

Osteoarthritis of the knee in the middle-aged recreational athlete

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A painful osteoarthritic knee in a middle-aged recreational athlete is one of the most difficult problems to manage. Initially, all patients should be treated conservatively; however, when exacerbations become frequent as the degenerative changes progress, surgical treatment should be considered. This article outlines the treatment options for this difficult condition.

■ For the purposes of this discussion we will define middle-aged as between 35 and 60 years. There are two major types of osteoarthritis in this age group – post-traumatic and nontraumatic.

Post-traumatic osteoarthritis occurs in patients who have had a previous knee injury as a young adult. The previous injury is commonly a combined ligament and meniscal injury that resulted in surgical removal of one or both menisci. The loss of the cushioning effect of the meniscus commonly results in arthritic changes 10 to 20 years later.

Nontraumatic osteoarthritis occurs in patients who have not had a previous knee injury and in whom the osteoarthritis is strongly genetically determined. Such patients often report a family history of early osteoarthritis.

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Pathophysiology

Although osteoarthritis is the most common form of arthritis, very little is known about its pathological basis. On a cellular level, osteoarthritis may be the result of a failed attempt of chondrocytes to repair the damaged cartilage, as well as an increased water content and altered proteoglycan and collagen content of the affected cartilage. The changes that occur in osteoarthritis begin with the deterioration and loss of the weight-bearing surface, followed by the development of osteophytes and the breakdown of the osteochondral junction. Finally, the cartilage disintegrates and subchondral microfractures occur, exposing the bony surface.

Clinical features

Symptoms

The predominant symptoms of osteoarthritis of the knee are pain, swelling and a decreased activity level. The pain generally worsens with activity and improves with rest. The pain can be present along the joint

line or it may be felt as a generalised anterior ache. Commonly, reflex inhibition of the quadriceps occurs, resulting in wasting of this muscle. This in turn may exacerbate anterior patellofemoral type pain and may also cause symptoms of giving way due to poor muscular control. Mechanical symptoms associated with a large effusion and pinpoint joint line tenderness, such as locking, catching and giving way, may be superimposed if an unstable meniscal tear or a loose chondral flap is present.

Signs

The patient with osteoarthritis of the knee commonly has an antalgic gait. Genu varum or valgum may be present, indicating a loss of joint space resulting in deformity. An effusion is often present and is usually large if the patient has an unstable meniscal tear or a loose chondral flap. Knees that have previously been injured may be ligamentously unstable. In this situation it is usually the anterior cruciate ligament that is damaged and this is best illustrated with the Lachman test (anterior translations of the tibia on the femur with the knee at 30° flexion).

The joint should be assessed for quadriceps wastage and palpated for tenderness, osteophytes and cysts. Baker's cysts are commonly felt in the popliteal region, and pseudocysts are usually felt along the joint line and are associated with degenerative meniscal tears. Rotational tests (for example, McMurray's test) should be performed to assess for meniscal

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pathology. An important test is to check for pain and crepitus whilst loading the affected compartment and moving the knee through a range of motion. This will elicit wear on the weight-bearing surface and often allows painful bone-on-bone crepitus to be felt.

X-ray findings

The minimum x-ray requirement for the assessment of osteoarthritis of the knee includes the following views:

- weight-bearing anterior-posterior
- lateral
- intercondylar
- patellar skyline
- weight-bearing posterior-anterior with 30° knee flexion.

This last view, known as the Rosenberg view, is more sensitive for demonstrating joint space narrowing because initially the weight-bearing surface tends to wear at the position of 30 to 40° of knee flexion.

The classical radiographic findings in osteoarthritis include subchondral sclerosis, subchondral cyst formation (secondary to subchondral microfractures), osteophytes and joint space narrowing. Three-foot weight-bearing alignment views are not required in the initial assessment but need to be performed preoperatively by a specialist if an osteotomy is to be performed.

Differential diagnosis

If the patient does not display the typical characteristics of osteoarthritis, other possible diagnoses should be considered. These include spontaneous osteonecrosis of the knee, inflammatory arthritis and crystal deposition diseases. Further studies should then be considered to document the true cause of the arthritis, and specialist rheumatological referral should be arranged if necessary.

