NASAL ADMINISTRATION

DESCRIPTION

Field of the Disclosure

The present disclosure, in one embodiment, relates to the nasal administration of substances, in particular drugs, and in particular substances which require a rapid onset of action, such as in the treatment of pain, including headaches, for example, cluster headaches and migraine, and neuropathic pain. It relates, in another embodiment, to nasal delivery of carbon dioxide gas or nasal pH adjustment as a supplement a therapeutic treatment, such as for the treatment of pain.

SUMMARY OF THE DISCLOSURE

In one aspect, the present disclosure relates to the use of a therapeutic amount of at least one of carbon dioxide or a pH adjusting material and at least one therapeutic agent in the preparation of a medicament for therapeutically treating a patient, wherein said therapeutic agent is to be administered before, after, before and after and/or at the same time as said carbon dioxide or pH adjusting material, and wherein said carbon dioxide or pH adjusting material is to be delivered to a location at an interior of a nasal passage of the patient.

In another aspect, there is disclosed the use of about 5% to about 6% vol/vol carbon dioxide in the preparation of a medicament for increasing a therapeutic effect of a pharmaceutical agent delivered to a patient, wherein said carbon dioxide is to be delivered as a fluid flow to a posterior region of a nasal passage of the patient; and wherein said patient has been administered with a dose of the pharmaceutical agent.

In another aspect, there is provided the use of carbon dioxide in a concentration of about 5% to about 6% vol/vol in the preparation of a medicament for providing a therapeutic or pharmacokinetic effect wherein said carbon dioxide is to be administered to a nostril of the patient to lower a pH of an upper posterior region of the nasal passage by at least about 0.1 pH units.

Referring to Figure 1(a), the nasal airway 1 comprises the two nasal cavities separated by the nasal septum, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 3 and the tubal ostia 5, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx 7, the oral cavity 9 and the lower airway 11, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx 7

and the oral cavity 9 by opening and closing of the oropharyngeal velum 13. The velum 13, which is often referred to as the soft palate, is illustrated in solid line in the closed position, as achieved by providing a certain positive pressure in the oral cavity 9, such as achieved on exhalation through the oral cavity 9, and in dashed line in the open position.

The present inventors have surprisingly identified that a rapid systemic uptake and a rapid response rate can be achieved, as compared, for example, to the conventional delivery of an equivalent liquid substance, by the delivery of substance and at least one gas to the posterior region of the nasal airway.

The posterior region of the nasal airway is that region which is posterior of the nasal valve NV, as illustrated in Figure 1(b). The nasal valve comprises the anterior bony cavum which contains inferior turbinate erectile tissue and septal erectile tissue, which are supported respectively by compliant ala tissue and the rigid cartilaginous septum (Cole, P (The Respiratory Role of the Upper Airways, a

WHAT IS CLAIMED IS:

1. An apparatus or method for therapeutically treating a patient, comprising:

administering, in a first step, a therapeutic agent; and

delivering, in a second step, to a location at an interior of a nasal passage of the patient a therapeutic amount of at least one of carbon dioxide or a pH adjusting material, wherein the first step is performed before, after, before and after and/or at the same time as the second step.

2. The apparatus or method of claim 1, wherein the first step is performed before the second step.

3. The apparatus or method of claim 1, wherein the first step is performed after the second step.

4. The apparatus or method of claim 1, wherein the second step is performed both before and after the first step and/or the first step is performed at the same time as the second step.

5. The apparatus or method of claim 1, wherein the location includes an upper posterior region of the nasal passage.

6. The apparatus or method of claim 1, wherein the therapeutic agent includes sumatriptan, optionally in the form of sumatriptan succinate, optionally administered as a powder aerosol.

7. The apparatus or method of claim 1, wherein the therapeutic agent includes a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

8. The apparatus or method of claim 7, wherein the therapeutic agent is delivered in amount of at least 100 ug, optionally twice daily.

9. The apparatus or method of claim 8, wherein the therapeutic agent is delivered in amount of at least 200 ug, optionally twice daily.

10. The apparatus or method of claim 9, wherein the therapeutic agent is delivered in amount of at least 400 ug, optionally twice daily.

11. The apparatus or method of claim 8, wherein the delivering comprises:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece; and

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the therapeutic agent when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability of 50 ug of the therapeutic agent when intranasally administered without the delivering.

12. The apparatus or method of claim 1, wherein the second step adjusts a pH in the nasal passage location by an amount ranging from about 0.01 to about 0.5 pH units.

13. The apparatus or method of claim 12, wherein the amount ranges from about 0.1 to about 0.2 pH units.

14. The apparatus or method of claim 1, wherein the second step comprises delivering a concentration of carbon dioxide from about 1% vol/vol to about 10% vol/vol carbon dioxide.

15. The apparatus or method of claim 14, wherein the concentration of carbon dioxide is from about 5% to about 6% vol/vol carbon dioxide.

16. The apparatus or method of claim 1, wherein delivering comprises:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient;

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece; and

directing the fluid flow to the location within the nasal passage.

