Description: Problem list info for PCPs: hemangioma treatment recommendations for timolol and propranolol

INFANTILE HEMANGIOMAS--TIMOLOL/PROPRANOLOL TREATMENT RECOMMENDATIONS

Timolol maleate treatment protocol:
0.5% ophthalmic GEL FORMING SOLN, 15 ml bottle
(not on formulary, so you need to order it as a "special exception")
(approx. 15 ggt per ml, 225 ggt per bottle)
Sig: apply 3-6 drops as needed to cover entire lesion twice daily, massage into lesion with fingertip, then wash hands.
(use until approx. 1 year of age, ideally start 1-6 months of age)
Pediatrics 2013;131;e1739

Propranolol treatment protocol:

In general, for patients on propranolol, see their PCP for a vitals check (no glucose) prior to the dose, then take their first dose in the PCP office and recheck the vitals 1 hour after the dose. Then have them come back in for vital checks 2 other times in a period of 10 days when the medication is tapered up. Start at 0.5 mg/kg/day div twice a day and then slowly increase up to a goal of 2 mg/kg/day div twice a day depending on pt tolerance over a 10-day period. **There are also many special cases in treatment so there is not a completely universal protocol.** For example, patients under 2 mo of age, start it inpatient. For premature infants, divide the dose TID. Provide parents with the propranolol instructions that were published for parental guidance - this provides great detail on feeding practices and also things for parents to monitor for (**see *Pediatrics* 2013;131:128-140 and see Parent Information below**). For any kids with pre-existing heart conditions, they would require more of a workup by cardiology prior to starting. For kids with PHACE syndrome, complete the work up for PHACE first (including the MRI/MRA of their head) prior to starting.

Parent Information on the Use of Propranolol

WHAT IS AN INFANTILE HEMANGIOMA? An infantile hemangioma is a common type of birthmark. Hemangiomas are benign collections of extra blood vessels in the skin and are one of the most common skin problems of the first year of life. They appear most frequently during the first one to four weeks after birth and occur in about 5% of all children. After appearing, hemangiomas grow fast for the first few weeks or months of life. A hemangioma is a tumor, but it is not cancer. It is benign. The cells of a hemangiomas multiply at a rate that is faster than normal. By around 8 months, these cells stop multiplying and most hemangiomas stop growing. They begin to shrink around 1 year and slowly improve over time on their own, and this often takes many years. Larger ones will take longer to go away and have a higher chance of scarring. Each hemangioma is unique. Even in the same baby, one hemangioma may not grow and another may become quite large. About one in four hemangiomas will need some form of treatment.

WHEN IS PROPRANOLOL USED TO TREAT A HEMANGIOMA? A small number of hemangiomas require treatment for complications caused by the growth of the hemangioma. Sometimes treatment is needed if the hemangioma is growing too large on the eye, lip, and nose or in the airway. Treatment is also needed if there is a real risk of permanent scarring. Sometimes propranolol is used to help with healing when skin breakdown occurs on the hemangioma. During the first couple of months of life when a hemangioma is growing rapidly, it can be difficult to determine how big it will become, so your child may need to be seen in the clinic often; as babies get older the office visits are usually less frequent. WHAT IS PROPRANOLOL? Propranolol is a medicine that has been used for many years to treat high blood pressure and an irregular heart rate. Propranolol is also used to treat migraine headaches. Recently, propranolol has been shown to shrink hemangiomas in some infants. Propranolol is approved by the FDA, but not for treating hemangiomas in children. In fact, there is no medicine approved by the FDA for the treatment of infantile hemangiomas.

