia, the distal tibia, the humerus, the distal femur, the sternum, the calcaneus and the styloid of the radius. A specific mechanical system for intraosseous needle insertion system facilitates needle insertion with minimal risk of perforation or infection of mediastinal structures.

Equipments

The following items should be assembled in preparation for the drill based insertion:

- EZ-IO drill and appropriate sized needle
- Chlorhexidine or iodine solution for site preparation
- Sterile gloves
- Sterile towels for draping the site
- 10 cc syringe for aspiration and infiltration
- 1% lidocaine for analgesia if the patient is conscious
- Standard Luer-Lok tubing for the delivery of fluids or medication
- A pressure bag if large volumes of fluid need to be administered through the intraosseous system
- Gauze and tape for securing the device

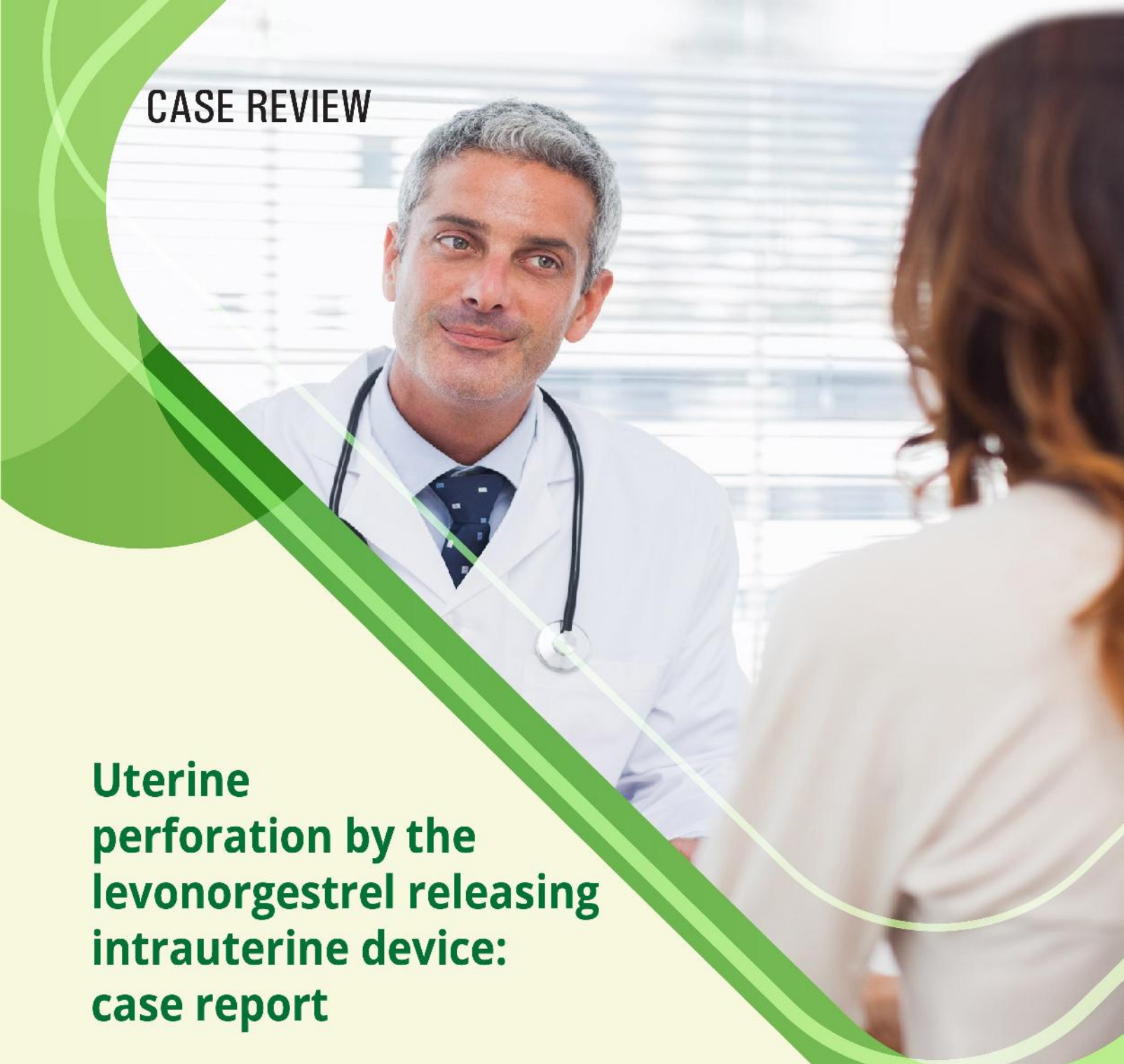
Intraosseous needle insertion with the help of a mechanical device

- Explain procedure to patient, if possible, explain the risks and benefits of the procedure to the patient and obtain consent
- When a mechanical device is used, the proximal tibia is the preferred site in adults. Secondary sites are the distal tibia and the humeral head
- The patient's leg should be positioned in slight flexion by placing a rolled towel under the knee
- The site should be cleaned with chlorhexidine or iodine solution and then it should be draped in a sterile fashion. If the patient is conscious, the skin, subcutaneous tissues and the periosteum should be infiltrated with 20 to 30 mg of 1% lidocaine
- The tibial tuberosity should be identified. The desired insertion site is the flat medial surface of the tibia, medially one finger's width away from the tibial tuberosity (Figure-1)

Figure-1: Site for mechanical intraosseous needle insertion

- The leg should be stabilized with the nondominant hand. By holding the drill in the dominant hand, the needle tip should be positioned at a 90 degree angle to the surface of the bone
- The trigger should be pressed and held and the needle should be gently guided through the tissues, avoiding excess pressure. A sudden loss of resistance indicates that the needle has penetrated the cortex and has reached the medullary cavity
- The stylet should be removed and the needle should be connected to a 10 cc syringe with standard Luer-Lok tubing
- If the needle is correctly placed within the marrow cavity, it should be possible for it to stand upright without support. Aspiration of blood and marrow confirms adequate placement of the needle. Obtain confirmation of placement by infusing a 10 cc bolus of saline solution through the syringe; the fluid should flow easily with no resistance. If the fluid does not flow, another insertion site should be selected
- After correct placement has been confirmed, the test syringe can be disconnected and the intraosseous needle can be connected to regular infusion tubing. Fluids can be infused by means of gravity, but infusing fluids through a pressure bag produces better flow rates. A pressure bag should be used in patients requiring resuscitation, once it is certain that the needle has been correctly placed and is functioning
- While infusing fluids, it should be carefully watched for extravasation and increased calf circumference. The needle and tubing should be secured to the leg with tape, and the leg should be immobilized to prevent dislodgement of the needle. To remove the catheter, disconnect the intravenous tubing and attach a sterile syringe to the hub. The leg should be stabilized, and gently pulled back while rotating the needle clockwise