17. The method of claim 16, wherein delivering further comprises:

adjusting a pH at the location by controlling the fluid flow.

18. The apparatus or method of claim 17, wherein controlling the fluid flow includes at least one of controlling a duration, a rate, a pressure, and a composition of the fluid flow.

19. The apparatus or method of claim 18, comprising controlling the fluid flow duration to be in a range of from about 2 to about 3 seconds.

20. The apparatus or method of claim 19, comprising controlling the fluid flow rate at at least 10 L/min, optionally at least 20 L/min, and optionally at about 30 L/min.

21. The apparatus or method of claim 16, wherein the delivering further comprises:

placing the nosepiece into a second nostril of the patient;

the patient exhaling a breath into the mouthpiece to create a second fluid flow out of the nosepiece; and

directing the second fluid flow to a second location within a second nasal passage.

22. An apparatus or method for increasing a therapeutic effect of a pharmaceutical agent delivered to a patient, comprising:

delivering a fluid flow to a nasal passage of the patient to deliver about 5% to about 6% vol/vol carbon dioxide to a posterior region of the nasal passage; and

administering a dose of the pharmaceutical agent to the patient.

23. The apparatus or method of claim 22, further including lowering a pH of the posterior region of the nasal passage.

24. The apparatus or method of claim 22, wherein the pharmaceutical agent includes sumatriptan, optionally in the form of sumatriptan succinate, optionally administered as a powder aerosol.

25. The apparatus or method of claim 22, wherein the pharmaceutical agent includes a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

26. The apparatus or method of claim 25, wherein the pharmaceutical agent is delivered in amount of at least 100 ug, optionally twice daily.

27. The apparatus or method of claim 26, wherein the pharmaceutical agent is delivered in amount of at least 200 ug, optionally twice daily.

28. The apparatus or method of claim 27, wherein the pharmaceutical agent is delivered in amount of at least 400 ug, optionally twice daily.

29. The apparatus or method of claim 26, wherein the delivering comprises:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece; and

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the pharmaceutical agent when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability or pharmacokinetic (PK) profile of 50 ug of the pharmaceutical agent when intranasally administered without the delivering.

30. An apparatus or method for treating a patient, comprising delivering a concentration of about 5% to about 6% vol/vol carbon dioxide to a nostril of the patient to lower a pH of an upper posterior region of the nasal passage by at least about 0.1 pH units to provide a therapeutic or pharmacokinetic effect.

31. The apparatus or method of claim 30, further including administering a therapeutic agent to the patient at least one of orally, intranasally, intravenously, and sub-cutaneously.

32. The apparatus or method of claim 30, further including administering a dose of sumatriptan powder intranasally.

33. The apparatus or method of claim 32, the low dose includes less than 20 mg of a sumatriptan powder, optionally about 16 mg of sumatriptan powder, optionally in the form of sumatriptan succinate.

34. The apparatus or method of claim 30, further including administering a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

35. The apparatus or method of claim 34, wherein the steroid is delivered in amount of at least 100 ug, optionally twice daily.

36. The apparatus or method of claim 35, wherein the steroid is delivered in amount of at least 200 ug, optionally twice daily.

37. The apparatus or method of claim 36, wherein the steroid is delivered in amount of at least 400 ug, optionally twice daily.

38. The apparatus or method of claim 30, wherein the delivering comprises:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece; and

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the steroid when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability or pharmacokinetic (PK) profile of 50 ug of the steroid when intranasally administered without the delivering.

39. The apparatus or method of claim 30, wherein the therapeutic or pharmacokinetic effect treats at least one of migraine and allergic rhinitis.

40. The apparatus or method of claim 30, further including substantially closing a soft palate of the patient during the delivery step.

WHAT IS CLAIMED IS:

1. Use of a therapeutic amount of at least one of carbon dioxide or a pH adjusting material and at least one therapeutic agent in the preparation of a medicament for therapeutically treating a patient, wherein said therapeutic agent is to be administered before, after, before and after and/or at the same time as said carbon dioxide or pH adjusting material, and

wherein said carbon dioxide or pH adjusting material is to be delivered to a location at an interior of a nasal passage of the patient.

2. The use of claim 1, wherein the therapeutic agent is to be administered before the carbon dioxide or pH adjusting material.

3. The use of claim 1, wherein the therapeutic agent is to be administered after the carbon dioxide or pH adjusting material.

4. The use of claim 1, wherein the carbon dioxide or a pH adjusting material is administered both before and after the therapeutic agent and/or the therapeutic agent is administered at the same time as the carbon dioxide or pH adjusting material.

5. The use of claim 1, wherein the location includes an upper posterior region of the nasal passage.

6. The use of claim 1, wherein the therapeutic agent includes sumatriptan, optionally in the form of sumatriptan succinate, optionally administered as a powder aerosol.

7. The use of claim 1, wherein the therapeutic agent includes a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

8. The use of claim 7, wherein the therapeutic agent is delivered in amount of at least 100 ug, optionally twice daily.

9. The use of claim 8, wherein the therapeutic agent is delivered in amount of at least 200 ug, optionally twice daily.

10. The use of claim 9, wherein the therapeutic agent Is delivered in amount of at least 400 ug, optionally twice daily.

11. The use of claim 8, wherein the delivering comprises:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece; and

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the therapeutic agent when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability of 50 ug of the therapeutic agent when intranasally administered without the delivering.

