The effects of altitude/hypoxic training on oxygen delivery capacity of the blood and aerobic exercise capacity in elite athletes – a meta-analysis

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INTRODUCTION

Since the 1968 Mexico City Olympics, studies have been conducted to perform training in altitude/hypoxic environment for the enhanced performance of athletes; currently, these training methods are commonly being applied to many athletes and coaches. In the past, training in altitude/hypoxic environment was only performed at high altitude areas, including Chamonix in France, Albuquerque in United States, and Kunming in China; however, a variety of artificial altitude/hypoxic environment (normobaric hypoxia, hypobaric hypoxia) equipment, such as hypoxic masks, hypoxic tents, hypoxic trucks, hypoxic hotels, and hypoxic training centers have been developed since the 1990s.

The performance at sea-level can be improved by 3 ways through the training in both natural and artificial altitude/hypoxic environments. Living High Training High (LHTH), was the first design of living and training at 1500 - 4000 m in the natural altitude environments that enhance Red Blood Cell (RBC) count, Hemoglobin (Hb) concentration, Hematocrit (Hct), Maximal Oxygen Consumption (VO2max), and aerobic exercise capacity. Several studies demonstrated that altitude/hypoxic acclimation (e.g., increased RBC count and Hb concentration) and sea-level training (i.e., maintenance of training intensity). In addition, many elite-athletes in other countries plan to participate in the training camps in altitude environments such as Albuquerque in United States, Kunming in China, and Chamonix in France. However, LHTH has a major limitation, which is failure to perform training of the same intensities (e.g., running speed), as compared with sea-level training. Buskirk et al. reported that the collegiate distance runners who completed 880 yard, 1 mile, and 2 mile runs in the LHTH decreased by 3 - 8 % in exercise performance. Moreover, several studies demonstrated that absolute training intensity during continuous and interval workout was significantly decreased at 2500 m, as compared with sea-level.

The living high training low (LHTL) was developed by Dr. Benjamin Levine and James Stray-Gundersen of the United States in the early 1990s, as a potential modification to the limitation of LHTH. Basically, LHTL simultaneously offers athletes the beneficial effects of altitude/hypoxic acclimation (e.g., increased RBC count and Hb concentration) and sea-level training. In addi-
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METHODS

Study design

This study determined effectiveness of natural altitude and artificial hypoxic training based on the results of oxygen delivery capacity of the blood (e.g., RBC, Hb, Hct, and EPO) and aerobic exercise capacity (e.g., VO2max) in Korean athletes through meta-analysis.

Reference search and data extraction

All relevant studies in systematic reviews and meta-analyses via PICO (Participants, Interventions, Comparisons, Outcomes, and Study Design) on the Cochrane guidelines were selected. Furthermore, for the systematic review and aggregate data meta-analysis using by PRISMA flowchart with 5 phases, we considered eligible studies that investigated the effects on oxygen delivery capacity of the blood and aerobic exercise capacity in altitude/hypoxic environments.

We identified relevant studies through a database of Research Information Service System (RISS), Korean studies Information Service System (KISS), and National Assembly Library (NANET) without any publication year restriction until December 15, 2015. We further identified studies for confidence by reviewing the reference lists of KCI in the field to identify published data only (Figure 1). We used 161 citations to collect information on the following: hypoxic exercise, hypoxic training, hypobaric exercise, hypoxic training, altitude exercise, and altitude training. From a total of 161 eligible studies identified, 85 were included in the aggregate data meta-analysis and 76 were excluded due to the overlapping study designs after title/abstract scan. In addition, 60 that were not relevant determinants or out-

Figure 1. PRISMA chart of the search and study inclusion process
come data for enhanced athletic performance were excluded. Thus, 25 retrieved selected full texts were reviewed so that the excluded were as follows: not elite athletes (e.g., healthy humans, the elderly, and patients), no control group, not relevant dependent variables on oxygen delivery capacity of the blood and aerobic exercise capacity, and no data used in the meta-analyses (e.g., mean, standard deviation, and sample size). Therefore, based on study characteristics of 161 references initially identified, 8 were included in the aggregate meta-analysis.

