Excessive sweating-induced by interaction between agomelatine and duloxetine: A cooperation with clinical pharmacist

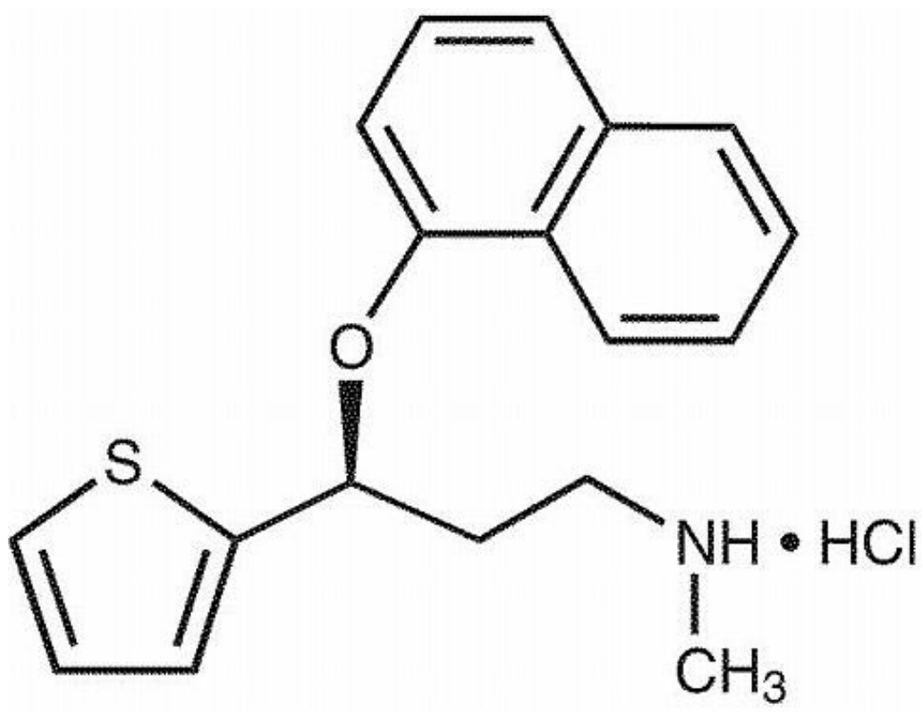
Matej Stuhec[1 2] Pharm.D., Psychiatric Clinical Pharmacist Specialist.
[1]Psychiatric Hospital Ormoz, Department for Clinical Pharmacy, Ormoz, Slovenia.
[2]Faculty of Pharmacy Ljubljana, Department for pharmacokinetics, Ljubljana, Slovenia.

OBJECTIVE

Duloxetine hydrochloride induced sweating has been reported frequently, but excessive sweating induced by agomelatine and duloxetine hydrochloride, has not been reported in the literature. **The aim of this report is to describe a case in which the clinical pharmacy team was asked to provide recommendations on possible continued use of combination antidepressants in a 62-year-old Slovenian female patient following agomelatine and duloxetine hydrochloride-induced excessive sweating.**

CASE SUMMARY

A 62-year-old Caucasian female with major depressive disorder developed 7 days after intake of 90 mg of duloxetine hydrochloride and 25 mg of agomelatine excessive sweating. **When agomelatine was administered as an additional treatment, drug-induced excessive sweating was observed.** The excessive sweating continued and patient reported difficulties with daily activities such as shopping, cooking and visiting friends. There were no abnormalities in cardiovascular status. Baseline laboratory results included a normal platelet count, normal liver enzymes and liver function tests. Hypomania was also excluded.

