湍泰低™ 注射液 5公絲/公撮

衛署藥製字第032350號 G-1700

(拉貝他樂)

【成分】
湍泰低注射液每安瓿5 ml含25 mg labetalol hydrochloride,為透明無色水溶液。Labetalol hydrochloride之化學名為2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenyl-propylamino) ethyl] benzamide hydrochloride 。

【適應症】
高血壓。

【用途】
湍泰低注射液適用於：緊急迅速控制嚴重高血壓，包括嚴重妊娠高血壓；需要降低血壓的麻醉術；以及伴隨急性心肌梗塞的偶發性高血壓。

【作用方式】
湍泰低注射液的降血壓作用係藉由阻滯周圍小動脈中的腎上腺α接受體以減少周邊血管阻力，而湍泰低注射液本身也同時具有β-阻斷作用，可保護心臟免於受到因周圍血管舒張所引起的反射交感神經傳動的影響。使用湍泰低注射液後其心輸出量在休息狀態或適度運動之後並無明顯的減少，雖然收縮壓在運動當中會升高但舒張壓的相對變化則依然正常。而所有此類作用應係有利於高血壓患者。

【用法用量】
本藥限由醫師使用。
湍泰低注射液係專供住院病人靜脈注射使用。注射本劑時患者應採仰臥或側左之姿勢。靜脈注射湍泰低注射液後三小時內患者應避免呈直立姿勢以免可能造成過度的姿勢性低血壓。
成人
使用一次全劑量注射方式(Bolus injection)時：在必須迅速降低血壓時，應給予靜脈注射50 mg之劑量(注射時間至少要一分鐘以上)，且必要時，可每隔5分鐘重複一次直至獲得理想反應為止，惟總劑量不得超過200 mg。通常5分鐘內即可產生最大作用，而作用時間大都約6小時，但也有可能長達18小時。
使用靜脈點滴輸注時：應使用1 mg/ml之湍泰低溶液，亦即，將8安瓿（200 mg）之湍泰低稀釋成共200 ml含Sodium chloride及Dextrose Injection BP（或5% Dextrose Intravenous Infusion BP）之溶液。妊娠高血壓一開始之點滴輸注劑量為每小時20 mg，然後每隔30分鐘給予加倍之劑量直至獲得令人滿意之反應或達到每小時160 mg之劑量為止。必要時，偶爾可給予較此為高之劑量。伴隨急性心肌梗塞的偶發性高血壓一開始之劑量為每小時15 mg，之後依血壓的控制情況逐漸增加至最大劑量為每小時120 mg為止。其他因素引起的高血壓一開始之點滴輸注率為每分鐘約2 mg，直至獲得理想反應後即停止注射。其有效劑量通常為50-200 mg，但必要時亦可給予較高之劑量，尤其是親鉻細胞瘤患者。點滴輸注的速率可由醫師判斷視反應情況加以調整。注射後或點滴輸注當中應監視血壓及心率。大多數患者都會有心率稍微降低的現象，至於嚴重心動徐緩情形則較少發生，可靜脈注射atropine 1-2 mg加以控制。對於呼吸功能應加以觀察，尤其是已知有功能障礙的患者。只要血壓一經全劑量注射或點滴輸注加以適度控制後，應即以湍泰低錠進行維持療法，其初劑量為一天兩次，每次100 mg。湍泰低注射液使用於曾接受其他降血壓藥，包括β阻斷劑之患者，經證實無不良反應。
須降低血壓的麻醉術：應使用標準麻醉劑<例如sodium thiopentone>加以誘導，並以加有halothane抑或不加halothane的nitrous oxide及氧氣維持麻醉過程。湍泰低注射液的建議初劑量為10-20 mg靜脈注射，視患者年齡及情況而定，對halothane有禁忌症的患者通常須較高的初劑量(25-30 mg)。若注射後5分鐘仍未獲滿意的降低作用，則需再增加5-10 mg直至達到理想的血壓為止。由於halothane和湍泰低具有互相加強的作用，因此halothane的濃度不應超過1-1.5%的範圍，以免造成血壓的過度降低。在使用湍泰低注射液後可藉由改變halothane的濃度以及調整床種的傾斜度迅速而簡易地調整血壓。使用湍泰低20-25 mg後的平均降低血壓的作用時間為50分鐘。湍泰低注射液的降血壓作用可隨時以atropine 0.6 mg及停止使用halothane的方式加以中止。為維持手術中呼吸暢通，於必要時，可使用tubocurarine及pancuronium加以輔助及控制。而IPPV則可能會進一步加強湍泰低注射液或halothane的降血壓作用。
孩童
本劑對孩童的安全性及有效性尚未確立。