12. The use of claim 1 , wherein the carbon dioxide or pH adjusting material adjusts a pH in the nasal passage location by an amount ranging from about 0.01 to about 0.5 pH units.

13. The use of claim 12, wherein the amount ranges from about 0.1 to about 0.2 pH units.

14. The use of claim 1, wherein the carbon dioxide is in a concentration of from about 1% vol/vol to about 10% vol/vol carbon dioxide.

15. The use of claim 14, wherein the concentration of carbon dioxide is from about 5% to about 6% vol/vol carbon dioxide.

16. The use of claim 1 , wherein delivering comprises: placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient;

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece; and

directing the fluid flow to the location within the nasal passage.

17. The use of claim 16, wherein delivering further comprises: adjusting a pH at the location by controlling the fluid flow.

18. The use of claim 17, wherein controlling the fluid flow includes at least one of controlling a duration, a rate, a pressure, and a composition of the fluid flow.

19. The use of claim 18, comprising controlling the fluid flow duration to be in a range of from about 2 to about 3 seconds.

20. The use of claim 19, comprising controlling the fluid flow rate at at least 10 L/min, *optionally at least 20 L/min, and optionally at about 30 L/min.*

21. The use of claim 6, wherein the delivering further comprises:

placing the nosepiece into a second nostril of the patient;

the patient exhaling a breath into the mouthpiece to create a second fluid flow out of the nosepiece; and

directing the second fluid flow to a second location within a second nasal passage.

22. Use of about 5% to about 6% vol/vol carbon dioxide in the preparation of a medicament for increasing a therapeutic effect of a pharmaceutical agent delivered to a patient, wherein said carbon dioxide is to be delivered as a fluid flow to a posterior region of a nasal passage of the patient; and wherein said patient has been administered with a dose of the pharmaceutical agent.

23. The use of claim 22, wherein a pH of the posterior region of the nasal passage is lowered.

24. The use of claim 22, wherein the pharmaceutical agent includes sumatriptan, optionally in the form of sumatriptan succinate, optionally administered as a powder aerosol.

25. The use of claim 22, wherein the pharmaceutical agent includes a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

26. The use of claim 25, wherein the pharmaceutical agent Is delivered in amount of at least 100 ug, optionally twice daily.

27. The use of claim 26, wherein the pharmaceutical agent is delivered in amount of at least 200 ug, optionally twice daily.

28. The use of claim 27, wherein the pharmaceutical agent is delivered in amount of at least 400 ug, optionally twice daily.

29. The use of claim 26, wherein the delivering comprises:
placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece;

and the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the pharmaceutical agent when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability or pharmacokinetic (PK) profile of 50 ug of the pharmaceutical agent when intranasally administered without the delivering.

30. Use of carbon dioxide in a concentration of about 5% to about 6% vol/vol in the preparation of a medicament for providing a therapeutic or pharmacokinetic effect wherein said carbon dioxide is to be administered to a nostril of the patient to lower a pH of an upper posterior region of the nasal passage by at least about 0.1 pH units.

31. The use of claim 30, wherein the medicament further comprises a therapeutic agent to be administered to the patient at least one of orally, intranasally, intravenously, and sub-cutaneously.

32. The use of claim 30, wherein the medicament further comprises a dose of sumatriptan powder, which is to be administered intranasally.

33. The use of claim 32, wherein the dose of sumatriptan powder includes less than 20 mg of a sumatriptan powder, or about 16 mg of sumatriptan powder, optionally in the form of sumatriptan succinate.

34. The use of claim 30, wherein the medicament further includes a topical steroid, optionally fluticasone, optionally in the form of fluticasone propionate, optionally administered as a liquid aerosol.

35. The use of claim 34, wherein the steroid is delivered in amount of at least 100 ug, optionally twice daily.

36. The use of claim 35, wherein the steroid is delivered in amount of at least 200 ug, optionally twice daily.

37. The use of claim 36, wherein the steroid is delivered in amount of at least 400 ug, optionally twice daily.

38. The use of claim 34, wherein said carbon dioxide is to be administered by a delivery step comprising:

placing a mouthpiece into a mouth of the patient and a nosepiece into a nostril of the patient, the mouthpiece being fluidly connected to the nosepiece; and

the patient exhaling a breath into the mouthpiece to create a fluid flow out of the nosepiece;

and wherein the steroid when intranasally administered has a systemic bioavailability or pharmacokinetic (PK) profile which is equivalent to or not greater than the systemic bioavailability or pharmacokinetic (PK) profile of 50 ug of the steroid when intranasally administered without the delivering.

39. The use of claim 30, wherein the therapeutic or pharmacokinetic effect treats at least one of migraine and allergic rhinitis.

40. The use of claim 38, wherein the patient has a substantially closed soft palate during the delivery step.