Special investigations

Bone scan

A bone scan is helpful if spontaneous osteonecrosis around the knee is suspected. Typically this condition is seen in women nearing the age of 60. Although it is most common in the medial femoral condyle it can also appear in the tibial plateau or on the lateral side of the femur. A bone scan will show focally increased uptake before the radiographs are abnormal.

The cause of spontaneous osteonecrosis is unknown, but vascular ischaemia or microfractures in osteoporotic bone are suspected. Many patients have a benign course followed by resolution of symptoms. Because of this, conservative management is indicated initially. However, if progressive collapse occurs, surgical treatment in the form of osteotomy or arthroplasty may have to be considered.

Aspiration of joint fluid

If the history is not typical of osteoarthritis, aspiration of joint fluid is worthwhile. In osteoarthritis, joint fluid analysis usually reveals a straw-coloured aspirate with normal viscosity and a low white blood cell count ($0.2 \times 10^9/L$ with 25% polymorphonuclear cells). Glucose and protein levels are equal to those found in serum.

In an inflammatory arthritis, a yellow-green coloured aspirate with low viscosity is found and the white blood cell count is elevated (2 to $75 \times 10^9/L$ per mL with 50% polymorphonuclear cells). The glucose level is moderately decreased (1.39 mmol/L lower than the serum level).

An infected knee produces an opaque fluid with a white cell count greater than $80 \times 10^9/L$ and 75% polymorphonuclear cells. The glucose level is low (more than 1.39 mmol/L less than serum values), and Gram stain and culture are often positive.

In crystal deposition disease, joint fluid analysis shows an inflammatory aspirate with crystals evident. In gout the crystals are thin, tapered, intracellular and strongly negatively birefringent (yellow). In chondrocalcinosis (pseudogout) the crystals are rhomboid-shaped rods that are weakly positively birefringent (purple).

MRI scan

MRI scanning has very little to offer in the work up of an osteoarthritic knee. The results can be misleading since 50% of the asymptomatic normal population aged 40 will show changes in their menisci on MRI. Clinical and radiological investigations are far more accurate and less expensive.

Management

Initially, all patients should be treated conservatively. The reason for this is that degenerative knees have a natural history of acute exacerbation which settles over several weeks, followed by remission. Ultimately, the exacerbations become more frequent as the degenerative changes progress, and when this happens surgical treatment should be considered.

Conservative treatment

Conservative treatment consists of a four-week course of analgesic or nonsteroidal anti-inflammatory medications. We prefer the regular dosage of an analgesic, such as paracetamol, because they are safe and effective. Anti-inflammatory agents are used infrequently because they have significant side effects and the inflammatory component of osteoarthritis is usually minimal.

Physiotherapy should be used to strengthen the quadriceps muscle, as this improves the mechanics of the knee joint and thus reduces symptoms. Local therapies for tender areas around

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the joint are also helpful. Weight reduction is important if the patient is obese. The patient should be given advice on avoiding high impact activities and should be encouraged to stay fit by cycling and swimming rather than running.

It is not uncommon for intra-articular corticosteroids to be used in the treatment of osteoarthritis. The aim of using corticosteroids is to control pain by decreasing inflammation. As degenerative osteoarthritis is mostly a biomechanical disorder with minimal inflammation, we generally avoid corticosteroid treatment. There are also known deleterious effects of corticosteroids on chondrocytes and the menisci as well as systemic side effects, such as infection and suppression of the hypopituitary-adrenal axis. Patients awaiting total knee arthroplasty may gain some short term pain relief, but there is no documented long term benefit for the use of corticosteroids in large weight-bearing joints. Certainly in a middle-aged recreational athlete with osteoarthritis of the knee, the risks of corticosteroid use outweigh the benefits.

If conservative measures fail, consideration can be given to surgical treatment.

Arthroscopy

If the history and physical findings suggest the presence of a torn degenerative meniscus or a loose body and minimal wear on the weight-bearing surface, an arthroscopic procedure may be worthwhile. Unfortunately, in middle-aged patients the success of arthroscopic meniscectomy in knees with minimal wear is only approximately 80%. The remaining 20% of patients have subclinical degenerative changes that cause persistent pain and swelling – frequently the symptoms with which the patient first presented. Accordingly, arthroscopy should only

be carried out if conservative measures have failed and the patient has been made clearly aware of the likelihood of success of this type of surgery. It should also be stressed that the middle-aged athlete is unlikely to be able to return to high impact activities, such as jogging and running, following arthroscopy, and that frequently the joint becomes asymptomatic with cessation of these activities without arthroscopy.