【禁忌症】
湍泰低注射液禁忌使用於第二或第三期的心臟傳導阻斷、心臟休克以及其他伴有嚴重及持續低血壓或嚴重心動徐緩狀況的患者。當周圍血管收縮顯示低心輸出量時，湍泰低注射劑即禁忌使用於控制伴隨急性心肌梗塞的偶發性高血壓。Labetalol禁忌使用於已知對本劑有過敏反應者。

【警語】
有極少數以labetalol治療而伴隨肝細胞受損的報告。惟肝受損現象係可逆性的，此種現象曾發生於短期及長期治療後。因此，當一有肝功能異常的初症狀時即應做適當的檢查。若檢查結果證實有肝受損現象或患者罹患黃疸，則應停止labetalol治療且不宜再使用。除非別無其他治療方式，否則β阻斷劑，即使是具有明顯心選擇性者，皆不宜使用於氣喘或曾有障礙性呼吸道病史者，必須使用於此類患者時，應事先防範可能導致支氣管痙攣的危險性。萬一使用湍泰低注射液後發生支氣管痙攣的現象，則可給予吸入β2催動劑，例如Salbutamol（所使用之劑量可能須較使用於氣喘的常用量稍大），必要時可給予靜脈注射atropine 1 mg。

【注意事項】
對於心儲量不足者，在謹慎使用湍泰低注射液之前，宜先以強心配醣體及利尿劑加以控制。麻醉施行之前不宜停用湍泰低注射液，惟應於麻醉誘導之前先給予靜脈注射atropine。湍泰低可能會增強halothane的降血壓作用。在麻醉過程中湍泰低可能會掩蓋了突發性出血的生理反應<心動過快及血管收縮>，因此須密切注意失血及維持血體積。Labetalol若與第一類抗心律不整劑或verapamil類的鈣拮抗劑併用時須加以小心注意。

【懷孕及哺乳】
雖然動物試驗未顯示湍泰低有致畸胎作用，但只有在可能產生的益處大於可能引起的危險性時，才可使用於懷孕頭三個月的孕婦。湍泰低可通過胎盤障礙，因此不可忽略了對胎兒及新生兒會有產生α及β腎上腺接受體阻斷的可能性。曾有極少數出生前後及新生兒障礙的報告（症狀包括心動徐緩、低血壓、呼吸抑制、低血糖、低體溫等），有時此類症狀在出生一天或兩天後才會顯現，此時通常須迅速地給予支持療法<例如靜脈注射液體及葡萄糖等>，但由於嚴重的子癇先兆，且尤其持久性地靜脈注射labetalol，因此復原時間會較慢，這可能和早產兒的肝代謝功能不完全有關。雖然也曾有子宮內及新生兒死亡的報告，但可能與其他藥物（如，血管舒張劑、呼吸抑制劑）以及子癇先兆、子宮內成長遲滯和早產等作用有關。以上這些臨床經驗警示不可有不適當的長期高劑量使用labetalol、延遲分娩以及併用hydralazine。湍泰低可從乳汁中排出，但未有任何報告指出對哺乳的嬰兒有不良反應。Labetalol很少會引起可逆的肝臟性及膽汁鬱滯性黃疸，萬一有黃疸現象應即停藥。

【副作用】
湍泰低注射液通常耐受性良好。若在使用湍泰低注射液後三小時內即讓患者成直立狀態則可能會引起顯著的姿勢性低血壓。極少數報告指出有過敏性反應、皮膚疹、搔癢、血管水腫及呼吸困難等現象。少部分會有鼻充血症狀。有極少數報告指出有肝功能測試數據升高、黃疸（包括肝細胞性及膽汁鬱滯性）、肝炎及肝壞死等現象。惟所有反應及症狀通常爲可逆性的，只要停藥即可恢復正常。少數報告指出有心動徐緩及心臟傳導阻斷的現象。

【過量】
過量所引起的反應主要可能爲心血管方面的作用，例如，高度的姿勢敏感性低血壓以及有時或可能發生的心動徐緩。此時應讓患者仰臥同時抬高雙腳。若有心衰竭現象則給予強心配醣體及利尿劑；若引起支氣管痙攣則給予吸入β2催動劑。對於心動徐緩反應則靜脈注射atropine 0.25-3 mg。在改善循環方面若靜脈注射noradrenaline由5-10 mcg (μg)開始，視情況再重覆注射給藥，其效果比isoprenaline理想。或者是將noradrenaline以每分鐘5 mcg (μg)的速率點滴輸注直至獲得理想的結果。若係嚴重過量則靜脈注射glucagon可能較理想，其初期劑量爲5-10 mg配以dextrose或生理食鹽水，再繼之以每小時5 mg之速率做靜脈點滴或至足以維持正常心輸出爲止。可能需要使用經靜脈的整律器。大量地口服過量的labetalol曾發現有尿量減少性腎衰竭的現象。曾有一病例顯示使用dopamine增高血壓可能會加重腎衰竭作用。血液透析法可自循環中除去1%以下的labetalol。