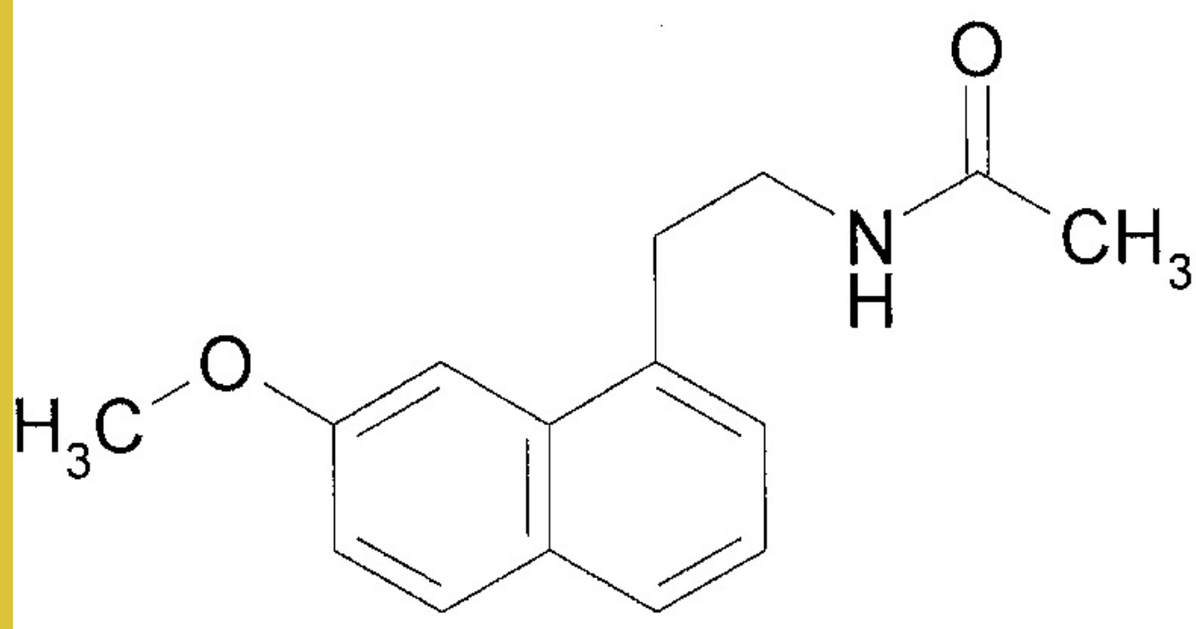


Agomelatine

After agomelatine discontinuation, symptoms improved. Adverse effect was determined by clinical pharmacist with the Naranjo probability scale and was probably associated with agomelatine use (6 points) and possibly associated with duloxetine hydrochloride use (4 points). After discussing the benefits and risks with the patient, a clinical pharmacist advised discontinuation of agomelatine and switching to trazodone 50 mg daily at bedtime. The physician accepted our recommendations and the symptoms completely disappeared in three days after agomelatine discontinuation. **Symptoms of major depression disorder were treated successfully with a combination treatment of duloxetine hydrochloride 90 mg daily and trazodone 50 mg daily at bedtime.** She left health center after 2 weeks on 90 mg daily of duloxetine hydrochloride, 50 mg daily of trazodone and 2,5 mg daily of lorazepam and she tolerated this therapy very well.

DISCUSSION

No case of agomelatine-induced sweating has been described. The interactions with agomelatine are reported to be mediated by cytochrome CYP1A2 enzymes. CYP1A2 and CYP2D6 have a major role in the metabolism of duloxetine hydrochloride and duloxetine hydrochloride increases the exposure of drugs that metabolized with CYP2D6, but not CYP1A2 [1]. **Consequently any pharmacokinetics drug interaction between agomelatine and duloxetine hydrochloride had not occurred in this patient.** An adverse effect was not induced by duloxetine hydrochloride itself, but pharmacodynamic drug–drug interaction between duloxetine hydrochloride and agomelatine could occur, which led to small additive adrenergic overstimulation.



Duloxetine Hydrochloride

Such case has not yet been described in literature, however an adverse effect associated with drug-drug interaction can occur, as this report clearly demonstrates. Pharmacodynamic drug–drug interaction between agomelatine and duloxetine hydrochloride could occur, which led to small additive adrenergic overstimulation. Daily dose of duloxetine hydrochloride was not changed in switching time.

Based on published data, we believe that agomelatine discontinuation and switching to trazodone are the most appropriate approach for our patient.

This case serves to illustrate how clinical pharmacy can help ensure a satisfactory clinical outcome and prevent a potentially life threatening adverse drug reaction, similar to other case reports of timely recognition of adverse drug reactions from other psychotropic medications by clinical pharmacy that were followed by close collaboration between clinical pharmacy and psychiatry for successful management of the clinical disorder in question [2, 3].

CONCLUSIONS

- **The benefit of this antidepressant combination needs to be carefully balanced with the risks associated with its use.**
- **Antidepressant combination treatment is common in some clinical practice settings, there is limited evidence to support this practice.**
- **Trazodone in small doses could be used in treating patients with agomelatine associated excessive sweating.**

DISCLOSURE

The authors have no personal affiliations, financial relationship or any commercial interest to disclose relative to this article.

KEYWORDS

Pharmacokinetics; Drug monitoring; Neuropharmacology.

REFERENCES

[1] Knadler, M.P., Lobo, E., Chappell, J., Bergstrom, R., 2011. Duloxetine: clinical pharmacokinetics and drug interactions. Clin Pharmacokinet 50, 281–294.

[2] Štuhec, M., 2013. Solifenacin-induced delirium and hallucinations. Gen Hosp Psychiatry 35, 682.e3–4.

[3] Stuhec, M., 2014. Oxcarbamazepine Associated With Serious Skin Reaction: A Case Report. J Clin Psychopharmacol 34, e2-3.

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M. Stuhec[1]

[1]*Psychiatric Hospital Ormoz, Clinical Pharmacy, Ormoz, Slovenia*

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Discussion: No case of agomelatine-induced sweating has been described. The interactions with agomelatine are reported to be mediated by cytochrome *CYP1A2* enzymes. *CYP1A2* and *CYP2D6* have a major role in the metabolism of duloxetine hydrochloride and duloxetine hydrochloride increases the exposure of drugs that metabolized with *CYP2D6*, but not *CYP1A2* [1]. Consequently any pharmacokinetics drug interaction between agomelatine and duloxetine hydrochloride had not occurred in this patient. An adverse effect was not induced by duloxetine hydrochloride itself, but pharmacodynamic drug–drug interaction between duloxetine hydrochloride and agomelatine could occur, which led to small additive adrenergic overstimulation. Such case has not yet been described in literature, however an adverse effect associated with drug–drug interaction can occur, as this report clearly demonstrates. No case of agomelatine-induced sweating has been described. Pharmacodynamic drug–drug interaction between agomelatine and duloxetine hydrochloride could occur, which led to small additive adrenergic overstimulation. Daily dose of duloxetine hydrochloride was not changed in switching time. This case serves to illustrate how clinical pharmacy can help ensure a satisfactory clinical outcome and prevent a potentially life threatening adverse drug reaction, similar to other case reports of timely recognition of adverse drug reactions from other psychotropic medications by clinical pharmacy that were followed by close collaboration between clinical pharmacy and psychiatry for successful management of the clinical disorder in question [2,3].

Conclusion: The benefit of this antidepressant combination needs to be carefully balanced with the risks associated with its use. Antidepressant combination treatment is common in some clinical practice settings, there is limited evidence to support this practice. Trazodone in small doses could be used in treating patients with agomelatine associated excessive sweating.

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