Comparison between Toxtyper™ and LC-Quadrupole-Time-of-Flight-MS in post-mortem toxicology

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Background

Various screening techniques exist for comprehensive toxicology screening, all having their advantages and disadvantages in terms of costs, turn-around-times, sample reprocessing, and available toxicology libraries. The LC-Ion trap-MS (Bruker; Toxtyper™ [Ion trap]) and the LC-QTOF-MS (Waters; Xevo™ G2-S Quadrupole Time-of-Flight Mass Spectrometer [QTOF]) are both powerful screening techniques for toxicology.

Aim

To assess the comparability in the outcomes of post-mortem toxicology after Ion trap and QTOF screening of samples.

Methods

Sample selection

Seventy-one whole blood and 21 urine samples from post-mortem cases were analyzed with both Ion trap and the QTOF in two different laboratories.

Sample preparation

[1] Ion trap-analysis (UPLC-Ion-Trap-MS):

- *Whole blood:* 100 µl sample + 200 µl acetonitrile + centrifugation; 5 µl injection.
- *Urine:* 100 µl sample + 500 µl acetonitrile + centrifugation; evaporation under N2, reconstitution in 50 µl mobile phase; 5 µl injection.

[2] QTOF-analysis (UPLC-QTOF-MS):

- *Whole blood:* 100 µl sample + 300 µl acetonitrile + centrifugation. 100 µl supernatant + 300 µl ammoniumformate buffer; 5 µl injection.
- *Urine:* 200 sample + 200 µl water. SPE: washing with 500 µl water; elution with 2x200 µl methanol. Addition of 2 mL ammoniumformate; 5 µl injection.

Primary outcome

The occurrence of similar and deviating qualitative findings was evaluated, and whether this would have led to a different interpretation.

Results

Table 1 shows the results of the number of detected and missed components in whole blood

Table 1: number of compounds detected by Ion trap and QTOF

	Whole blood (n=71)		Urine (n=21)	
	Ion trap	QTOF	Ion trap	QTOF
Compounds	209	249	90	110
number of ‘missed’ compounds but found by comparator	81	44	68	37
number of compounds missing in the library (not unique)	36	11	21	15

The Ion trap found nothing in 17 (24 percent) of all cases, while the QTOF found something in 5. The QTOF could identify nothing in 14 (20 percent) of all cases while the Ion trap found anything in 2.

Figures 1 & 2 display the accordance in interpretation of the different post-mortem cases for whole blood and urine samples respectively.

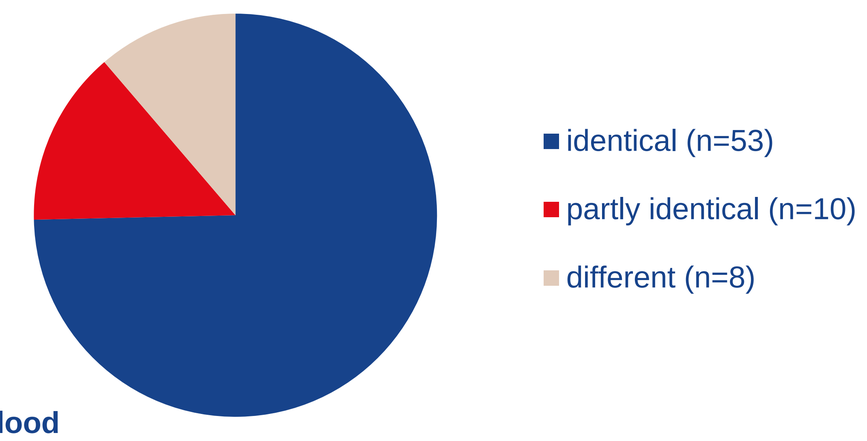

Figure 1: whole blood

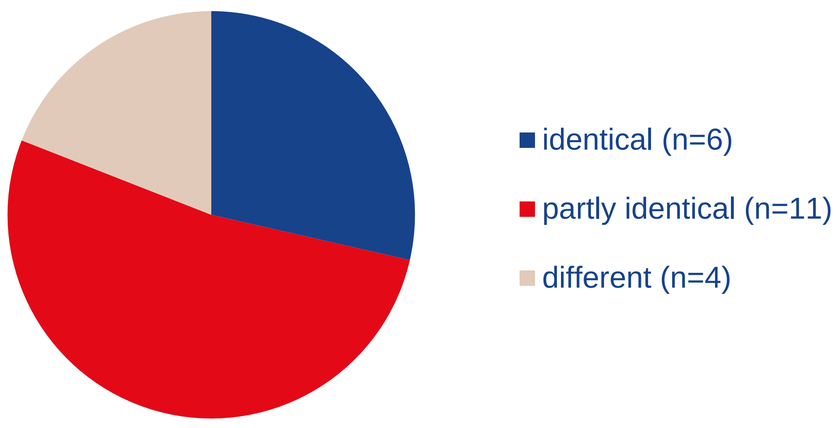

Figure 2: urine

The following inconsistencies were found in the 8 'definitely different' cases: [1] In five of the 8 cases, QTOF identified: 3x amiodarone (and its metabolite), 1x ocfentanil and 1x m-trifluorophenylpiperazine (TFMPP).
[2] In 3 out of 8 cases TT identified: 2x ethylglucuronide (EtG; GC-MS positive alcohol) and 1x tranexaminic acid.

All cocaine-intoxications were reported identically (whole blood n= 9, 13% ; urine n=3, 27%)

Discussion

- The interpretation of the results was solely based on analytical data. The autopsy report was not taken into account.
- Results of the whole blood analysis using QTOF were once reprocessed with parameter optimization (resolution, integration) as the previous integration approach was only appropriate for urine analysis.
- Discrepancies may have been due to an incomplete library, recovery (owing to sample preparation variations) and/or ionization/detection difficulties

Conclusion

Most toxicological analyses in post-mortem samples using Ion trap and QTOF have been reported as similar, although some substantial differences remain. These results require a general screening approach based not only on the lower detection limit but also on a semi-quantitative value in the upper therapeutic to toxic range of drugs that are regularly used or abused to improve interpretation.