(54) Title: AUTOMATED DELIVERY OF AEROSOLIZED DRUGS DURING ANESTHESIA WITH SYNCHRONIZED VENTILATION

(57) Abstract: A system for delivery of drugs to a patient while connected to a general anesthesia machine is disclosed, the system comprising (A) a breathing circuit comprising (1) an inhalation tube; (2) an exhalation tube; and (3) a connector having a first side adapted to fluidly connect with the inhalation and exhalation tubes, a second side adapted to fluidly connect with an endotracheal tube or face mask, and a special port adapted to connect with a nebulizer machine or a therapeutic vaporizer; (B) a programmable control module to regulate the timing and volume of anesthetic gases and oxygen delivered to the patient; (B) a ventilator; (C) a nebulizer machine comprising at least two interchangeable liquid or aerosolized drug containers or chambers; the nebulizer machine connected to the breathing circuit via the special port. A method of delivering drugs from a nebulizer while a patient is intubated and connected to a general anesthesia machine using the novel system is also disclosed.
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AUTOMATED DELIVERY OF AEROSOLIZED DRUGS DURING ANESTHESIA WITH SYNCHRONIZED VENTILATION

BACKGROUND OF THE INVENTION

[0001] This invention relates to the field of anesthesiology, more particularly to the field of aerosolized drug delivery during general anesthesia.

[0002] During general anesthesia or mechanical ventilation, anesthesia machines with sophisticated electronic controllers are typically used in a hospital setting. Such anesthesia machines include integrated general anesthesia drug delivery units which integrate patient management, anesthesia delivery, and information management. Modern anesthesia machines include flow meters, or rotameters, for oxygen, air, and nitrous oxide, one or more anesthetic vaporizers to accurately add volatile anesthetics to the fresh gas flow, a ventilator, patient monitoring devices, and breathing circuits. One example of such machines is the Datex-Ohmeda S/5 general anesthesia system.

[0003] During general anesthesia, after the patient’s trachea is intubated and an endotracheal tube is connected to the circuit of the anesthesia machine for mechanical ventilation, handheld nebulizer devices are often employed for aerosol therapy to deliver a fine mist of medication into the patient’s lungs. The handheld nebulizers have a source of oxygen or air and other gases which blows into a nebulizer cup, changing the liquid in the cup to a mist. The nebulizer also has a mouthpiece for the patient and just one chamber cup for liquid medication. Conventional nebulizers are not programmable or fully compatible with the anesthesia machine respiratory cycle, and they require disconnection of the breathing system during nebulizer drug administration.

[0004] Conventional nebulizers are designed with only one cup and for delivery of only one drug at a time. Typical drugs delivered during general anesthesia by nebulizers are corticosteroids to reduce inflammation and swelling in tissues of airways, bronchodilators which help open the airways and relax the airway muscles, mucus thinning drugs to reduce the risk of lung infections and improve lung function, counteracting the mucus-thickening effect of anesthetic gases.
Various improvements in the nebulizer art have been proposed by others, for example Sosiak, U.S. Pat. 6,425,392, disclosed a battery powered nebulizer with breath activation, recording and control of dosage, and enhanced atomization of liquid medication, addressed to overcoming problems with prior nebulizers which were bulky, non-portable, require AC power, and vary in output between units and type. Tobia, et al., U.S. Pat. Pub. 2005/0284469, disclose a nebulizer connected to a ventilator system for use in respiratory therapy, wherein a control unit obtains a control value based on one or more ventilatory control parameters associated with respiratory therapy, generating a modification signal from the control unit to automatically modify an operating condition of the nebulizer based on the control value, where the nebulizer is operated at predetermined dosing periods. The Tobia system is not directed to an general anesthesia system and does not provide for automated selection of drugs from a plurality of drugs. Von Hollen, et al., U.S. Pat. Pub. 2006/0201500, discloses a nebulizer installed in a ventilator circuit with an aerosol generator disposed in a base module, directed to overcoming the problem of having to open the housing to replenish drug solution when the drug solution is depleted, which causes a problem in some ventilator systems in that the ventilator circuit is opened to atmospheric air. Von Hollen, et al., disclose a seal arrangement to seal the inlet port and outlet port from ambient atmosphere when the base module is uncoupled from the ventilator interface module so the intake gas can be communicated from the inlet port to the outlet port.