Unfortunately, patients with more

advanced degenerative changes do not appear to benefit from arthroscopic procedures. This is particularly true of patients with advanced varus or valgus deformity or associated chondrocalcinosis. It has been fashionable to perform arthroscopic debridement, which removes loose pieces of articular cartilage, shaves rough surfaces and removes tags of torn cartilage. Some 'freshening up' of the exposed subchondral bone (abrasion osteoplasty) may also be carried out. Another

Osteotomy for osteoarthritis in a varus knee

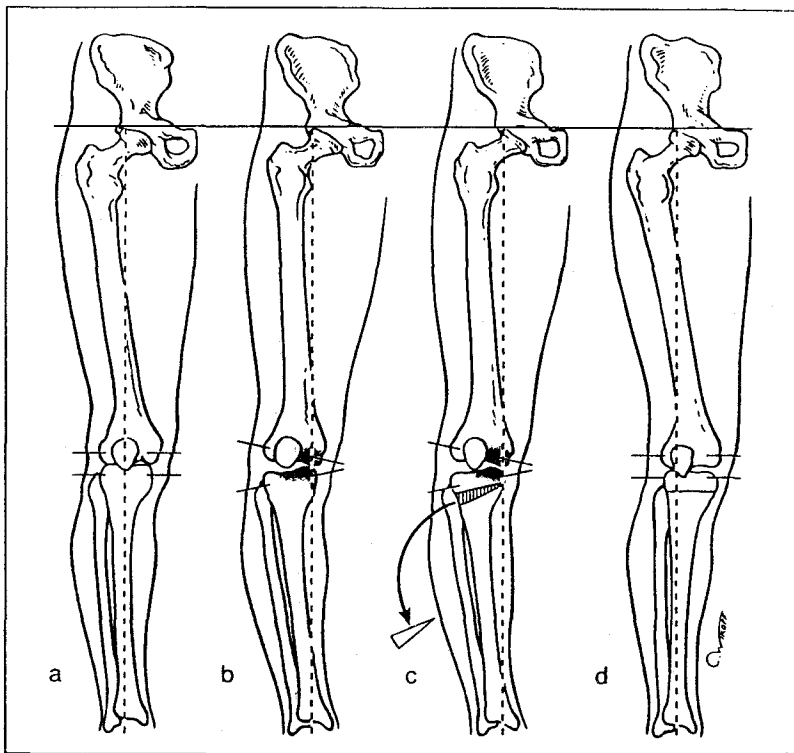


Figure 1. a. In a normally aligned leg the weight-bearing axis (dotted line) runs through the centre of the hip, knee and ankle. b. With a varus deformity, the weight-bearing axis runs through the centre of the hip and ankle, but through the diseased medial side of knee. c. A lateral closing wedge high tibial osteotomy removes a wedge of bone from the lateral side of the proximal tibia. d. Postosteotomy the leg is aligned in an appropriately over-corrected valgus position and the healthy lateral compartment takes the majority of the load. This relieves the pain and gives the medial compartment a chance to heal.

Illustrations for *Modern Medicine* by Chris Wikoff.

The inflammatory component of osteoarthritis is usually minimal; therefore, anti-inflammatory agents are infrequently used.

High tibial osteotomy

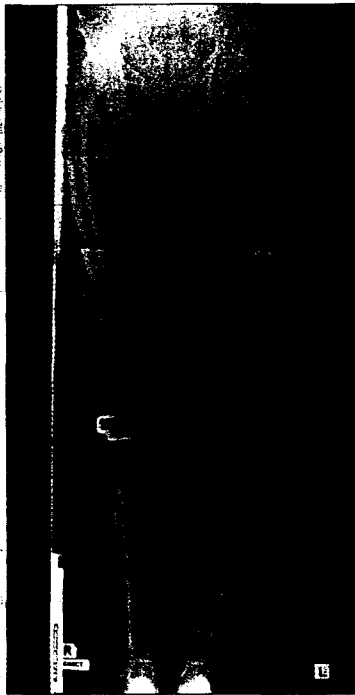


Figure 2. A patient, formerly with a bilateral varus deformity, after recent high tibial osteotomy of the right leg.

commonly performed operation is a lavage, in which loose fragments are washed from the joint using the arthroscope.