Reference: N. Eng. J. Med., 24 January 2019, Vol. 380(4):e4



Uterine perforation by the levonorgestrel releasing intrauterine device: case report

Introduction

We demonstrate a case report of the uterine perforation by the levonorgestrel releasing intrauterine device (LNG-IUD) in a 33 year old asymptomatic woman after an 18 month period after insertion. The device was not localized in utero during routine control with transvaginal sonography. After abdominal radiography examination the device was removed by laparoscopy. The possibilities of transuterine migration of intrauterine device (IUD) are discussed. An IUD is one of the commonly used forms of contraception. The local effect of levonorgestrel in the uterine cavity, sperm mobility inhibition, changes of endometrium structure, and cervical mucus changes are specific effects of LNG-IUD. A serious complication associated with the insertion of IUD is uterine perforation. The risk of perforation ranges from 0 to 1.3 per 1,000 insertions. Several cases of LNG-IUD related uterine perforation have been reported.

Case report

A 33 year old woman, gravida 2, para 2, with history of regular menstrual cycles after discussion with her physician opted for an

levonorgestrel releasing intrauterine device for contraception. The device was inserted 12 weeks after her last delivery. The woman was not lactating at the time of an insertion. The procedure of the insertion was reported as uneventful. Routine transvaginal sonogram (TVS) performed immediately after the insertion showed LNG-IUD in uterine cavity. She was amenorrheic after insertion. During routine control after 18 months TVS failed to demonstrate the device in the uterus. An antero-posterior radiograph of the abdomen confirmed the diagnosis of a misplaced intra-abdominal IUD.

The woman had no history of abdominal pain or irregular uterine bleeding during the last 18 months. Laparoscopy for IUD removal was scheduled. During laparoscopy uterus and adnexae appeared normal. The perforation site on the uterine wall was not identified. IUD was observed in the omentum encased in mild peritoneal adhesions (Figure-1). A simple laparoscopic procedure with the removing of IUD was accomplished. The patient was discharged 24 hour after laparoscopy.

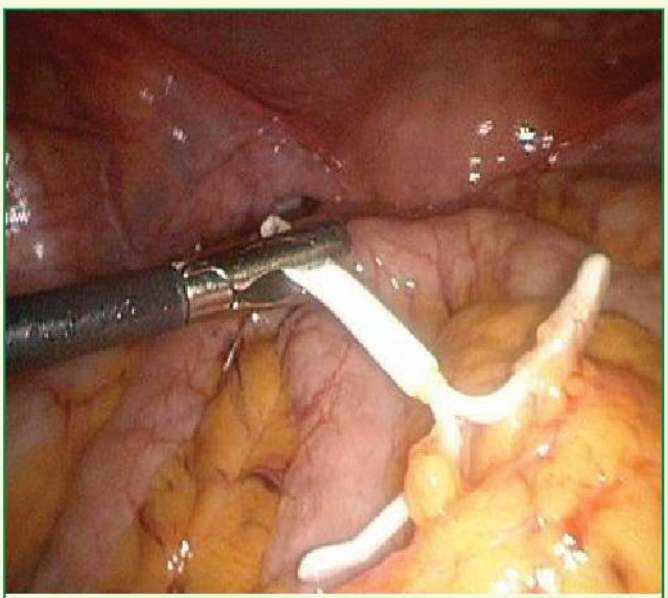


Figure-1: IUD in the omentum encased in mild peritoneal adhesions

Discussion

The hypothesis of uterine perforation during IUD insertion is perforation of the uterine wall by the sound or by the inserter tube or by IUD itself. Another mechanism might be partial perforation at the time of insertion, resulting in uterine contractions causing complete perforation. One reason for perforation is the failure to establish the size and orientation of the uterus by careful pelvic examination.

This is particularly important where there is sharp ante or retroflexion of the uterus, and where it is not straightened with traction using a tenaculum prior to insertion. Complexity of the insertion procedure of the LNG-IUD might have played a role in the (partial) perforation of the fundus: as the arms of the IUD are retracted in the tube, creating a narrow protruding element, pushing the IUD out instead of retracting the tube would increase the risk of perforation. Abdominal pain is a common symptom.

The insertion during lactation even beyond 6 weeks after delivery is an important risk factor for perforation and is associated with less pain. Such cases may therefore easily pass unnoticed. Studies have shown that cervical traction in a caudal direction reduces the median uterocervical angle, from 75° to 10° and moderate cervical traction straightens the uterus, and the routine use of a tenaculum theoretically should make insertion of an IUD safer. A prerequisite, however, is that traction should be applied until the insertion of the IUD has been completed. In addition, clinical experience shows that access to the uterus, and straightening of the utero-cervical axis, is facilitated by using the lithotomy position which should be recommended for all IUD/IUS insertions.

It is recommended that postpartum insertions of LNG-IUD should be postponed until 8 weeks postdelivery. IUD insertion immediately after a first trimester abortion seems to be both safe and practical. A routine check-up 6 weeks after insertion of a LNG-IUD including TVS is recommended. Intraperitoneal dislocated LNG-IUD resulted in plasma levonorgestrel levels ten times higher than the plasma level of levonorgestrel observed with LNG-IUD placed in uterus. High plasma levonorgestrel level supresses ovulation. When pregnancy is desired a misplaced LNG-IUD should be removed. There is a consensus for removal of a perforated IUD mainly because of the potential for adhesion formation . The effect of high levonorgestrel concentrations on the cytoplasm was identified in the submesothelial cells. The pseudodecidual changes also known as ectopic peritoneal decidua were described as developing solely in relation to pregnancy when there were found in the sites such as the submesothelial stroma of the uterus, the uterine ligaments, adnexae, appendix and omentum.

