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Comparing Prevention Efficacy of Different Medicines for Acute Mountain Sickness: A Network Meta-analysis

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Purpose

To compare the efficacy of different medicines in the prevention of acute mountain sickness (AMS).

Methods

We searched PubMed, Embase, Clinicalkey, and Cochrane Library for randomized controlled trials (RCTs). According to 2014 Wilderness Medical Society Practice Guidelines, inclusion criteria about the ascent profile in moderate-to-high risk for AMS were: (1) ascending form < 1200 m to > 2800 m in 1 day (2) ascending > 500 m/d at altitudes above 3000 m. Study subjects were healthy adults aged 18-65 and had no history of AMS. We applied a Microsoft-Excel-based tool called NetMetaXL, which provided an interface for conducting a Bayesian network meta-analysis with WinBUGS.

Main Outcome Measure

The outcome measure was the incidence of AMS based on 2018 Lake Louise AMS score. A total score ≥ 3, in the presence of a headache, was considered diagnostic for AMS.

Results

5 RCTs and 838 subjects were included (Table 1). A Cochrane risk-of-bias tool was used to assess these RCTs (Figure 1). In pairwise comparisons between 8 arms (Figure 2), the trend of lower AMS incidence compared with placebo had showed as odds ratio(OR) and 95% credible interval(CRI). However, the study showed that oral 50mg spironolactone BID does not prevent AMS(Table 2). There were no significant differences about AMS incidence between oral 125mg acetazolamide BID and 250mg acetazolamide BID: 0.29(0.05-1.55). The surface under the cumulative ranking curve area(SUCRA, Table 3) and Rankogram (Figure 3) of 8 arms showed that the best choice is oral 125mg acetazolamide BID (0.8807), and the worst choice was oral 50mg spironolactone BID (0.04869).

Characteristic	Number
Number of Interventions	8
Number of Studies	5
Total Number of Subjects in Network	838
Total Number of Events in Network	215
Total Possible Pairwise Comparisons	28
Total Number Pairwise Comparisons With Direct Data	12
Number of Two-arm Studies	2
Number of Multi-Arms Studies	3
Number of Studies With No Zero Events	5
Number of Studies With At Least One Zero Event	0
Number of Studies with All Zero Events	0

Table 1. Network Characteristics

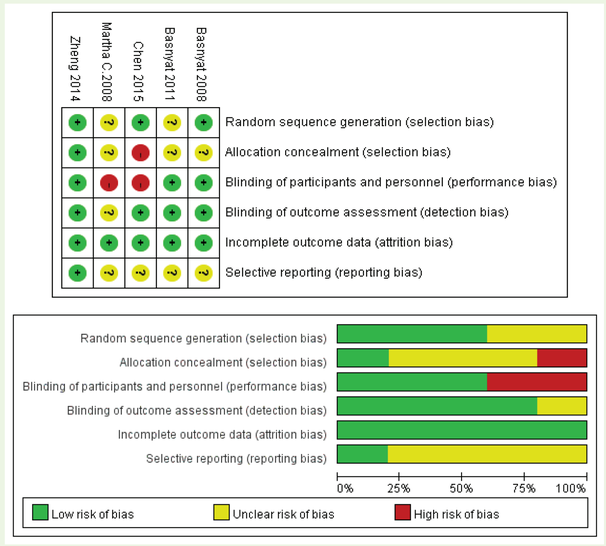

Figure 1. Risk of bias

Drug	Abbreviation
Oral 50mg Spironolactone BID	A
Oral 250mg Acetazolamide BID	B
Placebo	C
Inhaled 200μg Budesonide BID	D
Oral 4mg Dexamethasone BID	E
Oral 25μg Procaterol BID	F
Inhaled 160μg Budesonide/ 4.5μg Formoterol BID	G
Oral 125mg Acetazolamide BID	H