These arthroscopic techniques, although commonly performed, rarely afford a successful outcome. Anecdotally, in my experience, approximately one-third of patients improve, one-third of patients remain unchanged, and one-third of patients suffer a deterioration of symptoms necessitating more major surgery. Several studies have been performed which scientifically support this anecdotal evidence.^{1,2} A recent well-designed, double-blind, randomised pilot study has also shown that some or all of the favourable effects of arthroscopy for osteoarthritis of the knee may be due to a placebo

effect.³ In this study, patients who only had arthroscopic porthole puncture wounds continued to have better symptom relief at six months than those who had arthroscopic debridement or lavage.

Osteotomy

Osteotomy is an appropriate surgical option in selected cases of unicompartmental degenerative arthritis with an associated varus or valgus malalignment. The purpose of osteotomy is to transfer the load to an uninvolved tibial-femoral joint surface.

Osteotomy is most commonly performed for medial compartment disease with a varus deformity. In this situation, high tibial osteotomy is performed (Figure 1). The normally aligned leg is in a slightly valgus position, with the weight-bearing axis passing directly through the centre of the hip, knee and ankle (Figure 1a). Once varus deformity occurs, the weight-bearing axis passes through the painful degenerative medial compartment and the healthy lateral compartment carries minimal load (Figure 1b). This becomes a progressive disorder and worsens exponentially – there are minimal symptoms for many years and as symptoms worsen the deterioration accelerates. The reason for this is that the force through the affected compartment is related to the square of the distance of the weight-bearing line from the centre of the knee joint.

A lateral closing wedge high tibial osteotomy removes a lateral wedge from the proximal tibia and places the leg in a slightly over-corrected valgus position, thus unloading the medial compartment. (Figures 1c, d and 2). The healthy lateral compartment takes the majority of the load and gives the medial compartment a chance to heal with the production of new fibrocartilage. The patient will

be in hospital for the first five to seven days after surgery and will be required to wear a straight leg cast for six weeks. The leg should not bear weight for the first four weeks in the cast, so the patient will need to use crutches.

In lateral compartment disease with a valgus deformity a distal femoral osteotomy is performed. A medial wedge of bone is removed from the distal femur, placing the leg in a varus position and thus unloading the lateral compartment.

It should be stressed that these osteotomies are designed to allow patients to walk without discomfort, not to return them to sporting activities. If adequate correction is achieved, the success rate of high tibial osteotomy is 90% at the 12 month mark and 65% at 10 years. Those patients who fail to achieve such long term relief usually obtain at least a few of years of relief and are then eligible for joint replacement.

Osteotomy is strongly recommended in the middle-aged patient with osteoarthritis and deformity. If the patient is nearing the age of 60, it is worth considering continuing with conservative measures for as long as possible so that when complete deterioration of the joint has occurred, joint replacement may be performed.

Arthroplasty

Unfortunately, joint replacement surgery is not a realistic option in middle-aged patients with osteoarthritis. Even with today's technology there is no currently available implant that will not wear or fail prematurely. Revision procedures are likely to be required, carrying increased risk and limitations for the patient. Also, joint replacement does not allow the patient to return to running and jumping sporting activity, which is often the goal of treatment. We prefer to wait

until the patient nears the age of 60 and has exhausted all other treatment options such that they are willing to accept the risks of undergoing major surgery.

Arthrodesis

Arthrodesis is indicated only in young patients with severe, painful articular cartilage damage throughout the joint which is not amenable to other surgical options. Other indications for arthrodesis include uncontrollable septic arthritis and complete joint destruction, neuropathic joint disease and failed total knee arthroplasty.

Experimental treatments

Experimental treatments include osteochondral allografts, as well as implantation of growth factors, cartilage cells and artificial matrices in an attempt to stimulate restoration of the articular surface. None of these approaches has led to successful regeneration of tissue that duplicates the structured composition, mechanical properties or durability of articular cartilage.