Grychowski, et al., U.S. Pat. Publs. 2004/0173209 and 2007/0023036, disclose a pressure sensitive nebulizer coordinated with a breathing cycle of a patient which includes a gas diverter that is moveable and diverts pressurized gas across a liquid outlet in response to a patient’s breathing cycle. Smaldone, et al., U.S. Pat. Publ. 2004/0011358, disclose a nebulizer for treating tracheobronchitis, bronchiectasis and pneumonia in the nosocomial patient with antibiotics administered in combination or serially into the ventilator circuit, either mechanically or by aerosol formulation. Dhuper, et al., U.S. Pat. Pub. 2006/0283447, discloses a ventilator system having an inhalation port and an exhalation port, a patient conduit for delivering to and removing gas from a patient, an inhalation conduit fluidly connected to the inhalation port and the patient conduit, an inhalation conduit connected to the inhalation port and patient conduit, and nebulizer device for generating aerosolized medication connected to the inhalation conduit so that the aerosolized medication is delivered to the patient as the patient inhales. The inhalation conduit has a variable length to position the device for generating aerosolized
medication a predetermined distance from the patient conduit. This device has no automated feature to deliver medications and shows a large dead space volume, thus is less effective for delivery of medication. This device has no compatibility with the anesthesia machine and does not access effect. King, U.S. Pat. Publ. 2006/0231090, disclosed an apparatus which delivers up to about 80% of the medication aerosolized in essentially the same particle size distribution as originating from the nebulizer which produces the mist. Kraft et al, U.S. Pat. Publ. 2008/0230053, disclosed methods and systems for pulmonary delivery of tocopherol-containing compositions and formulations and a novel nebulizer design to convert such formulations into aerosols having a particle size range of 2 to 12μm. The novel nebulizer design may be adapted to work in conjunction with a mechanical ventilator by injecting the drug mist directly into the ventilator circuit at the endotracheal tube or tracheal tube and directly into the pulmonary region of the patient via air tube.

[0007] It is an object of the present invention to provide aerosolized and/or vaporized drugs to a patient who is intubated with an endotracheal tube connected to the circuit of an anesthesia machine with a system which is not limited to delivering one drug at a time and is capable of simultaneously delivering two or more compatible drugs and having mechanisms of action where such simultaneous delivery is medically indicated, and also capable of delivering two or more drugs sequentially.

[0008] It is another object of the invention to provide an automated, programmable system of delivery of nebulized and or vaporized drugs during general anesthesia to an intubated patient.

SUMMARY OF THE INVENTION

[0009] These objects, and others which will become apparent from the following detailed description and drawings, are achieved by the present invention which comprises in one aspect a system for delivery of drugs to a patient while connected to a general anesthesia machine comprising (A) a breathing circuit comprising (1) an inhalation tube; (2) an exhalation tube; and (3) a connector having a first side adapted to fluidly connect with the inhalation and exhalation tubes, a second side adapted to fluidly connect with an endotracheal tube or face mask, and a port adapted to connect with a nebulizer machine or a therapeutic vaporizer; (B) a ventilator; (C) a programmable control module to regulate the timing and volume of anesthetic gases and
oxygen delivered to the patient; (D) either a nebulizer machine comprising at least two interchangeable liquid or aerosolized drug containers or chambers or a therapeutic vaporizer; the nebulizer or therapeutic vaporizer machine connected to the breathing circuit via the connector port. In some embodiments the inhalation tube (2) and exhalation tube (3) are concentric and are fluidly joined at a point near the first side of connector (4) so inhalation gases comprising oxygen, anesthetic gases, and/or aerosolized drugs from the nebulizer machine pass through the connector to the face mask or endotracheal tube and exhalation gases from the patient pass through the connector to the exhalation tube. In other embodiments the inhalation tube (2) and exhalation tube (3) are separate and are fluidly joined at a Y-connector. In such embodiments the port adapted to connect with the nebulizer machine is either at the Y-joint or is located on the patient side of the Y-connector or between the Y-connector and the patient.

[0010] Another aspect of the invention is the method of delivering drugs during general anesthesia while a patient is intubated comprising providing a programmable nebulizer or therapeutic vaporizer fluidly connected to a breathing circuit of the general anesthesia machine at a connection point beyond the Y-piece, automatically delivering to the circulation loop during controlled times during the respiratory cycle one or more drugs at a time from one or more chambers within the nebulizer machine or therapeutic vaporizer, synchronizing the automatic delivery of drugs to the general anesthesia machine respiratory cycle so as to effectively and efficiently treat preexisting problems or prevent respiratory complications occurring during the general anesthesia procedure.

