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Utility of urinary prostaglandins(DM, D2, F2α) & N-methyl histamine(NMH) measurements across mast cell disorders

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INTRODUCTION

- Mast cell disorders (MCDs) are a heterogeneous group of conditions comprising:
  - Systemic or cutaneous Mastocytosis, (SM,CM)
  - monoclonal mast cell activation syndrome (MMCAS),
  - non-clonal mast cell activation syndrome (nc-MCAS) and
  - hereditary alpha tryptasemia (HαT). – first described 2014
- Serum tryptase is stable & usually raised in SM, MMCAS and HαT but often normal in nc-MCAS.
- Abnormalities in urinary prostaglandins (PG) DM, D2 and F2 α, and N methyl histamine levels are an alternative way to show biochemical abnormalities of mast cell function for all the MCDs.
- Patients with MCAS may not have raised mast cell mediator levels unless they are symptomatic.
- Keeping sample chilled throughout is thought to be important to avoid degradation of samples.

AIM

The main aims of this study were to:

- Assess urinary PG levels and NMH levels across the MCDs
- Compare results of urinary PGs & NMH across all the MCDs
- A secondary aim was to assess the importance of keeping the samples chilled throughout collection and transit

METHOD

- A local data base of MCDs was used to access information on 94 of 145 patients with one of the mast cell diagnoses, whose results for urinary tests were available.
- Of these 6 had SM, 1 CM, 2 MMCAS, 75 MCAS and 10 HαT
- Patients' characteristics are summarised below:
- We noted if samples kept chilled throughout for each case

Type of MCD	SM	CM	MMCAS	MCAS	HαT
F:M (total 79F:15M)	5F:1M	1M	1F:1M	71F:4M	6F:4M
Baseline tryptase mean & range	46.2 23.7-74.5	7	11.78 5.76 -17.8	3.6 1.5-8.3	19.64 11.9-31.4
Median no. of * symptom groups	3	2	4	4	3
Median age & range (8-88)	3 (28-62)	38	36.5 (35-38)	43 (8-63)	46 (32-88)

- *Symptom groups: Gut, skin, neurological, respiratory, allergy, CFS

RESULTS

Table 1 shows the results of analysis of the urinary PGs and NMH.

This demonstrates the similarities between all the MCDs apart from a difference in number of positive PGs: SM & MMCAS have the highest percentage of elevated triple positivity PGs and NMH, whereas MCAS and HαT have less % triple positivity and more likely to have single positivity, and less positivity in NMH

Table 1

Diagnosis	%triple positive PGs (PGDM,D2,F2α)	% double positive PGs (PGDM,D2,F2α)	% single positive PGs (PGDM,D2,F2α)	Negative PGs (PGDM,D2,F2α)	%positive NMH
SM	33%	33%	33%	0%	100%
MMCAS	50%	50%	0%	0%	0%
MCAS	4%	26%	54%	10%	15%
HαT	10%	30%	20%	40%	0%
CM	0%	0%	0%	100%	0%

Prostaglandin D2,DM & F2α

are present in preformed granules in mast cells, activated by

1) antigen cross-linking IgE or
2) non-IgE mechanisms on cell surface, degranulating contents into circulation.

PGD2 is unstable with a short t½ (1-30m).

It is broken down into metabolites, especially PGF2α

24 hr urine sample is recommended for assessing MCAS as short t½ mediators can lead to a normal result in spot urine samples.

N-Methyl Histamine is the major metabolite of histamine, which is produced by mast cells

RESULTS

Analysis of samples which were negative for PGs and NMH:

1. These were spot samples rather than 24 hr.
   PG and NMH production vary across the 24 hrs, therefore less likely to be positive in a spot sample

2. Some patients had repeat tests which were then +ve for one or more PGs or NMH

Analysis of samples with single and double positive PGs

1. 26 had PGF2α only,
2. 13 had PGD2 only
3. 15 had PGF2α and PGD2;
4. 4 had PGF2α and PGDM

Analysis of NMH results

1. NMH showed positivity with all the SM patients, and a smaller positive % in MCAS and HαT,
2. NMH was negative in CM and MMCAS (but samples too small to make conclusions in these)

CONCLUSIONS

The results demonstrate the all mast cell disorders (except CM) have similarities in having higher levels of one or more prostaglandins known to be produced by mast cells.as long as:

1. the samples are kept chilled for the total time of collection and transit
2. 24 hr collection is preferred over spot sample. The latter may however be useful if patient is particularly symptomatic at that time

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