【藥物注意事項】
湍泰低注射液應避光貯存於30°C以下。
與其他藥物之配合性－湍泰低注射液可與下列靜脈點滴輸注液相配合：
5% Dextrose BP, 0.18% Sodium Chloride及4% Dextrose BP, 0.3% Potassium Chloride及5% Dextrose BP, Compound Sodium Lactate BP。未使用之混合液應於配製後24小時即丟棄。湍泰低注射液不可與Sodium Bicarbonate Injection BP 4.2% W/V相配合。

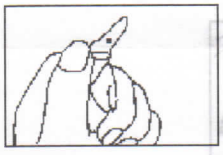
【藥物動力學】
Labetalol的血漿半衰期約4小時，大約有50%的血中labetalol會與蛋白質結合。Labetalol主要係經由與不活化的glucuronide代謝物結合而被代謝入尿液或經由膽汁隨排泄物排出。由動物試驗顯示穿過血腦障壁的藥物量僅為可忽視的微量。

【進一步之說明】
湍泰低對腎功能無不良作用，且特別適用於患有腎臟病的高血壓患者。湍泰低在鹼性溶液中可於334 nm波長及412 nm波長呈螢光反應，因此可能會干擾某些螢光物質包括catecholamines的檢驗。若以螢光法或光學方法檢驗尿中catecholamines，metanephrine， normetanephrine 及vanillymandelic acid <VAM>時可能會因labetalol代謝物的存在而誤導致濃度增高。在測定catecholamines濃度時，若欲篩檢疑似患有嗜鉻細胞瘤或可能正接受labetalol治療之患者時可使用HPLC方法加以檢驗。

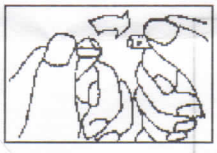
【包裝】
每安瓿5公撮裝，每盒5支。

使用前請依下列方式開啓安瓿

(1)一手握住安瓿瓶身，令圓點朝正面，若瓶子上方的管徑內遺留有注射液則輕敲或輕搖安瓿使其落回瓶身



(2)另一手握住圓點上方的管徑，如圖所示，向下折斷安瓿



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L863-U06-02

TRANDATE™ injection 5mg/ml

(labetalol)

Presentation

Trandate Injection: 5 ml ampoules each containing 25 mg (5 mg/ml) labetalol hydrochloride in an aqueous colourless solution. Labetalol hydrochloride is 2-hydroxy-5-[1-hydroxy-2-(1-methyl-3-phenyl-propylamino)ethyl] benzamide hydrochloride.

Uses

Indications

- Severe hypertension, including severe hypertension of pregnancy, when rapid control of blood pressure is essential.
- Anaesthesia when a hypotensive technique is indicated.
- Hypertensive episodes following acute myocardial infarction.

Mode of Action: Trandate lowers blood pressure by blocking peripheral arteriolar alpha-adrenoceptors, thus reducing peripheral resistance, and by concurrent beta-blockade, protects the heart from reflex sympathetic drive that would otherwise occur. Cardiac output is not significantly reduced at rest or after moderate exercise. Increases in systolic blood pressure during exercise are reduced but corresponding changes in diastolic pressure are essentially normal. All these effects would be expected to benefit hypertensive patients.

Dosage and Administration

Trandate Injection is intended for intravenous use in hospitalised patients. Patients should always receive the drug whilst in the supine or left lateral position. Raising the patient into the upright position within three hours of intravenous Trandate administration should be avoided since excessive postural hypotension may occur.

Adults

Bolus Injection

If it is essential to reduce the blood pressure quickly a dose of 50 mg should be given by intravenous injection (over a period of at least one minute), and if necessary, repeated at five minute intervals until a satisfactory response occurs. The total dose should not exceed 200 mg. The maximum effect usually occurs within 5 minutes and the duration of action is usually about 6 hours but may be as long as 18 hours.

