

Ask a Pharmacist First – A Case of Preventable Interaction Between Chromium and Levothyroxine

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Objective

To highlight the importance of clients with complex medical issues and their prescriber(s) consulting a pharmacist prior to adding any pharmacotherapeutic agent – even an Over-the-Counter agent perceived as a 'safe' adjunct medication, like chromium for blood glucose lowering.

Clinical Features

Mrs AS, a 76yo Italian widow, is supported by her 2 sons, one of whom daily organises her medications. Her complex medical history includes type II diabetes requiring insulin, ischaemic heart disease, depression, reflux and hypothyroidism.

Early September 2018 her basal insulin regimen was changed from Protaphane to Ryzodeg 70/30 due to worsening hyperglycaemia. Nil other medications were changed. A Rapid Access Clinic review was arranged 29.5.2019 for variability in glycaemic control, specifically more severe hypoglycaemic episodes in recent weeks. Insulin doses were decreased, sitagliptin was ceased and blood tests performed.

Current medications (pre-contact with client):

ST. VINCENT'S HOSPITAL MELBOURNE		HARP MEDICATION REVIEW		UR No. NAME: D.O.B:			
Generic name of medication	Brand(s) at home	Strength & dose/form	Prescribed dose and frequency	Indication for use	Start date	Cease / hold date	Comment / Plan of Action
aspirin	Astrix	100mg tab	1 midday	IHD	Ongoing		
irbesartan		150mg tab	1 morning	IHT	Ongoing	29.5.19: K: 4.8, Cr: 42, eGFR: >90	
metoprolol		50mg tab	1 TWICE a day	IHD	Increased		
rosuvastatin	Crestor	10mg tab	1 morning	Hyperlipidaemia	Ongoing		17.11.18: TCtot 4.4, Trig 1.9, HDL 0.95, LDL 2.6
GTN	NitroLingual Spray	400mcg	1 when needed	Angina	Ongoing		Kept in handbag.
metformin		1000mg tab	1 evening	T2DM	Ongoing		16.3.19: HbA1c 10.7% (prev 9.6)
metformin		500mg tab	1 evening x 3x/wk	T2DM	Ongoing		1000mg (TTSS) ALT 1500mg (MWF)
pioglitazone		30mg tab	1 morning	T2DM	Ongoing		
aspart insulin	NovoRapid Flexpen	100u/mL	30 units with BF	T2DM	Decreased	29.5.19	10 units midday if BSL > 10.
insulin degludec + aspart	Ryzodeg 70/30	100iu/mL	35 units pre evening meal	T2DM	Decreased	29.5.19	
thyroxine	Eutrosig	100mcg tab	1 morning	Hypothyroid	Ongoing		TSH monitored - dose for review tomorrow.
panoprazole		40mg tab	1 morning	GORD	Ongoing		
magnesium	Cenovis brand	325mg tab		Muscle cramps	Ongoing		
cholecalciferol	Oste-Vit-D	25mcg cap	2 midday	Supplement	Ongoing		16.3.19: 25(OH)vit D 65 nmol/L
citalopram	Citalopram-AN	20mg tab	1 morning	Anxiety/Depression	Ongoing		
doxosate + semosides	Coloxyl with Senna	50mg + 8mg tab	1-2 daily when required	Constipation	Ongoing		
CEASED							
sitagliptin	Januvia	100mg tab	1 morning	T2DM	Oct-16	29.5.19	Ongoing hypoglycaemia

ALLERGY: Sensitivity: pregabalin (drowsiness, 2015), tramadol, dapagliflozin (thrush, Oct 2016)

Insulin storage conditions were queried by both medical staff and Diabetes Educator and found to be appropriate. Medication mismanagement was not a suspected contributor to hypoglycaemic episodes.

The son had confirmed no medication changes had occurred when queried by medical and nursing staff.

Progress

The following day blood test results revealed an elevated Thyroid Stimulating Hormone (TSH) level of 11.11 µU/mL.

FINAL ENDOCRINOLOGY BEndoS					
Request No:	P061140	P142303	P197578		
Date:	06/02/19	16/03/19	29/05/19		
Time:	15:00	10:45	14:15	Units	Ref Range
SERUM/PLASMA					
TSH	1.38	1.49	11.11	uU/mL	0.35-4.94
Free T4			12	pmol/L	9-19

The weekend thyroxine dose was doubled to 200mcg in the morning and additional monitoring was scheduled. The CCS pharmacist was to discuss this with Mrs AS by phone and further investigate medication management.