The effects of progestogens on the formation of peritoneal adhesions are unclear. Progesterone has anti-inflammatory and immunosuppressive effects that could play a role in the prevention of peritoneal adhesion formation. Laparoscopy is the method of choice for removal of the displaced IUD. From the point of risks of adhesion formation after the laparotomy in the case with encapsulated IUD by the firm adhesions it may be safer to leave a misplaced device in place than to remove it by laparotomy. Conversion of laparoscopy to laparotomy is indicated only on the patients with the serious complications during laparoscopy.

Reference: Gyne. Sur., September 2009, Vol. 6(3):277-279

Human blood cells transformed into functional neurons

Scientists recently found a way to convert an immune system cell into a neuron, two cells with totally different shapes and very different functions. The hope is that the technique could help researchers study a patient's brain from a blood sample. Researchers at the Stanford University School of Medicine have found that human immune cells in blood can be converted directly into functional neurons in the laboratory in about three weeks with the addition of just four proteins. The dramatic transformation does not require the cells to first enter a state called pluripotency but instead occurs through a more direct process called transdifferentiation. The conversion occurs with relatively high efficiency, generating as many as 50,000 neurons from 1 milliliter of blood and it can be achieved with fresh or previously frozen and stored blood samples, which vastly enhances opportunities for the study of neurological disorders such as schizophrenia and autism. "Blood is one of the easiest biological samples to obtain," said Marius Wernig, MD, associate professor of pathology and a member of Stanford's Institute for Stem Cell Biology and Regenerative Medicine. "Nearly every patient who walks into a hospital leaves a blood sample, and often these samples are frozen and stored for future study. This technique is a breakthrough that opens the possibility to learn about complex disease processes by studying large numbers of patients." Marius Wernig and his colleague focused on highly specialized immune cells called T cells that circulate in the blood. T cells protect us from disease by recognizing and killing infected or cancerous cells. In contrast, neurons are long and skinny cells capable of conducting electrical impulses along their length and passing them from cell to cell. "It's kind of shocking how simple it is to convert T cells into functional neurons in just a few days," Wernig said. "T cells are very specialized immune cells with a simple round shape, so the rapid transformation is somewhat mind boggling." The resulting human neurons aren't perfect; the neurons they created can't form mature synapses spaces between neurons that are necessary for the cells to communicate with one another. According to the statement, Wernig and his team are hoping they can eventually improve the technique and have already begun to collect blood samples from children with autism.

References: 1. med.stanford.edu
2. www.livescience.com

Hyperhidrosis

Introduction

Hyperhidrosis (excessive sweating) is a chronic autonomic disorder that can be debilitating leading to emotional and social embarrassment, as well as occupational, physical and psychological disability. In a majority of cases, the cause of hyperhidrosis is unknown. Primary hyperhidrosis starts in childhood and affects 0.6%-1% of the population. A familial variant with autosomal dominant inheritance is now recognized with some families linked to an abnormality of chromosome 14q. The diagnostic criteria for hyperhidrosis includes excessive sweating that lasts at least six months without any obvious cause and has at least two of the following features: impairs daily activities, a bilateral and relatively symmetric pattern of sweating occurring at least once per week, an age of onset younger than 25 years, cessation of focal sweating during sleep or positive family history. Secondary hyperhidrosis can be drug induced (for example with sertraline), toxin induced (acrylamide), caused by a systemic illness (endocrine and metabolic disorders, neoplasms, spinal cord lesions), by congenital disorders such as familial dysautonomia (Riley-Day syndrome) or it can be compensatory. Compensatory hyperhidrosis is a phenomenon in which there is increased sweating in parts of the body unrelated to the location of treatment or in the case of surgery, unrelated to surgery or anatomy. It is often seen in segments below the level of sympathectomy, which is performed for treatment. Gustatory hyperhidrosis (usually involving the face) can be familial or occur in association with trauma or other local insults.

Epidemiology

Hyperhidrosis affects 1%-3% of the total population, yet less than one half of those affected discuss this with their physician. More than 90% of hyperhidrosis cases are primary and more than one half of these cases affect the axillae. More than one third of persons with axillary hyperhidrosis report that the condition is barely tolerable or completely intolerable, and it nearly always interferes with daily activities. Up to two thirds of patients report a family history suggesting a genetic predisposition. Although prevalence between sexes is roughly equal, women are more likely to report hyperhidrosis to their physician.

Function and pathology of sweating

Sweating is the most important effector in thermoregulation and is controlled through the hypothalamus. Sweat on the palms of the hands and soles of the feet help to provide a good grip, which has been important to human beings during evolution and having normal palm moisture is important to us when doing widely differing activities such as handicrafts, handling paper and sport. The palmoplantar sweating, sometimes called "emotional" is controlled through the cortex, the limbic system and through sympathetic (fight and flight) nerves (Figure-1).

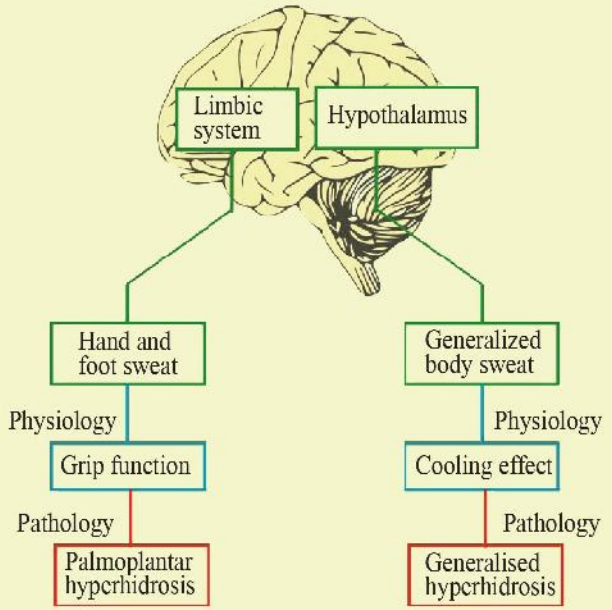


Figure-1: Sweating partly occurs to cool our body and partly to obtain a good grip function. These functions are controlled from different parts of the "old" part of the brain: grip function from the cortex and the limbic system, thermoregulation from nuclei in the hypothalamus. Since the hypothalamus is also a nucleus of the limbic system, factors such as stress also usually draw sweat from the whole of the body, and heat and/or exertion can make hand and foot sweat worse. What may be physiological can transform into pathological in 2.8% who are genetically predisposed.