Intravenous Infusion

A 1 mg/ml solution of Trandate should be used, i.e. the contents of eight ampoules (200 mg) diluted to 200 ml with Sodium Chloride and Dextrose Injection BP or 5% Dextrose Intravenous Infusion BP. Hypertension in pregnancy-Infusion should be started at 20 mg/hour, then doubled every 30 minutes until a satisfactory response is obtained or a dosage of 160 mg/hour is reached. Occasionally higher doses may be necessary. Hypertensive episodes following acute myocardial infarction-Infusion should be started at 15 mg/hour and gradually increased to a maximum of 120 mg/hour depending on the control of blood pressure. Hypertension due to other causes-Infuse at a rate of about 2 mg/min until a satisfactory response is obtained, then stop infusion.The effective dose is usually 50-200 mg but larger doses may be needed, especially in patients with phaeochromocytoma. The rate of infusion may be adjusted according to the response at the discretion of the physician. It is desirable to monitor the blood pressure and heart rate after injection and during infusion. In most patients, there is a small decrease in the heart rate; severe bradycardia is unusual but may be controlled by injecting atropine 1-2 mg intravenously. Respiratory function should be observed particularly in patients with any known impairment. Once the blood pressure has been adequately reduced by bolus injection or infusion, maintenance therapy with Trandate Tablets should be substituted with a starting dose of 100 mg twice daily. Trandate Injection has been administered to patients with uncontrolled hypertension already receiving other hypotensive agents, including beta-blocking drugs, without adverse effects.

Hypotensive anaesthesia- Induction should be with standard agents (e.g. sodium thiopentone) and anaesthesia maintained with nitrous oxide and oxygen with or without halothane. The recommended starting dose of Trandate Injection is 10-20 mg intravenously depending on the age and condition of the patient. Patients for whom halothane is contra-indicated usually require a higher initial dose of Trandate (25-30 mg). If satisfactory hypotension is not achieved after five minutes, increments of 5-10 mg should be given until the desired level of blood pressure is attained. Halothane and Trandate act synergistically, therefore the halothane concentration should not exceed 1-1.5% as profound falls in blood pressure may be precipitated. Following Trandate Injection the blood pressure can be quickly and easily adjusted by altering the halothane concentration and/or adjusting table tilt. The mean duration of hypotension following 20-25 mg of Trandate is fifty minutes. Hypotension induced by Trandate Injection is readily reversed by atropine 0.6 mg and discontinuation of halothane. Tubocurarine and pancuronium may be used when assisted or controlled ventilation is required. IPPV may further increase the hypotension resulting from Trandate Injection and/or halothane.

Children

Safety and efficacy in children have not been established.

Contra-indications

Trandate Injection is contra-indicated in second or third degree heart block, cardiogenic shock and other conditions associated with severe and prolonged hypotension or severe bradycardia. When peripheral vasoconstriction suggests low cardiac output, the use of Trandate Injection to control hypertensive episodes following acute myocardial infarction is contra-indicated. Labetalol is contra-indicated for patients known to have hypersensitivity to the drug.

Warnings

There have been rare reports of severe hepatocellular injury with labetalol therapy. The hepatic injury is usually reversible and has occurred after both short and long term treatment. Appropriate laboratory testing should be done at the first sign or symptom of liver dysfunction. If there is laboratory evidence of liver injury or the patient is jaundiced, labetalol therapy should be stopped and not re-started. Beta-blockers, even those with apparent cardioselectivity, should not be used in patients with asthma or a history of obstructive airways disease unless no alternative treatment is available. In such cases, the risk of inducing bronchospasm should be appreciated and appropriate precautions taken. If bronchospasm should occur after the use of Trandate Injection, it can be treated with a bata2-agonist by inhalation, e.g. salbutamol (the dose for which may need to be greater than the usual dose in asthma) and if necessary intravenous atropine 1 mg .

Precautions

Where cardiac reserve is poor, control with a cardiac glycoside and a diuretic should be obtained prior to the cautious use of Trandate Injection. Trandate Injection need not be discontinued prior to anaesthesia but patients should receive intravenous atropine prior to induction. Trandate may enhance the hypotensive effects of halothane. During anaesthesia, Trandate may mask the compensatory physiological responses of sudden haemorrhage (tachycardia and vasoconstriction). Close attention must therefore be paid to blood loss and the blood volume maintained. Care should be taken if labetalol is used concomitantly with either Class I antiarrhythmic agents or calcium antagonists of the verapamil type.

