

Changes in Altitude Cause Unintended Insulin Delivery From Insulin Pumps

Mechanisms and implications

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OBJECTIVE—Children and adults with type 1 diabetes who receive insulin pump therapy have reported hypoglycemia during air travel. We studied the effects of atmospheric pressure on insulin pump delivery.

RESEARCH DESIGN AND METHODS—Ten insulin pumps were connected to capillary tubes. The effects of changes in ambient pressure on insulin delivery, bubble formation, bubble size, and cartridge plunger movement were analyzed.

RESULTS—During a flight (200 mmHg pressure decrease), excess insulin delivery of 0.623% of the cartridge volume occurred ($P < 0.001$, Student *t* test). In hypobaric chamber studies, bubbles developed in the insulin when the pressure decreased and displaced the insulin out of the cartridge. Pre-existing bubbles changed in size consistent with Boyle law. Cartridge plunger movement did not occur in normal flight conditions but did occur when catastrophic plane depressurization was mimicked.

CONCLUSIONS—Atmospheric pressure reduction causes predictable, unintended insulin delivery in pumps by bubble formation and expansion of existing bubbles.

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A 10-year-old girl with well-controlled type 1 diabetes managed with insulin pump therapy developed recurrent hypoglycemia 60 to 90 min after commencing commercial air travel. Upon direct inquiry, we are now aware of 50 children and adults using insulin pumps who experience this phenomenon.

In 1994, Aanderud et al. (1) demonstrated that insulin pumps delivered “more insulin than the set rate during decompression.” At sea level, the ambient pressure is 760 mmHg (1 atmosphere). When commercial planes ascend to 40,000 feet, the cabin pressure decreases by 200 mmHg to 560 mmHg (cabin pressure equivalent of 8,000 feet) (2). The objective of this study was to investigate the effects of pressure changes during airplane flight on insulin pump delivery.

RESEARCH DESIGN AND METHODS

Five Animas 2020 pumps (IR1200/2020) and five Medtronic Paradigm pumps (1.8 mL cartridge) with 60-cm infusion systems were loaded with aspart insulin at sea level. Basal rates were 1 unit/h, and infusion sets were fixed in a 100 μ L/10 cm microtubule. The canula is open to ambient pressure. The validity of this model is discussed in the Supplementary Data.

Pressure studies

Insulin pumps were placed in a hypobaric chamber at 25°C. Pressure was changed to mimic normal flight in a commercial airliner (depressurization over 20 min) and an abnormal flight with catastrophic decompression.

Insulin delivery from 10 pumps was studied during the flight of a commercial

Boeing 767-338. Results were compared with predictions using Henry law of gas solubility (3).

Bubble study

Twenty syringes were filled with insulin or distilled water (control) and observed for bubble formation as ambient pressure was decreased. Bubbles were then placed in the microtubules and measured with changes in pressure in a hypobaric chamber. The changes were compared with predictions from Boyle law (4).

Plunger movement study

The pressure required to move the cartridge plunger in 5 Animas 2020 pumps was measured. All variables were normally distributed. Statistical significance was determined by using two-tailed Student *t* tests.

RESULTS

Hypobaric chamber studies mimicking airline flight

Ascent from 760 to 560 mmHg. Animas pumps delivered 0.776 units of excess insulin (SD 0.146 [range 0.645–1.04], $P < 0.000001$) and Medtronic pumps delivered 0.709 units excess insulin (0.186 [0.337–0.985], $P < 0.000001$).

Descent from 560 to 760 mmHg. Animas pumps delivered 0.663 units less than expected (SD 0.201 [range 0.37–0.94], $P < 0.000001$) and Medtronic pumps delivered 0.533 units less than expected (0.164 [0.29–0.82], $P < 0.000001$).

Catastrophic depressurization from 760 to 260 mmHg over 1 min. All the pumps delivered insulin due to plunger movement (>8 units delivered).

Airplane flight study

During ascent (ambient pressure decrease), Animas pumps delivered 1.37 (SD 0.09) units excess insulin (0.685% of cartridge volume; $P < 0.001$) and the Medtronic pumps delivered 1.01 (0.14) units excess insulin (0.561% of cartridge volume; $P < 0.001$).