Reflexes that are triggered by pressure on the palm of the hand and/or sole of the foot can trigger palmoplantar sweating. The eccrine sweat glands with cholinergic muscarinic receptors receive signals from sympathetic fibres with acetylcholine as the signal substance. The co-transmitters CGRP and VIP are potent vasodilators and lead to greater vascular permeability which is important when sweat is being produced. After NaCl has been reabsorbed into the sweat duct, the eccrine sweat turns into a hypo-osmolar salt solution. The presence of cystic fibrosis means that this reabsorption capacity is lacking leading to extra salty sweat, which is fairly often observed by parents of children with the disease. Armpits and groins have three types of sweat glands: eccrine, apocrine and hybrid apoeccrine (Figure-2).

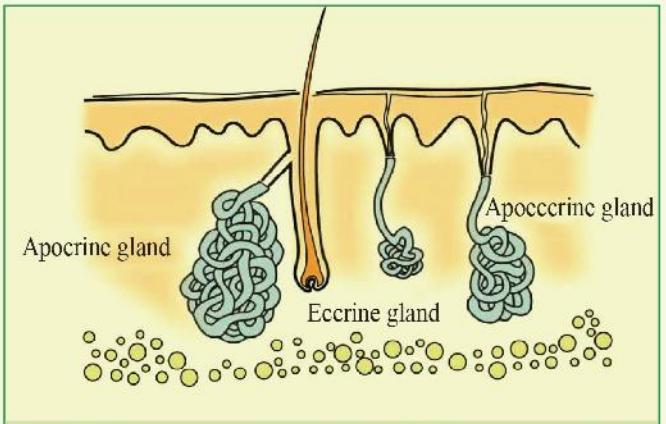


Figure-2: The armpits and groins have 3 different types of sweat glands which distinguish themselves histologically and functionally. The eccrine glands make the ample sweat which consists of a salt solution. The apocrine sweat constitutes a small amount of oily liquid which contains pheromones and when it breaks down skin bacteria it gives rise to the typical odour of sweat. The apoeccrine gland is a hybrid which is similar in function to the eccrine and which can produce large quantities of sweat in the form of a salt solution.

The eccrine and apoeccrine sweat glands produce the salt solution, "the normal sweat". The apocrine glands have some features of mammary gland secretion as the sweat is energy rich. The sweat consists of a small quantity which is of an oily consistency. The apocrine sweat is primarily odour free but the characteristic smell of sweat occurs when it breaks down skin bacteria in armpits and groins. A pronounced smell of sweat with its impact on an individual's quality of life is called bromhidrosis. The apocrine sweat contains pheromones whose odour signals may also be significant as regards sexual attraction in humans.

Hyperhidrosis is characterised by an abnormal response to heat, exertion and stress with pronounced sweating either in general or focally. This can be seen as an extension of the physiological response where general hyperhidrosis involves "the thermostat", the hypothalamus and focal, symmetrical hyperhidrosis cortex and the limbic system. Patients with hyperhidrosis display increased activity in the sympathetic nervous system (sudomotor) on arousal (pain, shouting, caressing).

Classification of hyperhidrosis

1. Primary hyperhidrosis (unidentifiable cause)
2. Secondary hyperhidrosis (with an underlying cause)
3. Secondary general hyperhidrosis
4. Secondary regional or asymmetrical hyperhidrosis

1. Primary hyperhidrosis

A major study shows that 2.8% of the population suffers from

hyperhidrosis. The majority have the primary form which is hereditary, probably autosomally inherited with incomplete penetrance. It can be divided into focal and general primary hyperhidrosis. The focal is bilaterally symmetrical: hands, feet, axillae or groins. Focal hyperhidrosis from the face/head does occur but is often part of the general form. Generalized sweating usually involves both the head and trunk and in severe cases also extremities and groins. Combined focal and general hyperhidrosis does occur. Other common combinations of focal hyperhidrosis are hands and feet, hands, feet and axillae and groins and axillae.

Hyperhidrosis from the hands and feet usually starts during early childhood but axillary hyperhidrosis often starts in the teenage years. Many people who have general hyperhidrosis start after the age of 50. For many women, if it starts late in life it is called postmenopausal hyperhidrosis, even if other climacteric symptoms are missing and oestrogen substitution is ineffectual.

Patients with general hyperhidrosis say that heat and/or exertion is the most deteriorative factor, and stress is the second most deteriorative. The reverse applies to focal hyperhidrosis from hands and feet where stress is the most deteriorative and heat and/or exertion come second. The fact that the "thermostat", the hypothalamus, is part of the limbic system may explain why the deteriorative factors of heat and/or exertion and stress covary with general and focal hyperhidrosis. The prognosis of hyperhidrosis is not known. For some, the problems pass but for many they remain for life. The disorder can also change in character; for example, it can start as axillary hyperhidrosis in the teenage years, followed by a problem free interval and later general hyperhidrosis in the 60s.

Hyperhidrosis has an extremely negative impact on quality of life. The Dermatology Life Quality Index (DLQI) can be used to objectivise this, to assess treatment results and compare results with other skin diseases which are surveyed using the same questionnaire. Patients with hyperhidrosis can have a heavily reduced quality of life on a par with the most severe psoriasis patients who are surveyed using the same questionnaire.

2. Secondary hyperhidrosis

Secondary hyperhidrosis may involve several specialties (Table-1). A small amount of anamnestic data is usually enough to differentiate between primary and secondary hyperhidrosis, but sometimes anamnesis and status in diagnostics are insufficient and that is when it becomes relevant to take samples and do further examinations.