WHAT ARE THE POSSIBLE RISKS OR SIDE EFFECTS OF PROPRANOLOL? Your doctor will review potential risks and side effects of propranolol with you. Allergic Reaction Your doctor will review potential risks and side effects of propranolol with you. As with any medicine, people can be allergic to propranolol, though this is very rare. Mild allergic reactions can include itching, hives or swelling of the face or hands. More severe allergic reactions include swelling or tingling of the mouth or throat, chest tightness or trouble breathing. You should stop your child's medicine and contact us if you suspect an allergic reaction. Slow Heart Rate Propranolol can make the heart rate slower, but most of the time the heart rate in infants taking propranolol for hemangiomas is still in a normal range. In some cases (if you agree) you may be taught how to take your child's heart rate and how many beats per minute is "normal" for your child's age group. Low Blood Sugar Propranolol can lead to low blood sugar. Low blood sugar can cause drowsiness or rarely seizures. Early signs of low blood sugar may include coldness, shakiness, and sweating. Low blood sugar with propranolol is more likely to occur when your child is not eating normal amounts or has gone for several hours without eating. To help prevent this, always give propranolol during or right after your child has eaten. Other instructions to prevent low blood sugar are listed below under "Important information when giving your infant propranolol". Breathing Problems or Wheezing Propranolol can worsen asthma or wheezing. Wheezing is frequently associated with colds or flu-like illnesses. Sometimes your child will be treated for wheezing with an inhaled medicine (one that is breathed in). If your child is wheezing, immediately contact your doctor. Propranolol may be held during these types of illnesses. Change in Sleep Pattern Propranolol can affect some children's mood or sleep pattern. These effects are usually noticed when your child first begins taking propranolol and may include difficulty getting to sleep or sleeping more than normal. Less often, night terrors (bad nightmares) have been reported. If you notice them and they are mild in your judgment, see if they decrease once your child has been taking propranolol for longer than a few weeks. Sometime the nightmares can be reduced by giving the last dose of propranolol before the evening feeding. If these side effects persist or are more than mild, report them to your doctor. Other Possible Side Effects Propranolol can much more rarely cause other side effects. If your child is having a new

problem or change in behavior, contact your pediatrician or the doctor prescribing the propranolol to see if it might be related.

WHAT CAN YOU DO TO REDUCE THE CHANCES OF A SIDE EFFECT DURING TREATMENT WITH PROPRANOLOL? If used properly, propranolol is a safe and effective medication for treatment of infantile hemangiomas. The following steps will help you use the drug safely.

- Propranolol's side effects can increase as the dose is increased. Propranolol will be prescribed in a liquid form and should be measured very carefully. It is very important to give the correct amount at the correct time. Determine who/which caregiver will give the baby the medication and at what time of the day. Give every dose of propranolol with a feeding (breast milk, formula, or solids), but do not mix in with food or milk.

- Always use a syringe to measure the medicine. Your doctor or pharmacist should provide you with the proper size syringe.

- Measure each dose of medicine carefully. It is best if the same person always gives the propranolol to avoid accidentally giving too much medicine. If this is not possible, measure the amount of propranolol in the syringes you will need for the entire day and give a prefilled syringe to the person that will be giving the dose.

- Doses should always be at least 6 hours apart.

- If you should miss a dose, never try to make up for missed doses by doubling the dose or giving more propranolol. Simply wait for the next time the dose is due and give it then.

- If your child spits up a dose or if you are uncertain whether they got all the medicine do not give another dose, just wait until the next scheduled dose.

- Feed your child frequently. Infants less than 6 months old should not go longer than 6 hours without feeding. Infants over 6 months old should not go longer than 8 hours without feeding. You may have to wake your baby during the night to feed them if they sleep longer than this.

- Have Pedialyte, or a similar drink, available at home. Give your child Pedialyte if they refuse to eat while on propranolol. This type of liquid is designed to promote quick fluid absorption while a child is sick and contains sugars and certain salts which are helpful during an illness.

- If your child is sick and will only drink small amounts, stop giving propranolol and contact your child's doctor. It is usually okay to stop the propranolol for a few days to give your child's body a chance to build up stores of sugar again after an illness.

- If your child needs to stop eating for a test or procedure (surgery, MRI scan or other procedure) be sure to let the doctors know that your child is on propranolol. It is possible that the propranolol will need to be stopped during procedure-related fasting (period of not eating).