Characteristics and variables of selected references

The 8 selected references were classified according to authors, published year, characteristics of subjects, number of subjects, and altitude/hypoxic environments training (e.g., type, duration, and frequency) (Table 1) and the number of subjects were 156 subjects (exercise group: 82 and control group: 74). All studies were conducted on elite athletes: 1 of high school soccer players, 2 of high school track players, 1 of national level fin swimmers, 1 of collegiate tennis players, 1 of national level swimmers, 1 of collegiate track players, and 1 of collegiate basketball players. Additionally, types of altitude/hypoxic environments training consisted of 2 LHTH, 1 LHTL, and 5 LLTH.

Of these 8 studies, meta-analyses included 8 oxygen delivery capacity of the blood (e.g., RBC, Hb, and Hct), 5 EPO, and 7 aerobic exercise capacity, in order to determine the comprehensive efficacy of oxygen delivery capacity of the blood and aerobic exercise capacity in altitude/hypoxic environments training for the enhanced athletic performance.

### RESULTS

The effect of altitude/hypoxic training on oxygen delivery capacity of the blood

Eight studies were selected for the effect of altitude/hypoxic training on RBC, Hb, Hct and 5 studies for the effect of altitude/hypoxic training on EPO. Among oxygen deliv-
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ery capacity of the blood, heterogeneity was identified in RBC (Q-value = 106.578, \(p = .000\), \(I^2 = 93.432\)) and effect size calculated by random effect model. Elite athletes in the altitude/hypoxic training group improved their RBC by \(4.499 \times 10^5\) cell/\(\mu l\) (95% CI: 2.469 - 6.529, \(p = .000\)) more than the sea-level training group (Table 2). Heterogeneity was also identified in Hb (Q-value = 119.043, \(p = .000\), \(I^2 = 94.120\)) and effect size calculated by random effect model. Elite athletes in the altitude/hypoxic training group improved their Hb by 5.447 g/dl (95% CI: 3.028 - 7.866, \(p = .000\)) more than the sea-level training group (Table 3). Likewise, heterogeneity was identified in Hct (Q-value = 104.973, \(p = .000\), \(I^2 = 94.120\)) and effect size calculated by random effect model. Elite athletes in the altitude/hypoxic training group improved their Hct by 3.639% (95% CI: 1.687 - 5.591, \(p = .000\)) more than the sea-level training group (Table 4). However, in EPO, homogeneity was identified (Q-value = 2.115, \(p = .715\), \(I^2 = .000\)) and effect size calculated by fixed effect model. Elite athletes in the altitude/hypoxic training group improved their EPO by

### Table 2. Effects of altitude/hypoxic training vs. sea-level training on RBC (10^5 cell/\(\mu l\)).

| Model               | Study name            | Std diff in means | standard error | variance | Lower limit | Upper limit | Z-value | p-value |
|---------------------|-----------------------|-------------------|----------------|----------|-------------|-------------|---------|---------|
| Sunoo et al. (2007) | 1.453                 | 0.491             | 0.241          | 0.490    | 2.415       | 2.958       | 0.003   |         |
| Shin and Cho (2003) | 31.752                | 5.635             | 31.756         | 20.707   | 42.797      | 5.635       | 0.000   |         |
| Yun and Lee (2014)  | 2.832                 | 0.708             | 0.501          | 1.445    | 4.219       | 4.003       | 0.000   |         |
| Park et al. (2011)  | 7.062                 | 1.203             | 1.447          | 4.705    | 9.420       | 5.871       | 0.000   |         |
| Sunoo and Hwang (2004) | 0.761              | 0.536             | 0.287          | -0.289   | 1.811       | 1.420       | 0.156   |         |
| Sunoo et al. (2005) | 2.292                 | 0.607             | 0.368          | 1.103    | 3.482       | 3.778       | 0.000   |         |
| Jung et al. (2004)  | 0.632                 | 0.458             | 0.210          | -0.266   | 1.531       | 1.380       | 0.168   |         |
| Kim et al. (2009)   | 15.891                | 2.085             | 4.348          | 11.804   | 19.978      | 7.621       | 0.000   |         |
| Random              | 4.499                 | 1.036             | 1.073          | 2.469    | 6.529       | 4.343       | 0.000   |         |