3. Secondary general hyperhidrosis

With general hyperhidrosis it can be difficult to clarify whether it is primary or secondary. A long anamnesis with no signs of other disease strongly suggests that it is not an endocrine, infectious or malignant disease. If there is a short anamnesis ask whether there are symptoms, medication has recently been started, there are signs

Table-1: Causes of secondary hyperhidrosis

Dermatology
Eccrine nevus
Idiopathic unilateral focal hyperhidrosis
Vascular deformities
Pretibial myxoedema
Gynaecology
Postmenopausal hyperhidrosis
Iatrogenic
Medicines:
• Methadone or other opiates
• Cholinergics such as galantamine
• SSRIs
Infection
Brucellosis
HIV
Chronic malaria
TBC
Endocarditis
Surgery
Compensatory hyperhidrosis after sympathectomy
Medicine
Diabetes (hyperhidrosis due to neuropathy or hypoglycaemia)
Endocrine diseases:
• Acromegaly
• Pheochromocytoma
• Hyperthyroidism
• Hypogonadism
• Insulinoma
Heart failure
Obesity
Neurology
Central or peripheral lesion
Harlequin syndrome
Horner's syndrome
Compensatory hyperhidrosis
Ross syndrome
Parkinson's
Polyneuropathies
Oncology
Carcinoid
Lymphoma
Orthopaedics
Hyperhidrosis from amputation stump
Psychiatry
Anxiety disorder
Psychotropic drugs
Social phobia

of endocrine disease or the menopause has started. If there are no signs of disease but there is a short anamnesis, a smaller screening is recommended with SR, CRP, blood status, liver and thyroid tests, IGF 1 (acromegaly), metanephrines in plasma (pheochromocytoma) and a lung X-ray. If there are symptoms other than sweating in the anamnesis, additional and more targeted examinations take place. In men, low levels of testosterone can lead to general hyperhidrosis but other symptoms such as loss of libido or erection problems can provide diagnostic guidance.

Obesity is rarely the reason for general hyperhidrosis but can be a deteriorative factor. Several medicines can cause increased sweating as a side effect and SSRIs and opioids are the most commonly reported. Of the opioids, methadone is particularly problematic.

Polyneuropathies where the sudomotor nerves are damaged cause less sweating from the extremities and compensatory sweating from the head and torso. This compensatory sweating can be misinterpreted as primary general hyperhidrosis. The polyneuropathy can be known as it is in a diabetic but can also be discovered during an examination and must then be investigated and treated if possible.

Sweating during the day and at night is a sub symptom of the menopause in many women. While other climacteric symptoms disappear, the sweating continues in a significant share of women. As many as 10% of all women suffer from postmenopausal hyperhidrosis 10 years after the menopause. Sweating with anxiety disorder or social phobia can be explained by sudden and powerful activation of the sympathetic nerves. Twenty years of experience of hyperhidrosis patients shows that hyperhidrosis is rarely primarily due to anxiety disorder. On the other hand hyperhidrosis can lead to anxiety, palpitations and escape behavior. The psychiatric disorder for patients with DSM IV-diagnosed generalized anxiety and axillary hyperhidrosis improved following the elimination of the sweat from their armpits with botulinum toxin. It means that patients with anxiety symptoms and hyperhidrosis should of course receive early help with their somatic disorder.

4. Secondary regional or asymmetrical hyperhidrosis

Regional or asymmetrical sweating is a strong indication of secondary hyperhidrosis and an underlying diagnosis should be sought. Loss of sweating from one area of the body can cause increased sweating from another. This "compensatory" hyperhidrosis was highlighted in the 1990s when the more common sympathectomise for hyperhidrosis were debated. The hands of the patients who underwent the operation certainly became dry but the majority instead sweated below the nipples. Many of these iatrogenically damaged patients can now receive help with botulinum toxin, sometimes combined with anticholinergics. Horner's syndrome with loss of sweating from one side of the face can cause compensatory hyperhidrosis from the contralateral side. With regional hyperhidrosis, it is important to examine the contralateral side with regard to deficit symptoms. Unusual asymmetrical sweating is seen with idiopathic unilateral focal hyperhidrosis. Attacks of profuse sweating occur from a delimited area, usually on the forehead or the upper side of one wrist. The patient perceives this as very troublesome.

Clinical presentation

Onset of primary hyperhidrosis is common in childhood or adolescence and it can persist throughout life. Patients will have focal sweating most often in palms, soles and axillae and less often in scalp, face and groin. Environmental humidity and psychological stress can worsen primary hyperhidrosis. It is not considered as psychological disorder. Patients note excessive sweating in affected areas. The most commonly affected sites are axillae, palms and soles, rarely other sites of the body are affected. Palmar hyperhidrosis can cause problems and fear of shaking hands, soiling of papers. Patients may have difficulty in performing tasks that require dry grip, these may result in social problems hyperhidrosis beginning later in life and generalized sweating and persisting during sleep should prompt a search for secondary causes.

Gustatory sweating

Sweating around the nose, lips and forehead, commonly occurs after consumption of hot, spicy food. It can also be due to sympathetic nerve damage by diabetic neuropathy.

Chromhidrosis

Coloured sweat is an uncommon idiopathic non-hyperhidrotic condition. Apocrine glands secrete coloured sweat- yellow, blue, green or black. This can occur over face, axilla, groin or areola. The pigment is due to lipofuscin granules.

Night sweats

It is defined as drenching sweats that require changing bed cloths at night. Benign increased sweat due to overheated room or too many bed coverings needs to be ruled out. Common causes could be malignancies like lymphoma, solid tumors like prostatic cancer, renal cell carcinoma and insulinoma. Common infections like tuberculosis, HIV, brucellosis and sub-acute bacterial endocarditis are other possibilities in those with predominant night sweats.

Consensus criteria for diagnosing primary hyperhidrosis

Focal, visible, excessive sweating of at least six months duration without apparent cause with at least any two of the six characteristics:

1. Bilateral and relatively symmetrical
2. Impairs daily activities
3. At least one episode a week
4. Age of onset less than 25 years
5. Positive family history
6. Cessation of focal sweating during sleep

Physical examination

Focal or generalized sweating is usually clearly notable. For direct visualization of the affected areas by hyperhidrosis, the iodine starch test may be used. This test requires spraying of the affected area with a mixture of 0.5-1 g of iodine crystals and 500 g of soluble starch. Areas that produce sweat turn black. Evidence of any diseases that can produce hyperhidrosis such as thyrotoxicosis, malignancy, pheochromocytoma and tuberculosis must be looked for. Hyperhidrosis is associated with increased incidence of other cutaneous disorders, common ones being dermatophytosis, pitted keratolysis and viral warts. Atopic eczematous dermatitis may have frequent association with hyperhidrosis.

