Antipsychotic drug use and hypothermia. Reported cases in literature and WHO database

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Introduction: Antipsychotic drugs (APDs) can influence thermoregulation. The hypothermic effect of antipsychotic drugs, often leading to ICU admission, seems less well known than the risks of developing hyperthermia. Risk factors for hypothermia in AP users are not well known.

Method: We performed a literature search for case reports of hypothermia in APD users in Medline and Embase. Secondly we searched the WHO international database for Adverse Drug Reactions for reports of hypothermia and APD use.

Results: Our search resulted in 31 publications (42 patients, 45 events) and 9 non-published cases. Characteristics are shown in table 1. In the WHO database, 339 reports of hypothermia associated with APD use were registered (compared to 326 reports of APD related hyperthermia) (table 2).

Conclusions:
1. Hypothermia risk is increased in the first days following start or dose increase of APDs.
2. 63% of hypothermia reports are for atypical APDs.
3. APDs with strong 5-HT2 antagonism seem to be more involved in hypothermia.
4. Patients with schizophrenia seem to be at increased risk.
5. Hypothermia incidence equals hyperthermia incidence.

Table 1
Characteristics cases in literature

Male	41%
Age (mean (SD))	52.5 (24.4)
Reported body temperature (mean (SD))	32.6 (2.0)
Diagnosis known (n = 34)	
Schizophrenia	59%
Mental retardation	18%
Bipolar disorder	15%
Dementia	9%
Drug change	
Start or dose increase	80%
No change	16%
Interval drug change detection hypothermia	
<2 days	58%
2–7 days	16%
Outcome	
Death	3.8%
ICU admission	22.6%
Hospitalisation (incl. prolonged)	69.8%

Table 2
No of reports of hypothermia in WHO-database (1970–2005)

Antipsychotic	Reports (n)	Reported OR (CI) Hypothermia
Pipamperon	10	42.40 (22.57–79.64)
Chloorprothixeen	4	22.58 (8.41–60.67)
Zuclopenthixol	11	22.26 (12.25–40.44)
Tiapride	3	10.95 (3.51-34-13)
Flupentixol	5	6.13 (2.54–14.78)
Haloperidol	31	4.68 (3.28–6.68)
Chloorpromazine	15	4.04 (2.43–6.71)
Perfenazine	2	1.78 (0.44–7.12)
Sulpiride	2	1.80 (0.45–7.21)
Droperidol	1	1.32 (0.19–9.37)
Risperidon	111	11.12 (9.18–13.46)
Quetiapine	10	4.92 (2.64–9.17)
Olanzapine	29	3.26 (2.26–4.71)
Clozapine	61	2.36 (1.83–3.04)
Ziprasidon	3	2.50 (0.81–7.78)
AP not available in the Neth.	41	

ROR = (a/c) / (b/d); (a = no. of reports of adverse drug reaction with suspected drug; b = no. of reports of adverse drug reaction in total database; c = no. of reports regarding the suspected drug in database; d = total no. of reports in database).

The association between antihypertensive drug combinations and the risk of myocardial infarction

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Introduction: In hypertension trials testing with individual antihypertensive drugs, thiazide diuretics and ACE-inhibitors were found to be most effective in reducing cardiovascular events. Most patients require more than one antihypertensive drug to control their hypertension. It is unresolved which combination of antihypertensive drugs has better effects on cardiovascular morbidity.

Aim: To compare different combinations of two antihypertensive drugs with the combination of thiazide diuretics and ACE-inhibitors (proved to be most effective) on the risk of myocardial infarction (MI).

Methods: In a population-based registry of pharmacy records linked to hospital discharge records (PHARMO) we used a nested case-control design to assess the association between antihypertensive 2-drug combinations and the risk of MI. Among users of antihypertensive drugs we selected subjects hospitalised for MI as cases if they had at least one prescription for antihypertensive drugs in the 3 months prior to their first MI and were registered in PHARMO for at least 1 year. Controls met the same eligibility criteria as the cases, but were not hospitalised for MI. To each case up to 12 controls were matched on age, gender and region.

All subjects were assigned an indexdate, for cases this was the date of their MI and for controls this was the same date as for the case to whom they were matched.

All subjects were recruited through community pharmacies that participate in PHARMO and were asked to fill in a questionnaire about demographics, cardiovascular diseases and risk factors. Only hypertensive subjects who used 2 antihypertensive drugs at the indexdate were included.

Logistic regression analysis was used to calculate odds ratios (OR) and 95% confidence intervals (CI) and to adjust for the potential confounding factors smoking, hypercholesterolemia, diabetes mellitus, obesity, use of aspirin, coumarins, statins and fibrates, history of cardiovascular disease, and family his tory of MI.

Results: We included 117 responding cases and 785 controls. Compared to users of thiazide diuretics and ACE-inhibitors combination, the risk of MI was statistically significant higher among users of thiazide diuretics and calcium channel blockers (OR 4.25; 95% CI: 1.45–12.50) and beta-blockers and calcium channel blockers