Heterogeneity: Q-value=106.572(\(p=.000\)), \(I^2=93.432\)

### Table 3. Effects of altitude/hypoxic training vs. sea-level training on Hb (g/dl).

| Model               | Study name            | Std diff in means | standard error | variance | Lower limit | Upper limit | Z-value | p-value |
|---------------------|-----------------------|-------------------|----------------|----------|-------------|-------------|---------|---------|
| Sunoo et al. (2007) | 4.834                 | 0.864             | 0.747          | 3.140    | 6.528       | 5.929       | 0.000   |         |
| Shin and Cho (2003) | 7.217                 | 1.370             | 1.878          | 4.531    | 9.903       | 5.267       | 0.000   |         |
| Yun and Lee (2014)  | 3.726                 | 0.827             | 0.684          | 2.105    | 5.347       | 4.506       | 0.000   |         |
| Park et al. (2011)  | 2.285                 | 0.575             | 0.331          | 1.158    | 3.412       | 3.974       | 0.000   |         |
| Sunoo and Hwang (2004) | 0.222              | 0.519             | 0.270          | -0.795   | 1.240       | 0.428       | 0.669   |         |
| Sunoo et al. (2005) | 1.102                 | 0.506             | 0.256          | 0.111    | 2.094       | 2.178       | 0.029   |         |
| Jung et al. (2004)  | 0.899                 | 0.469             | 0.220          | -0.021   | 1.819       | 1.916       | 0.055   |         |
| Kim et al. (2009)   | 56.258                | 7.272             | 52.888         | 42.004   | 70.511      | 7.736       | 0.000   |         |
| Random              | 5.447                 | 1.234             | 1.523          | 3.028    | 7.866       | 4.414       | 0.000   |         |

Heterogeneity: Q-value=119.043(\(p=.000\)), \(I^2=94.120\)

### Table 4. Effects of altitude/hypoxic training vs. sea-level training on Hct (%).

| Model               | Study name            | Std diff in means | standard error | variance | Lower limit | Upper limit | Z-value | p-value |
|---------------------|-----------------------|-------------------|----------------|----------|-------------|-------------|---------|---------|
| Sunoo et al. (2007) | 4.834                 | 0.864             | 0.747          | 3.140    | 6.528       | 5.929       | 0.000   |         |
| Shin and Cho (2003) | 7.217                 | 1.370             | 1.878          | 4.531    | 9.903       | 5.267       | 0.000   |         |
| Yun and Lee (2014)  | 3.726                 | 0.827             | 0.684          | 2.105    | 5.347       | 4.506       | 0.000   |         |
| Park et al. (2011)  | 2.285                 | 0.575             | 0.331          | 1.158    | 3.412       | 3.974       | 0.000   |         |
| Sunoo and Hwang (2004) | 0.222              | 0.519             | 0.270          | -0.795   | 1.240       | 0.428       | 0.669   |         |
| Sunoo et al. (2005) | 1.102                 | 0.506             | 0.256          | 0.111    | 2.094       | 2.178       | 0.029   |         |
| Jung et al. (2004)  | 0.899                 | 0.469             | 0.220          | -0.021   | 1.819       | 1.916       | 0.055   |         |
| Kim et al. (2009)   | 56.258                | 7.272             | 52.888         | 42.004   | 70.511      | 7.736       | 0.000   |         |
| Random              | 3.639                 | 0.996             | 0.992          | 1.687    | 5.591       | 3.654       | 0.000   |         |

Heterogeneity: Q-value=104.973(\(p=.000\)), \(I^2=93.332\)
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0.711 mU/mL (95% CI: 0.282 - 1.140, p = .001) more than the sea-level training group (Table 5).

The effect of altitude/hypoxic training on the aerobic exercise capacity

Seven studies were selected for the effect of altitude/hypoxic training on VO2max. Heterogeneity was identified in VO2max (Q-value = 56.328, p = .000, I² = 89.348) and effect size calculated by random effect model. Elite athletes in the altitude/hypoxic training group improved their VO2max by 1.637 ml/kg/min (95% CI: 0.599 - 1.400, p = .000) more than the sea-level training group (Table 6).