[0011] Another aspect of the invention is a method of delivering drugs during a general anesthesia procedure while a patient is intubated comprising providing a programmable nebulizer machine or therapeutic vaporizer fluidly connectable to a breathing circuit of a general anesthesia machine at a point at or near a Y-piece, automatically delivering to the breathing circuit during controlled times during the respiratory cycle from one to three drugs at a time from one to three liquid drug containers or chambers within the nebulizer machine and/or their mix into the therapeutic vaporizer, synchronizing the automatic delivery of drugs to the general anesthesia machine respiratory cycle so as to effectively and efficiently treat or prevent respiratory complications during the general anesthesia procedure.
[0012] In some embodiments the system includes pressure sensors and a recorder to register the frequency, type, amount, and/or time of drug delivery. Certain embodiments include an alarm system for detection of mechanical or drug delivery malfunction and/or a monitor. The system has a controller and monitor to provide selectability of one to three drugs to be delivered, the amount of each drug to be delivered, the time of delivery of each drug, wherein the monitor can report the progress and results of the delivery of the one or more drugs, either together or sequentially.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] These and other features and advantages of the present invention will be illustrated by certain embodiments set forth in the detailed description when considered in connection with the accompanying drawings, wherein:

[0014] FIG. 1 is a schematic illustration of a system according to the invention shown with an intubated patient comprising a general anesthesia machine, nebulizer device, and monitor.

[0015] FIG. 2 is a flow chart illustrating one embodiment of the method of the invention.

DETAILED DESCRIPTION

[0016] Referring now to Fig. 1, patient 11 is illustrated as being intubated with an endotracheal intubation tube 17, connected at distal (related to patient) end 28 to an elbow 36 which is proximal (related to patient) to and fluidly connected to divided tube 15. Divided tube 15 is clear plastic and ribbed to allow easy bending without kinking and has two lumens which are formed by flat plastic divider member 38, the flat plastic divider member 38 being molded longitudinally so as to form the two separate lumens, 41, 42 within divided tube 15. Lumen 41 is for ventilated gas from the ventilator 20 and lumen 42 is for exhaled gas from the patient 11. Divided tube 15 is well known in the general anesthesia machine art and such tubes are routinely used in the field of anesthetics, having advantages over two tubes connected with a Y-connector. The intubation tube 17, which has a single lumen carrying both ventilated gas and exhaled gas, two lumens 41, 42 formed in divided tube 15 and connected to inhalation and exhalation ports of the general anesthesia machine, combined with the ventilator, also known as the breathing circuit.
[0017] The general anesthesia machine has a ventilator 20. In an alternative embodiment, a face mask is substituted for the endotracheal intubation tube 17. In another alternative embodiment, two separate tubes connected to endotracheal intubation tube 17 or a face mask via a Y-connector and the tubes are connected to the inhalation and exhalation ports of the ventilator. An HME filter is usually provided in the circulation loop.

[0018] The nebulizer function can be integrated into the general anesthesia machine itself or can be a separate unit, in either case the nebulizer is connected to the breathing circuit at 43, which is proximal to divided tube 15 and would be proximal to or integrated with the Y-connector in the aforementioned two separate tube alternative embodiment.

[0019] The nebulizer machine or nebulizer module of the general anesthesia machine includes two or more interchangeable liquid drug containers/chambers for providing a selection of drugs to be delivered during the same general anesthesia procedure, or immediately before or after administration of general anesthesia. A tube connects the nebulizer machine to port 43 of the breathing circuit.

[0020] A recorder is provided in the illustrated embodiment in order to record the amounts, frequency, types, timing, success, and other factors associated with the delivery of drugs during the anesthetic procedure. The recorder can be integrated into the anesthetic machine control and record-keeping functions. Also, a nebulizer controller is provided in the illustrated embodiment. The medical professional can view the progress of drug delivery via the nebulizer monitor or a monitor which functions to monitor the drug delivery. In some embodiments the monitor functions to monitor both general anesthesia and drug delivery. An alarm system functioning to alert the medical professional of a failure event is present in the illustrated embodiment.