Investigations

There is no standard definition for excessive sweating. Normal sweating can be considered as less than 1 ml/m^2/min to the production of less than 100 mg of sweat in one axilla within 5 min, or less than 50 mg within 1 min.

Following investigations are done based on clinical clue:

1. Thyroid function tests- to confirm hyperthyroidism
2. Blood glucose levels- to confirm hypoglycemic episodes and diagnosis of diabetes mellitus (as diabetic dysautonomia can contribute to gustatory sweating)
3. Urinary metanephrine and vanillyl mandelic acid- to confirm pheochromocytoma
4. Uric acid levels- to detect gout
5. Tests to screen for infections such as tuberculosis, HIV, endocarditis and brucellosis
6. Chest radiography and ultra sound abdomen to evaluate tuberculosis or neoplasms

Treatment

Depending on the localization of hyperhidrosis, there are varying treatment options. The treatment should be individually adapted with respect to contraindications and theraphy failure. The availability of drugs can differ between countries due to lack of approval from the authorities. Various treatment options are described below and Table-2 displays recommendations based on the clinical guidelines from International Hyperhidrosis Society.

Topical treatment

Topical treatment e.g., aluminum chloride (AlCl), should be tried on all localized hyperhidrosis. Application may however be difficult on the scalp because of hairy skin. AlCl reacts with proteins in the sweat duct and forms a mechanical obstacle which prevents sweating. Solution is applied on completely dry skin once a week or more, preferably when going to bed and leave to work overnight. Some patients have problems using the solution due to skin irritation.

Botulinum toxin type A (BTX A)

Intradermal, local injections with BTX A constitutes a very effective treatment. Major, randomized multicenter studies have taken place concerning the indication of axillary hyperhidrosis and several studies have also shown a good effect for other locations. BTX A causes local chemical denervation by preventing the release of acetylcholine. The duration of the effect differs between individuals and the treatment usually needs to be repeated 1-4 times a year. Most commonly reported side effects are dryness of the skin and slight muscular weakness. Any side effects are usually local, transient and mild.

Botulinum toxin type B (BTX B)

The mechanism of action for BTX B is similar to that for BTX A but the effect on a motor neurons to muscles seems to be much less because 50-100 times higher doses are needed to treat cervical dystonia. However, new research shows that BTX B can be diluted to a low concentration to a greater extent and that the sweat inhibiting effect of 1 U BTX A corresponds to 1-2 U BTX B. These research results have generated possibilities of administering treatment to large areas or areas where there is a great risk of local muscular side effects, as in the palms or the face.

Patients with craniofacial hyperhidrosis, general hyperhidrosis or postmenopausal hyperhidrosis where oestrogen by mouth is unsuitable or ineffectual can receive treatment with relatively small doses of BTX B. The hands of children, musicians or others where local muscular weakness is not acceptable can also be treated with BTX B with a small risk of side effects. On group basis the duration of effect might be a bit shorter after treatment with BTX B compared with BTX A, but not for all individuals.

Iontophoresis

Iontophoresis may be an alternative in the treatment of palmar/plantar hyperhidrosis. Ions are conveyed to the sweat ducts using a weak current and cause an obstacle in the outermost section of the sweat duct. Initially, the treatment is administered 3-4 times per week for 20-30 minutes on each occasion. The interval is then lengthened and individually adapted with 1-4 treatments usually required per month. The treatment is time consuming for the patient.

Microwave thermolysis

In recent years, a non-invasive method which causes local destruction of sweat glands through microwaves has been developed with satisfactory and permanent results. Other invasive or minimally invasive methods are available for isolated axillary hyperhidrosis if is contraindicated.

Systemic medications

Different types of oral anticholinergic medications can work well for multifocal hyperhidrosis and alongside BTX, lead to additive effects. Monotherapy generally has an inadequate effect. Due to the

Table-2: Treatment recommendations based on the clinical guidelines from International Hyperhidrosis Society

Option	Axillary hyperhidrosis	Palmar hyperhidrosis	Plantar hyperhidrosis	Craniofacial hyperhidrosis	Gustatory hyperhidrosis	Torso (compensatory hyperhidrosis)
1st	Topical treatment (e.g., AlCl*)	Topical treatment (e.g., AlCl*)/ Iontophoresis	Topical treatment (e.g., AlCl*)/ Iontophoresis	Topical treatment (e.g., AlCl*)†	Topical treatment (e.g., AlCl*)/ Botulinum toxin	Botulinum toxin
2nd	Botulinum toxin/ microwave thermolysis	Botulinum toxin	Botulinum toxin	Botulinum toxin	Botulinum toxin/ Topical treatment (e.g., AlCl*)	Systemic medications (e.g., anticholinergics)
3rd	Local sweat gland ablation	Systemic medications (e.g., anticholinergics)	Systemic medications (e.g., anticholinergics)	Systemic medications (e.g., anticholinergics)	Systemic medications (e.g., anticholinergics)	
4th	Systemic medications (e.g., anticholinergics)	(ETS)**		(ETS)**		
5th	(ETS)**					

† Application on the scalp may be difficult because of hairy skin.

* AlCl (Aluminum chloride)

** In countries where Endoscopic Thoracic Sympathectomy (ETS) still is performed, patients must be carefully selected and educated to fully understand the possibility of limited efficacy and the risks of complications including, but not limited to, compensatory sweating.

systemic impact, the risk of side effects is greater compared with local treatment. Dry mouth is very commonly reported, furthermore, urinary retention, dry eyes and accommodation disturbance occur. Indications of an increased risk of dementia where there is higher cumulative use of anticholinergic medications has led to a demand for greater awareness of the potential risks of the use of anticholinergics and to reduce their use over time. In small studies, peroral preparations such as calcium channel blockers or carbonic anhydrase inhibitors (direct effect on the sweat glands calcium channels or carbonic anhydrase) and clonidine have proven to have an effect and can be tried.