Pregnancy and Lactation

Although no teratogenic effects have been demonstrated in animals, Trandate should only be used during the first trimester of pregnancy if the potential benefit outweights the potential risk. Trandate crosses the placental barrier and the possibility of the consequences of alpha and beta-adrenoceptor blockade in the fetus and neonate should be borne in mind. Perinatal and neonatal distress (bradycardia, hypotension, respiratory depression, hypoglycaemia, hypothermia) has been rarely reported. Sometimes these symptoms developed a day or two after birth. Response to supportive measures (e.g. intravenous fluids and glucose) is usually prompt but with severe pre-eclampsia, particularly after prolonged intravenous labetalol, recovery may be slower. This may be related to diminished liver metabolism in premature babies. Intra-uterine and neonatal deaths have been reported but other drugs (e.g. vasodilators, respiratory depressants) and the effects of pre-eclampsia, intrauterine growth retardation and prematurity were implicated. Such clinical experience warns against unduly prolonging high dose labetalol and delaying delivery and against co-administration of hydralazine. Trandate is excreted in breast milk: no adverse effects in breast feeding infants have been reported. Labetalol has been rarely associated with reversible hepatic and cholestatic jaundice. Trandate therapy should be discontinued if jaundice occurs.

Side effects

Trandate Injection is usually well tolerated. Pronounced postural hypotension may occur if patients are allowed to assume the upright position within three hours of receiving Trandate Injection. Rare reports of hypersensitivity, rash, pruritus, angioedema and dyspnea. A few reports of nasal congestion. There are rare reports of raised liver function tests, jaundice (both hepatocellular and cholestatic), hepatitis and hepatic necrosis. The signs and symptoms are usually reversible on withdrawal of the drug. There are rare reports of bradycardia and heart block.

Overdosage

Profound cardiovascular effects are to be expected, e.g. excessive, posture-sensitive hypotension and sometimes bradycardia. Patients should be laid supine with the legs raised. Use a cardiac glycoside and a diuretic in cardiac failure; for bronchospasm, administer a beta2-agonist per aerosol. Intravenous atropine 0.25 to 3 mg should be given to relieve bradycardia. Intravenous noradrenaline 5 to 10 micrograms initially, repeated according to response, may be preferable to isoprenaline to improve the circulation. Alternatively, noradrenaline may be infused at a rate of 5 micrograms per minute until the response is satisfactory. In severe overdose, intravenous glucagon may be preferred: an initial bolus dose of 5 to 10 mg in dextrose or saline should be followed by an intravenous infusion of 5 mg/hour or as sufficient to maintain cardiac output. Transvenous pacing may be required. Oliguric renal failure has been reported after massive overdosage of labetalol orally. In one case, the use of dopamine to increase the blood pressure may have aggravated the renal failure. Haemodialysis removes less than 1% labetalol HCl from the circulation.

Pharmaceutical Precautions

Potect from light. Store below 30°C

Compatibility: Trandate Injection is compatible with the following intravenous infusion fluids: 5% Dextrose BP, 0.18% Sodium Chloride and 4% Dextrose BP, 0.3% Potassium Chloride and 5% Dextrose BP, Compound Sodium Lactate BP. Unused admixtures should be discarded 24 hours after preparation. Trandate injection has been shown to be incompatible with Sodium Bicarbonate Injection BP 4.2% w/v.

Pharmacokinetics

The plasma half-life of labetalol is about four hours. About 50% of labetalol in the blood is protein bound. Labetalol is metabolised mainly through conjugation to inactive glucuronide metabolites. There are excreted both in the urine and via the bile, into the faeces. Only negligible amounts of the drug cross the blood brain barrier in animal studies.

Further Information

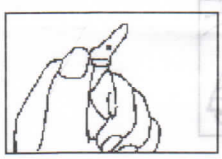
Trandate does not adversely affect renal function and is particularly suitable for use in hypertensive patients with renal disease. Trandate fluoresces in alkaline solution at an excitation wavelength of 334 nm and a fluorescence wavelength of 412 nm and may therefore interfere with the assays of certain fluorescent substances including catecholamines. The presence of labetalol metabolites in the urine may result in falsely elevated levels of urinary catecholamines, metanephrine, normetanephrine, and vanillylmandelic acid (VMA) when measured by fluorimetric or photometric methods. In screening patients suspected of having a pheochromocytoma and being treated with labetalol HCl, a specific method, such as high performance liquid chromatographic assay with solid phase extraction (eg, J Chromatogr 385:241, 1987) should be employed in determining levels of catecholamines.

Package quantities

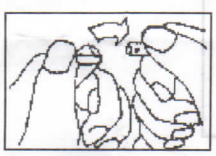
5 ml ampoules, boxes of 5

Break the ampoule as below before use:

(1) Hold the ampoule with the spot uppermost. If any of the solution is in the stem of the ampoule, tap or shake it down into the body of the ampoule.



(2) Hold the ampoule with the spot uppermost. Break the stem of the ampoule off in a downwards direction.



GlaxoSmithKline

L863-U06-02