[0021] According to the method of the invention two, three, or more drugs are stored in a nebulizer and one or more of the stored drugs are delivered during a general anesthesia procedure by an automated, programmable nebulizer which is connected to a breathing circuit of the general anesthesia machine at in elbow 28 at port 43, at controlled times during the respiratory cycle so as to effectively and efficiently treat or prevent respiratory complications during the general anesthesia procedure. The nebulizer can be fully integrated into the general anesthesia machine or can be a separate unit which receives data from the general anesthesia machine via an RS232 output, for example, sensing pressure and temperature in the breathing circuit to determine inhalation or expiration, and/or other parameters.
[0022] The drugs which are typically used in the invention are anti-spasmodic drugs, cardiovascular drugs, corticosteroids, bronchodilators, antibiotics, and/or mucus thinning drugs.

[0023] Referring now to Fig. 2, at step 31, a reference value or control parameter is obtained from the general anesthesia machine RS232 port. The control parameter may either be entered into the general anesthesia machine control panel 26 by a medical professional at step 32, or may be automatically determined by the general anesthesia machine 12 at step 33. Preferably, the control parameter comprises any one of a variety of parameters that are used to control the delivery for the nebulized drug therapy being delivered to the patient. Examples of such a parameter include (1) drug type; (2) information obtained during checkout of the ventilator; (3) patient circuit type; (4) type of ventilator setting; and (5) inspiratory flow rate of the ventilator.

[0024] At step 34, the general anesthesia machine 12 automatically determines the optimal delivery amount and time based upon one or more of the control parameters described above and then automatically controls the function of the nebulizer 19 at step 35. Such automatic control allows the medical professional to provide a selected amount of the aerosolized drug in the most efficient manner possible. The medical professional can also start or stop the dosing period manually at step 36.

[0025] The system can be modified to facilitate optimized nebulization during dosing periods controlled in step 37. Integration of the anesthesia machine and the nebulizer unit or module of the anesthesia machine further allows for automatic modification of general anesthesia delivery in response to operation of the nebulizer function and results such that: (1) bias flow is increased or decreased during periods of nebulizer dosing; (2) inspired breath profiles (e.g. pressure or volume) are modified during periods of nebulizer dosing; (3) inspired flow profiles are modified during periods of nebulizer dosing; (4) inspiratory time (including inspiratory pause) is modified during periods of nebulizer dosing; (5) expiratory time (including expiratory pause) is modified during periods of nebulizer dosing; and/or (6) breath rate is modified during periods of nebulizer dosing.

[0026] In other embodiments, a therapeutic vaporizer can be used instead of the nebulizer or in combination with the nebulizer to deliver vaporized drugs to the patient during general anesthesia. An advantage of a therapeutic vaporizer is that smaller particle sizes can be achieved by vaporization than by nebulization and the concentration of the drugs delivered to the patient can be much more accurate and manageable. A therapeutic vaporizer is a novel optional feature.
of the invention and is not similar to a conventional agent-specific (e.g., desflurane or isoflurane), anesthetic vaporizer of the type which is always included in modern general anesthesia machines.

[0027] While the invention has been described in conjunction with specific embodiments, it is not intended to limit the invention to one embodiment. Thus, the present invention is not intended to be limited to the embodiments described, but is to be accorded the broadest scope consistent with the disclosure set forth herein.
CLAIMS

What is claimed is:

1. A system for delivery of drugs to a patient while connected to a general anesthesia machine comprising (A) a breathing circuit comprising (1) an inhalation tube; (2) an exhalation tube; and (3) a connector having a first side adapted to fluidly connect with the inhalation and exhalation tubes, a second side adapted to fluidly connect with an endotracheal tube or face mask, and a port adapted to connect with a nebulizer machine or a therapeutic vaporizer; (B) a programmable control module to regulate the timing and volume of anesthetic gases and oxygen delivered to the patient; (B) a ventilator; (C) a nebulizer machine comprising at least two interchangeable liquid or aerosolized drug containers or chambers; the nebulizer machine connected to the breathing circuit via the connector port.

2. The system of claim 1 comprising the therapeutic vaporizer which is comprised of one chamber adapted to be filled with one or more different therapeutic agents, the therapeutic vaporizer adapted to deliver a selected concentration or dose of the one or more agents.