Endoscopic Thoracic Sympathectomy (ETS)

Owing to the frequency of severe and irreversible side effects, ETS is no longer performed. The side effects profile is unfavorable with acute and chronic side effects. The most common of reported side effects is compensatory sweating (incidence of 80% to 95% has been reported in several studies) and may constitute a lifelong disability, which for many is a significantly greater disorder than that which justified the operation.

In countries where ETS still is performed, patients must be carefully selected and educated to fully understand the possibility of limited efficacy and the risks of complications including, but not limited to, compensatory sweating. This treatment should be the last option.

Complications

Common complications are: psycho-social disturbances, anxiety neurosis and depressive illness. There can be increased incidences of fungal and bacterial infections.

Conclusion

Hyperhidrosis is a widespread disorder which is usually idiopathic but can be secondary to diseases involving several specialties.

Topical and oral agents are probably effective in hyperhidrosis and often are tried as first line remedies. In practice, most adults with axillary hyperhidrosis or palmar hyperhidrosis endure the pain of injections and find the benefit outweighing the discomfort. In teenagers (who constitute a sizeable number of patients with primary hyperhidrosis) however, pain is often not acceptable and the return rate for treatment is low.

The new data with iontophoresis are encouraging and may particularly prove useful for young individuals with this condition. Unfortunately, the magnitude of the response with iontophoresis is still suboptimal and less than that seen with the injection technique (only 30%–35% sweat reduction beyond two weeks). Refinement of the iontophoresis technique may lengthen the duration of response in axillary hyperhidrosis and palmar hyperhidrosis and prove to be especially helpful in young patients.

Examinations show that there is a strong negative impact on the quality of life of patients with hyperhidrosis. With today's treatment methods, individually adapted therapy can thus lead to very good results.

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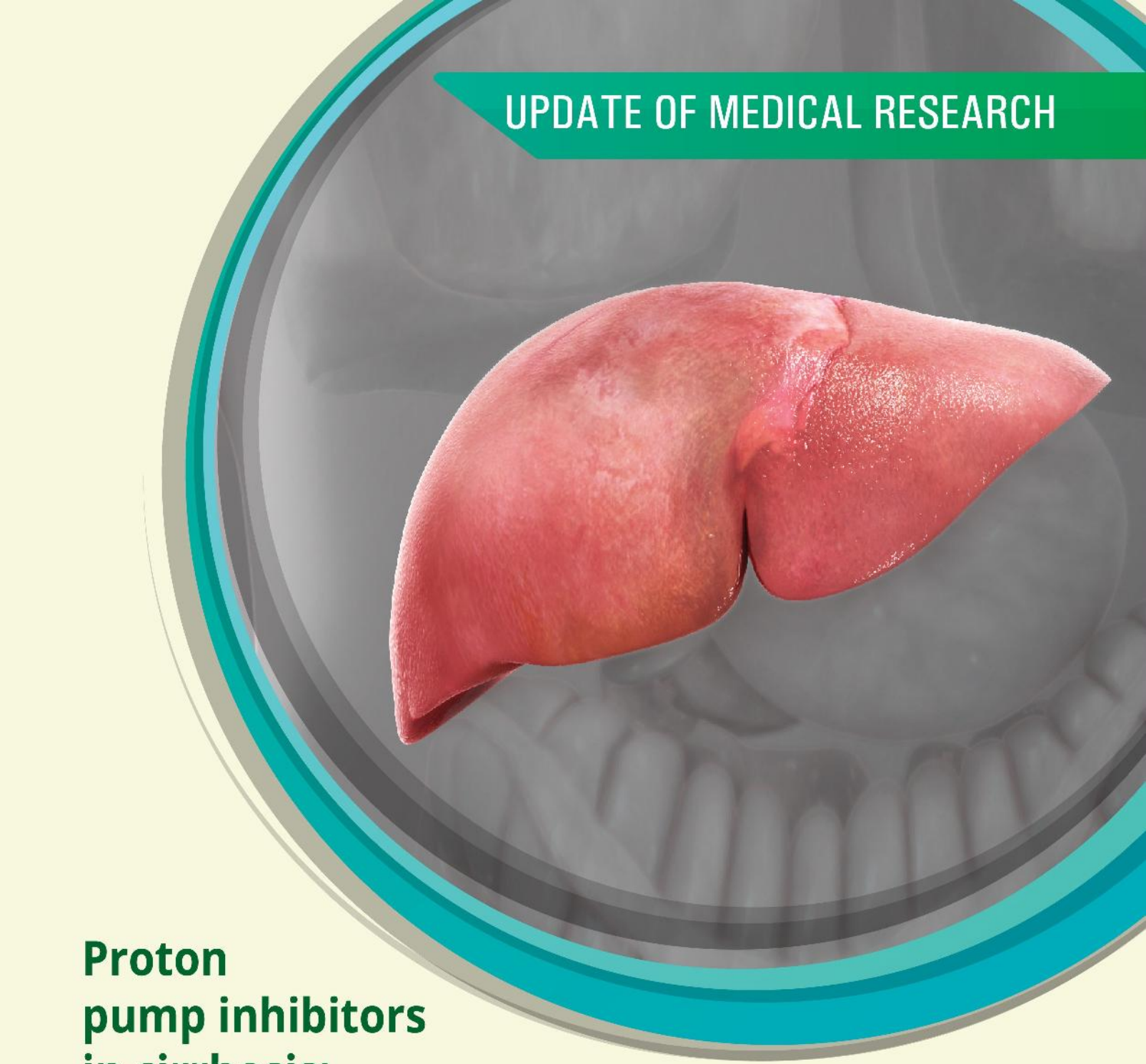

Proton pump inhibitors in cirrhosis: Tradition or evidence based practice?

Introduction

Proton Pump Inhibitors (PPIs) are extensively used in different acid related diseases. Their efficacy in inhibiting acid secretion is well known, and the use of this class of drugs has increased worldwide. They act through inhibition of the H+/K+ ATPase of parietal cells producing the so called "inhibitory complex" and blocking HCl secretion. They are metabolized in the liver by the CYP450 cytochrome. PPI are also often used in patients with liver cirrhosis sometimes in the absence of a specific acid related disease, with the aim of preventing peptic complications in patients with variceal or hypertensive gastropathic bleeding receiving multidrug treatment.