- Check all drugs that your child is taking with your child's doctor or pharmacist. Propranolol may interact with some other drugs. This includes medicines that are over the counter, herbal and Prescription.

INITIATING PROPRANOLOL THERAPY

We usually start at approximately 0.5-1 mg/kg/day divided twice a day and then slowly increase up to a goal of 2 mg/kg/day, if need be, divided twice a day depending on patient tolerance over a 10-day period. The clinic will obtain baseline vital signs, Heart Rate, Blood Pressure and Respiratory Rate before first dose, and then 1 -2 hours after. Pediatric clinic will do the same before/after each incremental step. Your child's pediatrician will be notified of these results. We may need to hold on increase or contact one of your child's specialists if vital signs are out of range. (newborn <1 mo, HR <70/min; infant 1mo-1 year, HR <80/min; children >1yr HR<70/min)

There are also many special cases in treatment, so there is not a completely universal protocol for treatment with propranolol. For example, patients under 2 mo of age, we generally would consider starting the medication as an inpatient. For premature infants, we may divide the dose into three doses per day. For any infant with pre-existing heart conditions, they require a more thorough workup by Pediatric Cardiology prior to starting treatment. For infants with suspected PHACE syndrome, we typically want to complete the work up for PHACE first (including the MRI/MRA of their head) prior to starting propranolol. (See below)

We frequently need to readjust dose periodically as the child's weight increases.

Treatment may be reinitiated if hemangiomas recur after stopping propranolol.

WHAT SHOULD YOU DO IF YOU NOTICE ANY SIDE EFFECTS THAT YOU THINK COULD BE CAUSED BY PROPRANOLOL? if your child should develop trouble breathing, is unresponsive, or has a seizure. If you think your baby may have low blood sugar, give him/her Pedialyte or other source of sugar. However, do not give anything to your baby by mouth if he/she is unresponsive. Contact/See your child’s doctor right away if you notice any of these side effects: - Allergic reaction: Itching or hives, swelling in the face or hands, swelling or tingling in the mouth or throat, chest tightness. - Trouble awakening or losing consciousness. - Cold sweats and/or bluish-colored skin. - Slow, fast, or uneven heartbeat. - Unusual tiredness or weakness. If you notice these less serious side effects, contact your child’s doctor to discuss: - Constipation, diarrhea, nausea or vomiting, or upset stomach. - Mood change. - Skin rash. - Trouble sleeping.

Formulations:

Liquid -- 20 mg/5 mL

Suspension -- 2 mg/mL

Hemangeol -- 4.28 mg/mL

PHACE(S) SYNDROME

Infants with large (>5 cm in diameter), segmental hemangiomas, particularly when located on the face, scalp, or posterior head/neck, are at risk for PHACE syndrome

P Posterior fossa brain malformations, most commonly the Dandy-Walker variant

H Hemangiomas, particularly large, segmental facial lesions

A Arterial anomalies

C Cardiac anomalies and coarctation of the aorta

E Eye abnormalities and endocrine abnormalities

S* Sternal cleft, supraumbilical raphe, or both

<u>Propranolol Treatment Guidelines:</u>

Advance in intervals of 4-6 days (for example, start with 0.5 mg/kg/d on Monday, then increase to 1 on Thursday then increase to 2 the next Monday).

For patients aged 6-8 weeks, use 1 week interval due to less reserves of hepatic glycogen.

For patients <6wks old, start as inpatient.

For patients 6-8wks old, start at 0.5 mg/kg/d divided TID, consider starting inpatient.

For patients >8wks old, OK to start outpatient with 1 mg/kg/d divided BID or TID.

Check blood pressure 1-2h after dose when starting and increasing.

Instruct parents to give dose 10 minutes (not more) after feeding.

Advance to 3 mg/kg/d for poor response, ulceration, or dangerous location.

Generally, plan to start weaning between age 10 and 12 months.

Hold dosage for significant emesis.

Hypoglycemia treatment - lollipop + go to ER/call 911, whichever is fastest.

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