DISCUSSION

A number of studies have been conducted on the effect of altitude/hypoxic training on oxygen delivery capacity of the blood and aerobic exercise capacity. These studies reported inconsistent results (positive and negative results) due to difference in physiological characteristics and training conditions (method, intensity, frequency, duration, and time of training)56. Altitude/hypoxic environments training has positive effects on VO2max, oxygen consumption (VO2), maximum ventilation, Hb, EPO, area of capillary blood vessel, 2,3-diphosphoglycerate (DPG), density of mitochondria, storage of glycogen, muscle buffer capacity, lactate threshold, strength and power, psychological limitation, hypoxic inducible factor (HIF)-1, vascular endothelial growth factor (VEGF), and glycolysis enzyme14, 22, 29, 35, 42, 47, 49. Together with positive effects, altitude/hypoxic environments training leads to negative effects on blood viscosity, muscle blood flow, cardiac output, HRmax, protein synthesis, and Na⁺-K⁺-ATPase activity, and decreases training quality and quantity5, 21, 28, 31. These controversial effects are dependent on sports event, performance level, support of nutrition and medical, fatigue level, training type, physiological state, psychological state of subject, and lead to inconsistent of study results.

Due to these positive or negative effects of altitude/hypoxic environments training, athletes, coaches, trainers, and researchers have continued argument about effect in oxygen delivery capacity of the blood and aerobic exercise capacity. In this study, we accordingly conducted meta-analysis on 8 research studies with elite athletes in Korea to verify practical applicability of altitude/hypoxic environments training, and propose the direction of training system development for athletic performance. Our results indicated that altitude/hypoxic environments training is more efficient than sea-level training in terms of oxygen delivery capacity of the blood (RBC, Hb, Hct, EPO) and aerobic exercise capacity (VO2max). Although, training type, exercise intensity, frequency, and duration were different in 8 research studies for meta-analysis, the result shows that training of more than 3 weeks, 3 times a week, and 1 hour can improve oxygen delivery capacity of the blood and aerobic exercise capacity. Also, the result is in agreement with previous meta-analysis studies that report-

Table 5. Effects of altitude/hypoxic training vs. sea-level training on EPO (mU/mL).

| Model     | Study name           | Std diff in means | standard error | variance | Lower limit | Upper limit | Z-value | p-value |
|-----------|----------------------|-------------------|----------------|----------|-------------|-------------|---------|---------|
| Sunoo et al. (2007) | 0.369 | 0.441 | 0.194 | -0.495 | 1.233 | 0.837 | 0.402 |
| Yun and Lee (2014) | 1.210 | 0.544 | 0.296 | 0.144 | 2.275 | 2.224 | 0.026 |
| Park et al. (2011) | 0.958 | 0.472 | 0.223 | 0.032 | 1.883 | 2.029 | 0.042 |
| Sunoo and Hwang (2004) | 0.384 | 0.522 | 0.273 | -0.639 | 1.408 | 0.736 | 0.462 |
| Sunoo et al. (2005) | 0.752 | 0.488 | 0.238 | -0.204 | 1.708 | 1.542 | 0.123 |
| Fixed     | 0.711 | 0.219 | 0.048 | 0.282 | 1.140 | 3.251 | 0.001 |

Heterogeneity: Q-value=2.115(p=.715), I²=0.000

Table 6. Effects of altitude/hypoxic training vs. sea-level training on VO2max (ml/kg/min).

| Model     | Study name           | Std diff in means | standard error | variance | Lower limit | Upper limit | Z-value | p-value |
|-----------|----------------------|-------------------|----------------|----------|-------------|-------------|---------|---------|
| Sunoo et al. (2007) | 0.171 | 0.438 | 0.192 | -0.687 | 1.029 | 0.390 | 0.697 |
| Shin and Cho (2003) | 0.313 | 0.503 | 0.253 | -0.673 | 1.299 | 0.622 | 0.534 |
| Yun and Lee (2014) | 1.425 | 0.560 | 0.313 | 0.328 | 2.523 | 2.546 | 0.011 |
| Sunoo and Hwang (2004) | 0.585 | 0.528 | 0.279 | -0.451 | 1.620 | 1.106 | 0.269 |
| Sunoo et al. (2005) | 0.200 | 0.473 | 0.223 | -0.726 | 1.126 | 0.423 | 0.672 |
| Jung et al. (2004) | 2.832 | 0.633 | 0.401 | 1.592 | 4.073 | 4.475 | 0.000 |
| Kim et al. (2009) | 7.232 | 1.005 | 1.011 | 5.262 | 9.202 | 7.194 | 0.000 |
| Random     | 1.637 | 0.641 | 0.411 | 0.381 | 2.894 | 2.554 | 0.011 |