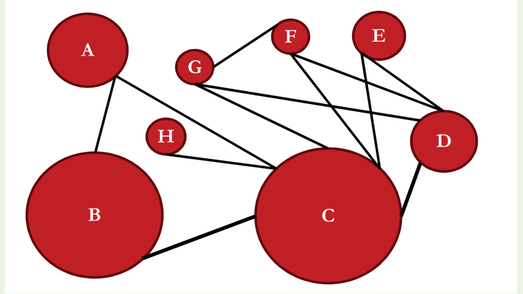

Figure 2. Network Diagram

OR <1 Means the Treatment in Top Left is Better

Oral 125 mg Acetazolamide BID							
0.70 (0.10 – 4.25)	Inhaled 200 μg Budesonide BID						
0.46 (0.06 – 3.06)	0.64 (0.20 – 2.11)	Oral 4 mg Dexamethasone BID					
0.29 (0.05 – 1.55)	0.41 (0.12 – 1.36)	0.63 (0.16 – 2.42)	Oral 250 mg Acetazolamide BID				
0.27 (0.03 – 2.20)	0.38 (0.09 – 1.54)	0.60 (0.11 – 3.09)	0.94 (0.19 – 4.63)	Oral 25 μg Procaterol BID			
0.26 (0.03 – 2.05)	0.38 (0.09 – 1.50)	0.58 (0.10 – 3.07)	0.91 (0.19 – 4.47)	0.97 (0.23 – 4.25)	Inhaled 160 μg Budesonide/ 4.5 μg Formoterol BID		
0.12 (0.02 – 0.56)	0.17 (0.06 – 0.45)	0.27 (0.08 – 0.83)	0.42 (0.20 – 0.89)	0.45 (0.11 – 1.85)	0.46 (0.11 – 1.82)	Placebo	
0.08 (0.01 – 0.48)	0.11 (0.03 – 0.43)	0.17 (0.04 – 0.76)	0.27 (0.10 – 0.73)	0.29 (0.05 – 1.63)	0.29 (0.05 – 1.61)	0.63 (0.24 – 1.69)	Oral 50mg Spironolactone BID

Table 2. League Table(OR and 95% CRI)

Treatment	SUCRA
Oral 125 mg Acetazolamide BID	0.8807
Inhaled 200 μg Budesonide BID	0.8428
Oral 4 mg Dexamethasone BID	0.6628
Oral 250 mg Acetazolamide BID	0.4909
Oral 25 μg Procaterol BID	0.4616
Inhaled 160 μg Budesonide/ 4.5 μg Formoterol BID	0.4518
Placebo	0.1607
Oral 50 mg Spironolactone BID	0.04869

Table 3. SUCRA

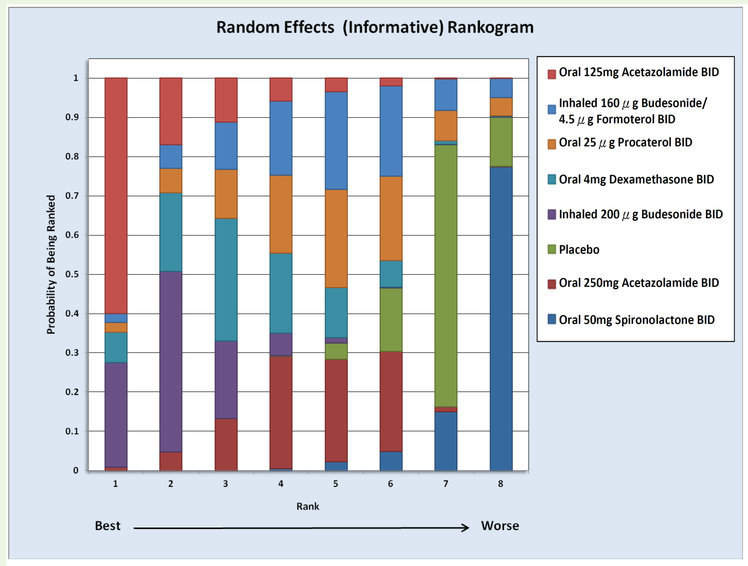

Figure 3. Rankogram

Conclusion

The standard medicines used for prevent AMS are acetazolamide and dexamethasone, however, other options such as ginkgo or ibuprofen can not be included in the study because of the criteria setting.