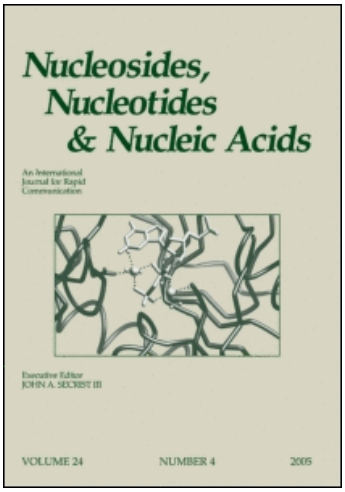

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Hypoxanthine Effects on Cyclic AMP Levels in Human Lymphocytes

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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 μM and 50 μM 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.

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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 μM and 50 μM 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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