Heterogeneity: Q-value=56.328(p=.000), I²=89.348
ed altitude/hypoxic environment training enhances aerobic exercise capacity and performance through increase of RBC mass, Hb mass and VO2max and exposure of altitude/hypoxic environment increases Hb mass in 2 weeks and improves aerobic exercise capacity and performance. An increase in investment by administration department for various types of altitude/hypoxic environments training facility (e.g., hypobaric/hypoxic lodging, hotel, mask, training truck, training center etc.) is needed for improved aerobic exercise capacity and performance among elite athletes in Korea. In addition, members of the athletic community including athletes, managers, and coaches should change the perception of altitude/hypoxic training and apply to elite athletes. Currently, U.S.A. has established Colorado Altitude Training (CAT) and possesses hypoxic tent, hypoxic hotel, hypoxic room, hypoxic swimming pool, hypobaric and hypoxic training center. Through altitude/hypoxic training in the facilities, long distance speed skating team in 2002 Salt Lake City Winter Olympic & 2006 Torino Winter Olympic and marathon team in 2004 Athens Olympic reported unprecedented success. Japan also has founded Japan Institute for Sports Science (JISS) in 2002 and possesses hypoxic room, hypoxic swimming pool, and hypobaric/hypoxic training center. In Japan, various events’ athletes have conducted hypobaric/hypoxic training and maintained high athletic performance since the 2004 Athens Olympics. These facts prove that investment in altitude/hypoxic training facility and efforts to apply altitude/hypoxic training are required acutely for increase of elite athletes and national competitiveness in sports.

Detail examination of previous studies applied in a meta-analysis reveals that elite athletes’ events are different (high school soccer players, high school runners, national team level pin swimmers, college runners, college basketball players) and applied altitude/hypoxic environments training type are also distinguished into 2 studies of LHTH, 1 study of LHTL, and 5 studies of LLTH. Therefore, in results of meta-analysis, variables except EPO showed heterogeneity of effect sizes. The results indicated that altitude/hypoxic environment training is more efficient than sea-level training in terms of oxygen delivery capacity of the blood and aerobic exercise capacity, but they cannot explain altitude/hypoxic environments training type, exercise intensity, frequency, and duration for increase of athletic performance. Therefore, meta-analysis should be conducted for various dependent variables, aerobic exercise capacity, and athletic performance after classification according to altitude/hypoxic environment training type and athletes’ event in previous Korean and other studies. These efforts would identify the most effective altitude/hypoxic environment training for increased oxygen delivery capacity of the blood, aerobic exercise capacity, and athletic performance.

CONCLUSIONS

This study was designed as a meta-analysis of randomized controlled trials comparing effectiveness of altitude/hypoxic training versus sea-level training on oxygen delivery capacity of the blood and aerobic exercise capacity of elite athletes in Korea. It comprised a five step process of the PRISMA flowchart after setting the selection criteria for the study based on PICOS introduced in the Cochrane guideline. Homogeneity was identified in EPO but heterogeneity was identified in RBC, Hb, Hct, and VO2max due to difference in the pattern of sporting event and altitude/hypoxic training type between each study. RBC, Hb, Hct, EPO, and VO2max were significantly increased following altitude/hypoxic training, as compared with sea-level training. For elite athletes in Korea, altitude/hypoxic training appears more effective than sea-level training for improvement of oxygen delivery capacity of the blood and aerobic exercise capacity. Therefore, increased investment in the various altitude/hypoxic training facilities (hypobaric and hypoxic room, hotel, mask, training truck, training center), change of awareness and application of altitude/hypoxic training are needed for improvement of athletic performance in elite athletes.

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