When Mrs AS was unable to be contacted a call was made to her son. The CCS pharmacist had noted that oral iron supplementation had been suggested at an earlier Outpatient appointment so informed the son of needing to check for any recent changes which could be altering the absorption of thyroxine. As with other clinicians, the son repeated that no new medications had been started. He stated that the only change was a "supplement" begun slightly more than a fortnight earlier upon recommendation from the general practitioner.

The son recalled being informed the supplement *might* help with managing the high blood sugar levels his mother had been experiencing in April. He could purchase it from "a natural health shop" as it was not really a 'medicine'. He did so and advised his mother to take 1 tablet daily as per the directions on the pack. A photo of the supplement revealed it to be chromium.



Timing of the chromium dose had been left at the discretion of Mrs AS. When checked by her son, she stated taking the tablet early in the morning with her thyroxine.

Literature Review

Micromedex search under levothyroxine revealed absorption being moderately impaired if dosed together with chromium.

Chromium

- Interaction Effect: decreased levothyroxine absorption
- Summary: Concomitant use of chromium picolinate and levothyroxine in healthy euthyroid individuals has resulted in reduced thyroxine (T4) absorption by 17%. Therefore, a separation of several hours between administration of chromium picolinate and levothyroxine is advised^[96].
- Severity: moderate
- Onset: rapid
- Substitution: probable
- Clinical Management: Concurrent use of chromium picolinate and levothyroxine decreased the absorption of levothyroxine. Patients should be advised to separate the administration of these drugs by several hours^[96].
- Probable Mechanism: unknown
- Literature Reports

a) In pharmacokinetics studies of levothyroxine conducted in healthy euthyroid volunteers (n=7; age range: 22 to 40 years), levothyroxine absorption was decreased (i.e., a smaller area under the serum thyroxine (T4) absorption curve) following the concurrent use of chromium picolinate and levothyroxine compared with the use of levothyroxine alone. In four 6-hour studies performed at least 2 weeks apart, participants who had fasted overnight received levothyroxine sodium 1 mg (five 0.2-mg tablets) orally alone in the first study and levothyroxine 1 mg with ezetimibe 10 mg, sevelamer hydrochloride 800 mg and chromium picolinate 1000 mcg, respectively, in the three subsequent studies. Blood samples were collected 15 minutes before, at the time of, and 30, 60, 120, 240, and 360 minutes after administration in each study. The area between baseline and the T4 absorption curve was 2176 +/- 195 mcg-minutes/dL for levothyroxine administered alone compared with 1766 +/- 171 mcg-minute/dL for levothyroxine administered with chromium picolinate (83% of T4 alone; p less than 0.05). The mean baseline serum of thyroxine-stimulating hormone (TSH) level was 2.81 +/- 0.59 microunits/mL for levothyroxine alone and 2.16 +/- 0.43 microunits/mL for levothyroxine plus chromium picolinate; none of the participants showed any symptoms of thyrotoxicosis. Although investigators postulated that the mechanism of this interaction between chromium picolinate and levothyroxine was the adsorption of thyroxine by chromium, other possible mechanisms (e.g., via drug-induced alterations in mucosal transport processes) could not be ruled out ^[96].

[96] John-Kalarickal J, Pearlman G, & Carlson HE: New medications which decrease levothyroxine absorption. Thyroid 2007; 17(8):763-765.

The study by John-Kalarickal *et al* appears the most cited study on this topic based on further Google searches.

Outcome

The CCS pharmacist contacted the son and recommended to either cease the chromium or dose it after midday to avoid the physical interaction. He opted to cease it.

- Bloods checked two weeks later showed return to normal TSH of 2.53 µU/mL.

FINAL ENDOCRINOLOGY BEndoS					
Request No:	P061140	P142303	P197578	P443334	
Date:	06/02/19	16/03/19	29/05/19	13/06/19	
Time:	15:00	10:45	14:15	13:45	Units
SERUM/PLASMA					Ref Range
TSH	1.38	1.49	11.11	2.53	uU/mL 0.35-4.94
Free T4			12		pmol/L 9-19

- Thyroxine weekend dose was reduced back to 100mcg.
- Although glycaemic control is still not ideal hypoglycaemic episodes have reduced in frequency.

Conclusion

This case highlights the need to consult a pharmacist when considering pharmacotherapeutic changes, especially for clients with complex medical issues and sensitive medications like levothyroxine. Pharmacists are uniquely skilled at interviewing and discussing medications with clients and carers, and a medication review may assist when unexplained issues arise.