During descent (ambient pressure increased), insulin was sucked back into the

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pump, causing a deficit of 0.87 (SD 0.21) units ($P < 0.01$) for Animas pumps and 0.58 (0.13) units ($P < 0.01$) for Medtronic pumps.

In all studies, the insulin excess or deficit seen was consistent with predictions of bubble volume due to pressure changes using Henry law (Fig. 1). There was no statistical difference between Animas and Medtronic when abnormal delivery was considered as a percentage of insulin volume.

Bubble study

Gas bubbles appeared in all the syringes when the pressure decreased by 50 mmHg. The bubbles disappeared when the pressure was returned to 760 mmHg. Air bubbles in the microtubules changed in size when pressure changed, consistent with Boyle law (4) (Supplementary Fig. A1).

Plunger movement study

The Animas cartridge plunger moved when the pressure was decreased by 273.48 mmHg (SD 25.39 [range 228–303.8]), equivalent to atmospheric pressure of 486.52 mmHg.

CONCLUSIONS—We demonstrated that decreases in ambient pressure cause predictable unintended insulin delivery by two independent mechanisms. The first mechanism is due to air coming out of solution and forming bubbles when pressure decreases. Air dissolves in

water proportional to ambient pressure (3). As airplanes ascend, ambient pressure decreases and air comes out of solution, forming bubbles. The bubbles displace insulin in a pump, causing excess delivery. The larger the volume of insulin, the more bubbles will form, displacing insulin. As the airplane descends, air pressure increases again and the bubbles redissolve, which stops insulin delivery until the deficit is “replaced.” If air bubbles are removed before descent, then the pump will deliver normally because water is not compressible.

The second mechanism of unintended insulin delivery is due to expansion of existing bubbles in the cartridge before takeoff. These bubbles will increase in size by 36%, displacing insulin during ascent (4).

Excess insulin delivered during ascent in an airplane may cause hypoglycemia 1–2 h later. Hyperglycemia may follow due to decreased insulin delivery during descent. Whether abnormalities in insulin delivery during flight cause clinical effects depend on factors such as insulin sensitivity, current glycemic control, food intake, and pump settings, among others.

The U.S. Food and Drug Administration requires that insulin pump mechanical function is not affected by “changes in ambient pressure which would reasonably be expected to be encountered according to the intended use of the device” (5). Built-in features of insulin pumps designed to prevent plunger movement are discussed in the Supplementary Data.

We demonstrated that changes in ambient pressure during commercial flights did not affect insulin pump mechanical function. Plungers may potentially move, however, causing insulin overdose with massive, rapid depressurization that occurs 40–50 times worldwide per year (6).

We recommend for flights:

- 1) The cartridge should only contain 1.5 mL of insulin.
- 2) Disconnect the pump before takeoff.
- 3) At cruising altitude, take the cartridge out of the pump and remove any air bubbles before reconnecting.
- 4) After the airplane lands, disconnect the pump and prime the line with 2 units. Then reconnect the pump.
- 5) During flight emergencies involving cabin decompression, disconnect the insulin pump.

Insulin pumps deliver excess insulin as ambient pressure decreases, which may cause hypoglycemia. We observed three mechanisms to explain this phenomenon.

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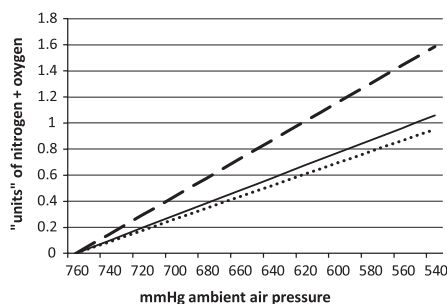


Figure 1—Henry law (3) was used to calculate the predicted volume of nitrogen and oxygen that comes out of solution from 1.8 (dotted line), 2 (solid line), and 3 mL (dashed line) of water when ambient pressure decreases from 760 to 560 mmHg at 25°C. In a pump cartridge, this gas would displace the insulin in the cartridge causing insulin delivery (1 unit = 10 μ L). A linear relationship exists between the ambient pressure and the amount of gas that comes out of solution. Larger fluid volumes cause larger volumes of insulin to be delivered.