Gastric acid secretion and liver cirrhosis

The role of gastric secretion in cirrhosis is controversial. Some studies report reduced acid production while others reported normal production. The evaluation of 24 hour acidity by gastric ph-metry in 49 patients with cirrhosis showed a marked hypoacidity in patients with cirrhosis compared to controls, mainly during the night hours. This may depend on hemodynamic alterations consequent to portal

hypertension and is supported by experimental studies showing reduced gastric acid secretion in animals with portal hypertension. These observations rule out the relevance of gastric acid in the pathogenesis of ulcers in cirrhotics.

Gastrin, the gastric hormone whose secretion is regulated by intragastric pH, and that regulates the production of HCl and pepsin, is partially metabolized by the liver and mainly by the kidneys. Gastrin is elevated in serum of patients with *Helicobacter pylori* infection or atrophic gastritis. Few studies have evaluated gastrin levels in cirrhosis, and their contribution towards understanding the pathophysiology of gastric acid secretion is very limited. The urinary gastrin output in patients with cirrhosis with and without hepato-renal syndrome. Serum gastrin levels were higher in cirrhotics compared to controls; and in cirrhotics with hepato-renal syndrome the difference was greater suggesting that impaired urinary gastrin secretion may contribute to their hypergastrinemia.

Progastrin and gastrin serum levels have been reported to be significantly higher in patients with cirrhosis of any Child-Pugh class compared to controls while there are no differences between controls and patients with chronic hepatitis B or C. Indeed, it is important to note that in this study, the prevalence of *H. pylori* infection in cirrhotic patients was 83% versus 50% in controls. Therefore, it is not clear whether the difference in progastrin and gastrin level was due to reduced liver metabolism, to *H. pylori* infection, or both. In summary, gastrin increase in patients with liver cirrhosis could be related to: (1) impaired hepatic gastrin catabolism; (2) impaired renal function, at least in those with HRS; (3) gastric mucosal alteration due to gastropathy related cirrhosis.

Peptic ulcers and liver cirrhosis

Many authors reported an increased prevalence of peptic ulcers in patients with cirrhosis and it was shown that cirrhotics have an increased risk of developing gastric or duodenal ulcers during an interval of one year compared to non cirrhotics. The prevalence of peptic ulcers ranges between 4.6% and 21% in patients with cirrhosis. However, the pathogenesis of this finding is far from being elucidated and different factors have been proposed in relation to increased ulcer prevalence in patients with cirrhosis. Furthermore the prevalence of duodenal and gastric ulcers in patients with liver cirrhosis increases with disease progression. Several theories have been postulated. It has been demonstrated that the gastric mucosa in rats with portal hypertension is more susceptible to aggressive agents such as bile acids, aspirin and alcohol. Some investigators have attributed to portal hypertension itself the increased risk of peptic ulcer, nevertheless no study has clarified the pathogenesis of peptic ulceration in cirrhosis.

Esophageal disorders and liver cirrhosis

It has been postulated in the past, that gastro-esophageal reflux may contribute to oesophagitis and variceal bleeding in cirrhotic patients, and acid reflux could be exacerbated by the presence of ascites and water retention. More recent papers do not confirm these hypotheses and report a high incidence of gastro-esophageal reflux only in patients with alcoholic cirrhosis, though the presence of reflux did not correlate with disease severity or bleeding episodes. Functional studies showed decreased lower esophageal sphincter function with low amplitude of primary peristalsis and acid clearance in patients with large varices. These phenomenon could also be due to a mechanical effect of the presence of varices. In conclusion, it is unclear whether the presence of cirrhosis itself could predispose to the onset of gastroesophageal reflux. It seems that the presence of varices is related to reflux episodes, although it is not clear whether these might contribute to bleeding from varices. In summary, expert opinion based on evidence of scarce value, advise PPI use in cirrhotic patients undergoing endoscopic treatment for varices, especially when treatment is performed by endoscopic variceal sclerotherapy (EVS), to prevent gastroesophageal reflux which may worsen the procedure related inflammation or ulceration.

PPI safety in cirrhotic patients

All PPIs are metabolized in the liver by cytochrome CYP450; two isoenzymes are involved in PPI metabolism (CYP2C19 and CYP3A4). CYP2C19 is the main metabolic pathway while CYP3A4 is activated only when the other enzyme is saturated. Nevertheless, the affinity of each isoenzyme for different PPIs is different and rabeprazole is metabolized mainly by a non enzymatic pathway. There are two CYP2C19 phenotypes: extensive and poor metabolisers. The poor phenotype is present in 2%-6% of Caucasians and 20% of the Asian population. Poor metabolisers have higher plasma levels of PPI, which could lead to higher efficacy but also to potential adverse events. The effects of these genotypes varies according to the specific PPI used and in general is greater when using omeprazole decreasing progressively to lansoprazole, esomeprazole, pantoprazole and finally rabeprazole.

PPI are metabolized in the liver and secreted by the kidney. Renal impairment has minimal effect on PPI clearance, and therefore there is no need to reduce PPI dosage in patients with renal diseases. This is not the case for liver impairment in which the Area under the Curve (AUC) of PPIs increases and their half-life becomes 4 hour to 8 hour greater with increasing risk of accumulation. This effect was also seen with rabeprazole although a dose reduction seems to be unnecessary with a 20 mg, once daily dose in patients with mild to moderate liver cirrhosis. When using other PPIs or rabeprazole at 40 mg/daily dose, dose reduction in patients with cirrhosis is advisable.

Reference: W. J. Gastr., May 21, 2008, Vol. 14(19):2980-2985

WORLD DIABETES DAY

14th November 2019

The Family and Diabetes

On December 20, 2006, the United Nations (UN) passed a resolution to designate November 14 as World Diabetes Day. The occasion aimed to raise awareness of diabetes, its prevention and complications and the care that people with the condition need. Governments, non-governmental organizations and private businesses are encouraged to increase awareness of the disease, particularly among the general population and the media. World Diabetes Day was first commemorated on November 14, 2007 and is observed annually.

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