

INDIANAPOLIS, Indiana — Women taking oral contraceptives are at significantly increased risk of developing altitude sickness and are less likely to respond to treatment compared with those not on the pill, according to preliminary research.

The study, the first of its kind, was presented here at the American College of Sports Medicine 60th Annual Meeting.

"We found that oral contraceptive use places individuals at an increased risk for developing acute mountain sickness," said lead investigator Michael Harrison, MD, who conducted the research at the Mayo Clinic, in Rochester, Minnesota. "Using acetazolamide prophylactically actually doesn't provide any benefit in this small population," he added.

Among 70 female workers traveling by plane from sea level to a high altitude, 13 were on oral contraceptives. The trip took the study cohort to the South Pole at an altitude of approximately 3200 meters.

During the first 7 days, the researchers found the majority of the women, 85% on oral contraceptives experienced acute mountain sickness compared with 51% of the remaining workers ($P = .04$).

Acetazolamide improved symptoms for about half of the people feeling sick, but it did not help any of the women on oral contraceptives ($P = .03$).

The possible mechanism, Dr. Harrison speculated, is progesterone, which has been considered in the past as playing a role in altitude sickness due to its association with factors including anti-inflammatory properties, respiratory smooth muscle relaxation, ventilatory stimulation, and antidiuretic characteristics.

Progesterone a Factor

"Our thought was that if subtle changes are causing acute mountain sickness, we should look at people who are on a medication that affects progesterone," explained Dr. Harrison, now affiliated with the Henry Ford Hospital, in Detroit, Michigan. "Oral contraceptive is an obvious one because it stabilizes the progesterone level, decreases what's circulating, and eliminates the progesterone peak that goes along with ovulation."

Baseline measurements from the women showed that, as would be expected, those in the oral contraception group had significantly lower progesterone levels at sea level compared with nonusers ($0.7 \text{ ng/mL} \pm 0.5$ vs $3.2 \text{ ng/mL} \pm 4.6$) and at the higher altitude ($0.7 \text{ ng/mL} \pm 0.7$ vs $3.1 \text{ ng/mL} \pm 4.6$).

In addition to the differences in acute mountain sickness and acetazolamide response, the women in the oral contraception group also had different blood pressure responses to the altitude exposure, with higher mean arterial pressures at the high altitude compared with the nonusers.

Dr. Harrison underscored that, while the preliminary study was small, an important strength that sets it apart from many previous studies is that there was consistency in the participants' rate of ascent.

"We controlled the mode and duration of travel to altitude," he explained. "All of our participants traveled in the same fashion to the same altitude — 3 to 4 hours unpressurized flight after approximately 14 days of acclimatization at sea level."

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This is important because numerous references suggest rate of ascent and manner, such as exhausting hike or leisurely drive, can affect the development of acute mountain sickness," Dr. Harrison pointed out.

The availability of blood samples provided essential data. "We collected two blood samples, at sea level and altitude, and analyzed an extensive set of variables from these samples," he added.

In follow-up work looking at possible prophylactic alternatives, Dr. Harrison and his team plan to evaluate spironolactone.

"The only other medication aside from acetazolamide that has been beneficial for acute mountain sickness that acts in the kidneys has been spironolactone, an inhibitor of aldosterone," he said.

High-altitude-medicine expert Andrew Luks, MD, said the findings raise some intriguing questions, but that women would probably be ill-advised to stop taking oral contraception to avoid mountain sickness.

Given its small size and relatively unique setting — flying by plane to Antarctica, Dr. Luks added, "I would not take the results as a reason to recommend against oral contraceptive use in women traveling to high altitude."

He pointed out that, in addition to higher numbers of participants, future studies should include diverse settings. "The way the study is set up, it may not be generalizable to a wider population of women," Dr. Luks said.

"I think you need to see a larger study in a different setting such as among trekkers in Nepal," he added, "before you would think about making any recommendations for women to change or stop their oral contraceptive use prior to any high altitude travel."

Dr. Harrison has disclosed no relevant financial relationships. Dr. Luks is the lead author on the Wilderness Medical Society's altitude illness guidelines.

American College of Sports Medicine (ACSM) 60th Annual Meeting: Abstract 2709. Presented June 1, 2013.