of increasing the dosage due to tolerance effects thereby promoting vascular irritation and overshoot reactions.

BRIEF DESCRIPTION

The object of the disclosure is solved by the present disclosure.

The present disclosure also provides in one aspect the use of a formulation of landiolol hydrochloride in the manufacture of a medicament for persistent reduction of the heart rate in a subject suffering from supraventricular tachycardia and/or hypertension, wherein said landiolol hydrochloride is a lyophilized powder reconstituted to obtain a ready to use solution or a formulation wherein landiolol is provided in a diluted ready to use solution which is to be administered at a constant dose of more than 5 μg/kg/min for a period of at least 2 hours.

The disclosure provides a formulation of landiolol hydrochloride in a therapeutically efficient amount for use in the treatment of a subject suffering from tachycardia, tachyarrhythmia and/or hypertension, wherein landiolol hydrochloride is administered at a constant dose of about 5 μg/kg/min, specifically more than (>) 5 μg/kg/min, preferably at least 10 μg/kg/min for a period of at least 2 hours, preferably for at least 4 hours, preferably for at least 6 hours, preferably for at least 12 hours, preferably for at least 20 hours, preferably for at least 24 hours, preferably for at least 2 days, preferably for more than two days and wherein the heart rate and/or blood pressure of said patient are persistently reduced during the administration period compared to the heart rate and/or blood pressure before treatment, specifically as opposed to other short acting beta blocker such as esmolol.

According to a further embodiment of the disclosure, the constant dose of landiolol hydrochloride is at least 15 μg/kg/min, specifically at least 20 μg/kg/min, specifically at least 25 μg/kg/min, specifically at least 30 μg/kg/min, specifically at least 35 μg/kg/min, specifically at least 40 μg/kg/min.

According to a further embodiment of the disclosure the heart rate and/or blood pressure are reduced at least 5%, preferably between 10% and 50% compared to the heart rate and/or blood pressure before treatment with landiolol.

Overshoot is not occurring after termination of administration and normal heart rate and/or blood pressure are attained within a few minutes, specifically within 5 to 20 minutes and more specifically, said normal heart rate and/or blood pressure are preserved for at least 30 minutes, preferably for at least 60 minutes, more preferred at least 120 minutes after termination of administration of landiolol-hydrochloride as opposed to esmolol where an overshoot occurs within minutes and may be maintained hours thus leading to increased heart rate and/or blood pressure.

CLAIMS

1. Use of a formulation of landiolol hydrochloride in the manufacture of a medicament for persistent reduction of the heart rate in a subject suffering from supraventricular tachycardia and/or hypertension, wherein said landiolol hydrochloride is a lyophilized powder reconstituted to obtain a ready to use solution or a formulation wherein landiolol is provided in a diluted ready to use solution which is to be administered at a constant dose of more than 5 μg/kg/min for a period of at least 2 hours.

2. The use according to claim 1, wherein the constant dose of landiolol hydrochloride is at least 10 μg/kg/min, at least 15 μg/kg/min, at least 20 μg/kg/min, at least 25 μg/kg/min, at least 30 μg/kg/min, at least 35 μg/kg/min, or at least 40 μg/kg/min.

3. The use according to claims 1 or 2, wherein landiolol hydrochloride is to be administered for at least 4 hours, for at least 6 hours, for at least 12 hours, for at least 24 hours, for at least 2 days, or for more than two days.

4. The use according to any one of claims 1 to 3, wherein the heart rate is reduced at least 5%, or between 10% and 50% compared to the heart rate before treatment.

5. The use according to any one of claims 1 to 4, wherein no overshoot effect occurs after termination of administration of landiolol hydrochloride.

6. The use according to any one of claims 1 to 5, wherein a normal heart rate is reached within 5 to 20 minutes after termination of administration.

7. The use according to any one of claims 1 to 6, wherein said landiolol hydrochloride is at a concentration of about 1 to 30 mg/mL, or about 5 to 15 mg/mL.

8. The use according to any one of claims 1 to 7, wherein said solution has a pH of up to 6.5.

9. The use according to any one of claims 1 to 8, wherein said solution is to be administered intravenously.

10. The use according to any one of claims 1 to 9, wherein said solution is to be administered as maintenance infusion at a dose of between 15 to 100 µg/kg/min, or between 10 to 50 µg/kg/min.

11. The use according to any one of claims 1 to 10, wherein said solution is local tissue tolerant at the infusion site, preventing local venous irritation or skin necrosis at the infusion site.

12. The use according to any one of claims 1 to 11, wherein said subject is suffering from supraventricular tachycardia and/or hypertension in perioperative, postoperative, or other circumstances where persistent control of the ventricular rate is desirable, wherein said supraventricular tachycardia is selected from the group consisting of atrial fibrillation and atrial flutter.

13. The use according to any one of claims 1 to 12, wherein said subject is having cardiac decompensation, renal decompensation, hypernatremia, hyperchloramic acidosis and/or hyperhydratation.

14. The use according to any one of claims 1 to 13, wherein said subject is receiving a positive inotropic drug, selected from the group of dobutamine, amrinone or a sympathomimetic drug, or selected from the group of beta 1, beta 2 agonists, phophodiesterease inhibitors or Calcium sensitizers.

15. The use according to any one of claims 1 to 14, wherein said subject is suffering from intoxication from positive inotropic and/ or chronotropic drug or sympathomimetic drug.