3. The system of claim 1 wherein the inhalation tube (2) and exhalation tube (3) are concentric and are fluidly joined at a point near the first side of connector (4) so inhalation gases comprising oxygen, anesthetic gases, and/or aerosolized drugs from the nebulizer machine or therapeutic vaporizer pass through the connector to the face mask or endotracheal tube and exhalation gases from the patient pass through the connector to the exhalation tube.

4. The system of claim 1 wherein the connector (4) is L-shaped and the port adapted to connect to the nebulizer is at the corner of the L.

5. The system of claim 1 further including an HME filter in the breathing circuit.

6. The system of claim 1 further including a recorder to register the frequency, type, amount, and time of drug delivery.

7. The system of claim 1 further including an alarm system for detection of mechanical or drug delivery malfunction.

8. The system of claim 1 wherein the nebulizer comprises a monitor and means to select one to three drugs to be delivered, the amount of each drug to be delivered, the time of delivery of each drug, wherein the monitor comprises means to report the progress and results of the delivery of the one to three drugs.
9. A method of delivering drugs during a general anesthesia procedure while a patient is intubated comprising providing a programmable nebulizer machine or a therapeutic vaporizer fluidly connectable to a breathing circuit of a general anesthesia machine at a point at or near a Y-piece, automatically delivering from one to three drugs at a time to the breathing circuit during controlled times during the respiratory cycle from one to three liquid drug containers or chambers within the nebulizer machine or therapeutic vaporizer, synchronizing the automatic delivery of the drugs to the general anesthesia machine respiratory cycle so as to effectively and efficiently treat or prevent respiratory complications during the general anesthesia procedure.

10. The method of claim 9 comprising connecting the nebulizer or therapeutic vaporizer to the general anesthesia machine via an RS232 output signal from the anesthesia machine, sensing pressure in the breathing circuit, and sensing temperature in the breathing circuit to determine inhalation or expiration.

11. The method of claim 9 wherein the drugs are selected from the group consisting of anti-spasmatic drugs, cardiovascular drugs, corticosteroids, bronchodilators, antibiotics, and mucus thinning drugs.

12. The method of claim 9 further including providing a failure alarm for detection of mechanical or drug delivery malfunction.

13. A system comprising a general anesthesia delivery machine comprising a breathing circuit within which anesthetic gases and oxygen are circulated by a ventilator to a Y-piece which connects the breathing circuit to a face mask or endotracheal tube with which a patient can be intubated, an endotracheal tube or face mask fluidly connected to the general anesthesia machine via the breathing circuit, an HME filter in the breathing circuit, a programmable control module to regulate the timing and volume of anesthetic gases and oxygen delivered to the patient, and means for delivery of aerosolized or vaporized drugs for treatment of or prevention of respiratory complications during general anesthesia comprising a nebulizer or therapeutic vaporizer machine comprising two or more interchangeable liquid or aerosolized drug containers or chambers, a tube fluidly connecting the nebulizer machine or therapeutic vaporizer to the breathing circuit at a point proximal to the Y-piece between the Y-piece and the endotracheal tube or face mask, the nebulizer machine or therapeutic vaporizer programmed to deliver aerosolized drugs controlled times during inhalation.
14. The system of claim 13 comprising a nebulizer machine and a therapeutic vaporizor.

15. The system of claim 13 wherein the therapeutic vaporizor is adapted to vaporize drugs and the nebulizer machine is adapted to aerosolize drugs.
REFERENCE VALUE OR CONTROL PARAMETER IS OBTAINED FROM THE ANESTHESIA MACHINE RS232 PORT 31

CONTROL PARAMETER ENTERED INTO THE ANESTHESIA MACHINE CONTROL PANEL BY A MEDICAL PROFESSIONAL OR MAY BE AUTOMATICALLY DETERMINED BY THE ANESTHESIA MACHINE 33

ANESTHESIA MACHINE AUTOMATICALLY DETERMINES THE OPTIMAL DELIVERY AMOUNT AND TIME BASED UPON ONE OR MORE OF THE CONTROL PARAMETERS 34

ANESTHESIA MACHINE AUTOMATICALLY CONTROLS THE FUNCTION OF THE NEBULIZER 35

MEDICAL PROFESSIONAL CAN ALSO START OR STOP THE DOSING PERIOD MANUALLY 36

Optimized Nebulization During Dosing Periods 37

FIG. 2