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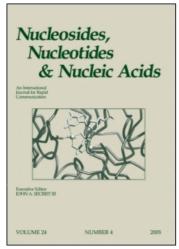
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Hypoxanthine Effects on Cyclic AMP Levels in Human Lymphocytes

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Hypoxanthine Effects on Cyclic AMP Levels in Human Lymphocytes

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ABSTRACT

We have measured hypoxanthine effect on cAMP levels in PBL in basal conditions (no agonist), and with the addition of 2-(p- [2-carboxyethyl] phenylethylamino)-5'-N-ethylcarboxamidoadenosine (CGS-21680, a specific A2 receptor agonist). We have found that hypoxanthine, at 25 μ M and 50 μ M concentrations, increases cAMP levels in PBL in basal and A2 agonist stimulated conditions.

Key Words: Hypoxanthine; Lesch-Nyhan; HPRT; Adenosine receptor.

INTRODUCTION

We have reported that hypoxanthine excess causes inhibition of adenosine transport in peripheral blood lymphocytes (PBL). Decrease adenosine transport could lead to accumulation of extra-cellular adenosine that binds to adenosine A2_A receptors and increases intra cellular cAMP production. We have tested this hypothesis by measuring hypoxanthine effect on cAMP levels in PBL.

1181

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Torres et al.

Table 1. Effect of hypoxanthine on cAMP levels in PBL.

Hypoxanthine (μM)	cAMP (fmol/10 ⁶ cells)	p vs. 5 μM	p vs. 0 μM
BASAL			
5	15 ± 5		
25	60 ± 10	P < 0.005	
50	74 ± 10	P < 0.005	
+ CGS 21680 5 μM			
5	601 ± 11		
25	705 ± 10	P < 0.001	
50	723 ± 10	P < 0.001	
+ CGS 21680 25 μM			
0	630 ± 24		
5	669 ± 32		NS
25	970 ± 27	P < 0.005	P < 0.0001

METHODS

Hypoxanthine effect on cAMP levels in PBL were tested: a) in basal conditions (no agonist) or b) with the addition of 2-(p- [2-carboxyethyl] phenylethylamino)-5'-N-ethylcarboxamidoadenosine (CGS-21680, a specific A2 receptor agonist) at 5 μM and 25 μM concentrations. Different hypoxanthine concentrations (0, 5, 25 or 50 μM) were added and cells incubated for 60 min at 37°C. Quantification of cAMP levels was determined using a commercially available enzyme-immunoassay kit (cAMP Biotrack, Amersham Biosciences).

RESULTS

Results are shown in Table 1. Basal cAMP levels were significantly increased with the addition of 25 μM and 50 μM hypoxanthine versus 5 μM hypoxanthine. cAMP levels in PBL stimulated with 5 μM CGS 21680 were significantly increased with the addition of 25 μM and 50 μM hypoxanthine versus 5 μM hypoxanthine. In PBL stimulated with 25 μM CGS 21680, no significant differences were found between cAMP levels with the addition of 5 μM hypoxanthine, or without hypoxanthine. However, 25 μM hypoxanthine caused a significant increase in cAMP levels compared with basal or 5 μM hypoxanthine concentrations.

CONCLUSIONS

Hypoxanthine, at 25 μ M and 50 μ M concentrations, increases cAMP levels in PBL in basal and A2 agonist stimulated conditions. Thus, increased hypoxanthine levels as excreted by HPRT deficient cells, [1,2] may decrease adenosine transport and lead to accumulation of extra-cellular adenosine that binds to adenosine A2_A receptors and increases cAMP production.

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