Conclusion

Osteoarthritis in the middle-aged recreational athlete is one of the most difficult problems to treat. Once all conservative measures have failed, the surgeon relies primarily on the success of osteotomy to afford pain relief for these patients. Unfortunately arthroscopy has only a limited role in the treatment of osteoarthritis, and joint replacement arthroplasty is not a reasonable option until patients near the age of 60. Hopefully, further advances in orthopaedic technology will give the treating physician more options for managing these patients. ■

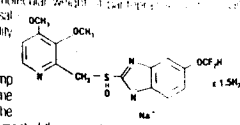
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Further reading

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FULL PRODUCT INFORMATION SOMAC®

TRADE NAME: Somac **NAME OF THE DRUG:** Pantoprazole sodium sesquihydrate **DESCRIPTION:** Pantoprazole is a proton pump inhibitor. Each 40 mg coated tablet contains 45 mg of pantoprazole sodium sesquihydrate. **Chemical Name:** 5-(diethylamino)-2-methoxy-3,4-dimethoxy-2-pyridinyl-methyl-sulfanyl-1H-benzimidazole sesquihydrate. The molecular weight is 459.5. **Structure of pantoprazole sodium sesquihydrate:** 

PHARMACOLOGY:- Pharmacodynamics Pantoprazole is a proton pump inhibitor. It inhibits specifically and dose proportionately H⁺/K⁺ ATPase, the enzyme which is responsible for gastric acid secretion in the parietal cells of the stomach. The substance is a substituted benzimidazole which accumulates in the acidic environment of the parietal cells after absorption. There it is converted into the active form, a cyclic sulphenamide which binds to the H⁺/K⁺ ATPase, thus inhibiting the proton pump and causing potent and long-lasting suppression of basal and stimulated gastric acid secretion. As pantoprazole acts distally at receptor level, it can influence gastric acid secretion irrespective of the nature of the stimulus. Acetylcholine, histamine and gastrin. Pantoprazole's selectivity is due to the fact that it only exerts its full effect in a strongly acidic environment (pH < 4) and is therefore mostly inactive at higher pH values. As a result, its complete pharmacological, and thus therapeutic, effect, can only be achieved in the acid secretory parietal cells. By means of a feedback mechanism this effect is diminished at the same rate as acid secretion is inhibited. The minimum effective dose of pantoprazole has not yet been determined and may be 30 mg/day. **Pharmacokinetic** Pantoprazole is rapidly absorbed and the maximal plasma concentration appears after one single 40 mg oral dose. After single or multiple oral doses, the median time to reach maximum serum concentrations was approximately 2.5 h, with a C_{max} of approximately 1.2 µg/mL. Terminal half life is approximately 1 h. Volume of distribution is approximately 0.15 L/kg and clearance is approximately 0.1 L/h/kg. Pharmacokinetics do not vary after single or repeated administration. The plasma kinetics of pantoprazole are linear after both oral and intravenous administration. Studies with pantoprazole in humans reveal no interaction with the cytochrome P450-system of the liver. There was no induction of the P450-system after chronic administration of pantoprazole and no interactions were observed after concomitant administration of pantoprazole with either antipyrine, dazepam, theophylline or digoxin. Concomitant administration of warfarin has no influence on its effect on coagulation factors. Pantoprazole is completely absorbed after oral administration. The absolute bioavailability of the tablet is approximately 77%. Concomitant intake of food had no influence on AUC, maximum serum concentrations and thus bioavailability. The serum protein binding of pantoprazole is approximately 98%. Pantoprazole is rapidly eliminated from serum and is almost exclusively metabolised in the liver. Renal elimination represents the most important route of excretion (approximately 80%) for the metabolites of pantoprazole. It is excreted with the faeces. The main metabolite in both the serum and urine is desmethyl-pantoprazole which is conjugated with the sulphate. The half life of the main metabolite (approximately 1.5 h) is not much longer than that of pantoprazole. In studies in healthy volunteers, 2% of subjects showed a slower elimination of pantoprazole from serum/plasma, with an increase in terminal elimination half life of up to 10 h. Patients with a half-life of greater than 3.5 h and with an apparent clearance of less than 2L/h/m² are considered to be slow metabolisers of pantoprazole. In patients with liver cirrhosis changes in kinetics are not clinically relevant because of good tolerability and once daily administration. The half-life increases to between 7 and 9 h and the AUC values are increased by a factor of 6.8 but the maximum serum concentration increases only slightly by a factor of 1.5. In comparison with healthy