

COMPLICATIONS ARISING DUE TO CODEINE CONTAINING COMPOUND ANALGESIC ABUSE IN PATIENTS PRESENTING WITH PRIMARY CODEINE DEPENDENCE

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Introduction

- In Australia codeine containing compound analgesics are available as either schedule 3 or 4 analgesics .
- Schedule 3 analgesics contain < 16 mg codeine phosphate per tablet and are available over-the-counter.^{1,2}
- Within Drug and Alcohol Services of South Australia there has been an increase in the number of patients presenting for assistance with primary codeine dependence.
- It has been observed that many of these patients have had a number of medical complications as a result of supra-therapeutic intake of ibuprofen/codeine compound analgesics.

Aims

The aims of this study were:

- to compare the complications arising in patients with primary codeine dependence who abused either paracetamol/codeine or ibuprofen/codeine containing compound analgesics *and*
- To compare demographic data in these two groups for variables that may have contributed to a possible difference in the number of complications observed.

Methods

This was a retrospective case review of patients who self referred to DASSA (Drug and Alcohol Services South Australia) for assistance with primary codeine dependence from 2009 - 2014.

The data from 60 patients abusing ibuprofen/codeine and 46 abusing paracetamol/codeine containing compound analgesics were compared.

Demographic data including age, sex, number of tablets ingested per day, average codeine content per tablet and cumulative codeine dose per day were collected .

Electronic hospital records were reviewed and complications arising due to supra-therapeutic use of ibuprofen or paracetamol were documented . The number of complications arising in the two groups was compared.

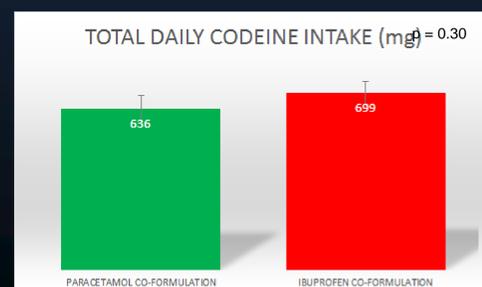
A p-value of < 0.05 was considered significant.

Results

Table 1 : Demographic data.

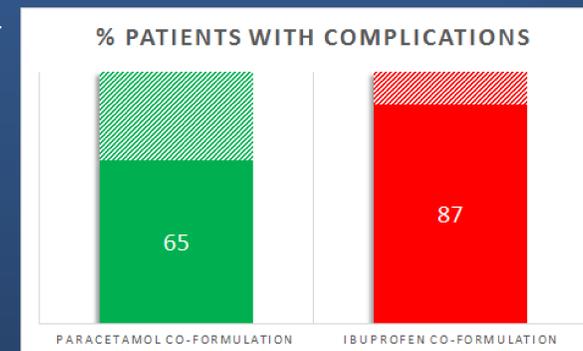
	Paracetamol/Codeine Co-formulation n = 46	Ibuprofen/Codeine Co-formulation n = 60	P-value
Age (yrs)	39±10	36±10	0.22
Female (% in brackets)	26(57)	42(70)	0.15
Admissions (median&range)	1(1-5)	1(1-6)	0.81
Number with > 1 admission (% in brackets)	19(41)	27(45)	0.70
Tablets/day (median plus IQR)	30[20;41]	60[30;74]	< 0.0001
Average codeine content per tablet (mg)	21±1.3	12.8	< 0.0001
Cumulative codeine dose/day (mg)	636±50	699±45	0.30
Average duration of use (±8 mths)	6 yrs 11 mths	5 yrs 2 mths	0.11
Cumulative lifetime tablets (per patient)	85624	107833	0.31
Cumulative lifetime codeine dose (g)	1543±203	1380±170	0.54
Nicotine dependent	15(33%)	30(50%)	0.07
EtOH dependent	15(33%)	9(15%)	0.03

- The data presented in the above table demonstrates similar demographic data for both groups.
- Ibuprofen/codeine compound analgesics contain a consistent amount of codeine per tablet – 12.8 mg.²
- Paracetamol/codeine compound analgesics contain varying amounts of codeine per tablet (8,15 or 30 mg depending on the preparation)² as result the average codeine content per tablet ingested was 21 mg.
- Patients consumed similar daily doses of codeine (699±45mg vs 636±50mg) with those consuming ibuprofen compound analgesics ingesting twice as many tablets per day (median 60 vs 30 tablets per day; P < 0.0001)



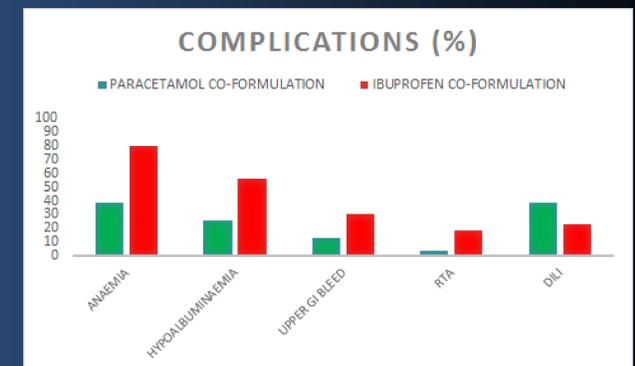
Results

Complications related to compound analgesic abuse occurred more commonly in patients taking ibuprofen/codeine containing compound analgesics (52/60; 87%) versus those taking paracetamol/codeine containing compound analgesics (30/46; 65%) (P < 0.01)



- Patients taking ibuprofen/codeine containing compound analgesics were more likely to have upper gastrointestinal bleeds (P < 0.05) and gastrointestinal perforation (2 cases in the ibuprofen/codeine abusing group)
- These patients were also more likely to have unexplained anaemia (P < 0.0001). This likely being related to gastrointestinal blood loss. (Macro- and microscopic)
- The patients abusing ibuprofen/codeine containing compound analgesics were also more likely to have renal tubular acidosis characterized by a raised chloride, hypokalaemia and hypophosphataemia.
- There was a trend for patients abusing paracetamol/codeine containing compound analgesics to have drug induced liver injury, however this did not reach statistical significance (P=0.08)
- All patients had a similar low incidence of liver failure and none of the patients in this study underwent liver transplantation as a result of drug induced liver injury.
- There were two deaths in the ibuprofen/codeine abusing group.

Results (continued)



Discussion

- This study demonstrates that in patients presenting with primary codeine dependence, who are abusing codeine containing compound analgesics, there were significantly more complications related to the abuse of ibuprofen versus paracetamol containing compound analgesics.
- Although both groups demonstrated similar daily average total codeine intake, the average number of tablets ingested per day was significantly higher in the ibuprofen group.
- This is likely linked to the lower codeine content per tablet in the ibuprofen/codeine containing compound analgesics as well as the consequential lower scheduling and easier over-the-counter access of *all* of the ibuprofen/codeine compound analgesics.
- Rescheduling of the ibuprofen containing compound analgesics is one aspect that needs to be considered in an attempt to minimize the harms observed.
- Further research is necessary to determine the health care costs related to the medical co-morbidities associated with the abuse of compound analgesics in primary codeine dependent patients.

References.

- "Codeine Schedule Changes" The Pharmacy Guild of Australia. www.guild.org.au
- "Combination Analgesics in Adult" B Murnion et al. Australian Prescriber 2010;33: 113-115