subjects, in patients with renal impairment, undergoing dialysis, no dose reduction is required. Although the main metabolite is moderately increased, there is no accumulation. The half-life of pantoprazole is as short as in healthy subjects. Pantoprazole is poorly dialyzable. The slight increase in AUC and C_{max} in elderly volunteers compared with their younger counterparts is also not clinically relevant. **INDICATIONS:-** For symptomatic improvement and healing of gastrointestinal diseases which require reduction in acid secretion, duodenal ulcer treatment up to 4 weeks, gastric ulcer and reflux oesophagitis, stage 2 and 3 treatment up to 8 weeks, gastrointestinal lesions refractory to H₂ blockers, treatment up to a maximum of 12 weeks Zollinger-Ellison Syndrome. Patients whose gastric or duodenal ulceration is not associated with ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation or if recurrence. **CONTRAINDICATIONS:-** Pantoprazole may not be used in cases of known hypersensitivity to any component of its formulation, or in cases of cirrhosis or severe liver disease. **WARNINGS AND PRECAUTIONS:-** In the case of suspected gastric ulcer malignancy of gastric carcinoma should be excluded as treatment could conceal the symptoms, and may delay diagnosis. Gastrointestinal system treatment with pantoprazole causes dose-dependent hypergastrinaemia as a result of inhibition of gastric acid secretion. Gastrin has a trophic effect on the gastric mucosa, and increases in gastric weight have been observed in rats at doses to be dependent upon both dose and duration of treatment. Accompanying histopathological changes in the gastric mucosa were increased height, dilatation of fundic glands, chief cell hyperplasia and/or atrophy and parietal cell hyperplasia or vacuolization/degeneration. Increased density of enterochromaffin-like (ECL) cells was observed after 12 months treatment at dose levels of 5 mg/kg/day in rats and 2.5 mg/kg/day in dogs. All changes were reversible after various recovery periods. Since these gastric effects are a consequence of the pharmacological effect of acid secretion inhibition, no effect doses were not established in instances. Genotoxicity: it was noted that a minute amount of radioactivity was bound to rat hepatic DNA after treatment with 200 mg/kg/day for 14 days. However, no distinct DNA adduct has been detected. Additionally, pantoprazole did not demonstrate any clear genotoxic activity in a number of tests of mutagenicity and clastogenicity in bacterial and mammalian cells. Thus there is no clear evidence of a genotoxic potential. Carcinogenesis: a two year carcinogenicity study in rats showed an increase in development of gastric carcinoma tumours after pantoprazole treatment at doses greater than 0.5 mg/kg/day in females and greater than 5 mg/kg/day in males. The development of gastric tumours is attributed to chronic elevation of serum gastrin levels with associated histopathological changes in the gastrointestinal system. The development of hepatocellular adenomas in rats was increased at doses greater than 5 mg/kg/day in males and females and hepatocellular carcinomas were increased at doses greater than 50 mg/kg/day in males and females. Hepatocellular tumours, which were also observed in female mice at oral doses greater than 25 mg/kg/day, may be associated with pantoprazole-induced increases in hepatic enzyme activity. Treatment with pantoprazole at doses greater than 50 mg/kg/day also increased the development of thyroid follicular cell adenomas in male and female rats. The mechanism behind thyroid tumour development is unknown, but may be secondary to hepatic thyroid hormone enzyme induction resulting in increased levels of the thyrotropic hormone, TSH. Consideration of the possible mechanisms involved in the development of the above drug-related tumour types suggests that it is unlikely that there is any carcinogenic risk in humans at therapeutic dose levels of pantoprazole for short-term treatment. Thyroid tissue changes have been observed in the absence of an increase in thyroxine levels in long term studies (5-12 months) in rats and dogs. The significance of these effects the short term treatment of humans is not known. Ocular toxicity and dermal phototoxicity/sensitivity: Studies have shown that pantoprazole is retained in low levels in the eyes and skin of pigmented rats. It is likely that the retention reflects a reversal association with melanin. Animal studies investigating the potential for phototoxicity/ photosensitivity have not been conducted. **Interactions with other drugs:** No drug interactions have been reported so far. In studies with pantoprazole in humans, interactions were observed after concomitant administration of pantoprazole with either antipyrine, dazepam, theophylline, digoxin. Concomitant administration of warfarin has no influence on its effect on coagulation factors. **Use in Pregnancy (Category B3):** Teratological studies in rats and rabbits gave no evidence of a teratogenic potential for pantoprazole. In rats, dose dependent fetotoxic effects were noted, increased pre- and postnatal deaths (450 mg/kg/day), reduced foetal weight and delay skeletal ossification (150 mg/kg/day), reduced pup growth (15 mg/kg/day). For the latter a no-effect dose was not established. Doses of 450 mg/kg/day were maternotoxic and may have been associated with dystocia and incomplete parturition. Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentrations pantoprazole in the foetus are increased shortly before birth regardless of the route of administration. The significance of the findings in humans is unclear. As there is no information on the safety of the drug during pregnancy in women, pantoprazole should not be used during pregnancy, unless the benefit clearly outweighs the potential risk to the foetus. **Use in Lactation:** A perivascular effect in rats found that treatment with pantoprazole at doses of 10 mg/kg/day or greater decreased pup growth. A trans effect on one of a series of development tests (startle response) was only evident in the 30 mg/kg/day group at an age when male and female offspring showed lower body weights, paralleled with lower brain weight, than the controls. The significance of the findings for humans is unknown, and there is currently no information on the safety of pantoprazole during breast feeding humans. Therefore, pantoprazole should only be used during lactation if the benefits clearly outweigh the risks. **ADVERSE REACTIONS:-** Somac is well tolerated. Most of the adverse events seen with treatment were of mild or moderate intensity. 1) following adverse events classified as possibly or definitely related to therapy, have been reported in clinical trials with an incidence of less than 1%: Dermatological: pruritis, rash. Central and peripheral nervous system: headache, dizziness, dry mouth, increased sweating. Gastrointestinal: diarrhoea, nausea. Biochemical: There were no consistent changes in any laboratory parameter. increase in levels of SGPT however, was seen with an incidence of 0.2%. Other: asthenia. **DOSE AND ADMINISTRATION:** Pantoprazole should not be chewed or crushed but swallowed whole with a little water either before or during breakfast. **Duodenal Ulcer:** Pantoprazole 40 mg (1 tablet) should be given once a day. In most patients freedom from symptoms is achieved rapidly and healing generally occurs within 2 weeks. If a 2 week period of treatment is not sufficient, healing will be achieved in almost all cases within a further 2 weeks. **Gastric Ulcer:** Pantoprazole 40 mg (1 tablet) should be given once a day. In most patients freedom from symptoms is achieved rapidly and healing usually takes 4 weeks. If a 4 week period of treatment is not sufficient, healing will usually be achieved in a further 4 weeks. **Reflux Oesophagitis (Stage 2 and 3):** Pantoprazole 40 mg (1 tablet) should be given once a day, in most patients freedom from symptoms is achieved rapidly and healing usually takes 4 weeks. If a 4 week period of treatment is not sufficient, the dosage may be increased up to 80 mg of pantoprazole a day. Healing will usually be achieved within a further 4 weeks. **Lesions Refractory to H₂ Receptor Antagonists:** Pantoprazole 40 mg (1 tablet) should be given once a day. In most patients freedom from symptoms is achieved rapidly and healing usually takes 4 weeks. If a 4 week period of treatment is not sufficient, healing is achieved in the majority of patients or a further 4 weeks in a small group of patients. It may be beneficial in extending pantoprazole therapy to a total of 12 weeks. **Zollinger-Ellison Syndrome:** The dosages should be individually adjusted so that the acid output remains below 10 mmol/L. No fixed period of time is proposed for treatment. **Zollinger-Ellison syndrome Use in children:** There are no data currently available on the use of pantoprazole in children. **Use in the elderly:** The usual daily dose of 40 mg is given. **Impaired Renal Function:** The usual daily dose of 40 mg is given. **Impaired Hepatic Function:** Pantoprazole is contraindicated in patients with cirrhosis or severe liver disease. **Contraindications:** With milder forms of liver disease, the minimum effective dose has not been determined and the initial dose should be reduced. **OVERDOSAGE:-** There are no known symptoms of overdosage in humans, in individual cases 240 mg were administered i.v. or p.o. and were well tolerated. Normal intoxication procedures apply. **STORAGE:-** Store below 25°C. **PRESENTATION:-** 40 mg tablets in PE bottles of 28s. The tablets are marked with the letter P on one side and the figure 40 on the reverse. **POISON SCHEDULES:-S4. Lastest amendment 5th October 1995. 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