June 22, 2021.

To the Listserve:
From: Lonny Shavelson, MD

All,

Here's a key, for those who are appropriately lost in the acronyms:
DDMP2: Digoxin 50 mg, Diazepam 1 gm, Morphine 15 gm, Propranolol 2 gm.
D-DMP2: As above, but digoxin is given separately, 30 minutes before the other medications.
DDMA: Digoxin 100 mg, Diazepam 1 gm, Morphine 15 gm, Amitriptyline 8 gm.
D-DMA: As above, but digoxin is given separately, 30 minutes before the other medications.
DDMAPh: Digoxin 100 mg, Diazepam 1 gm, Morphine 15 gm, Amitriptyline 8gm, Phenobarbital 5 gm.
D-DMAPh: As above, but digoxin is given separately, 30 minutes before the other medications.

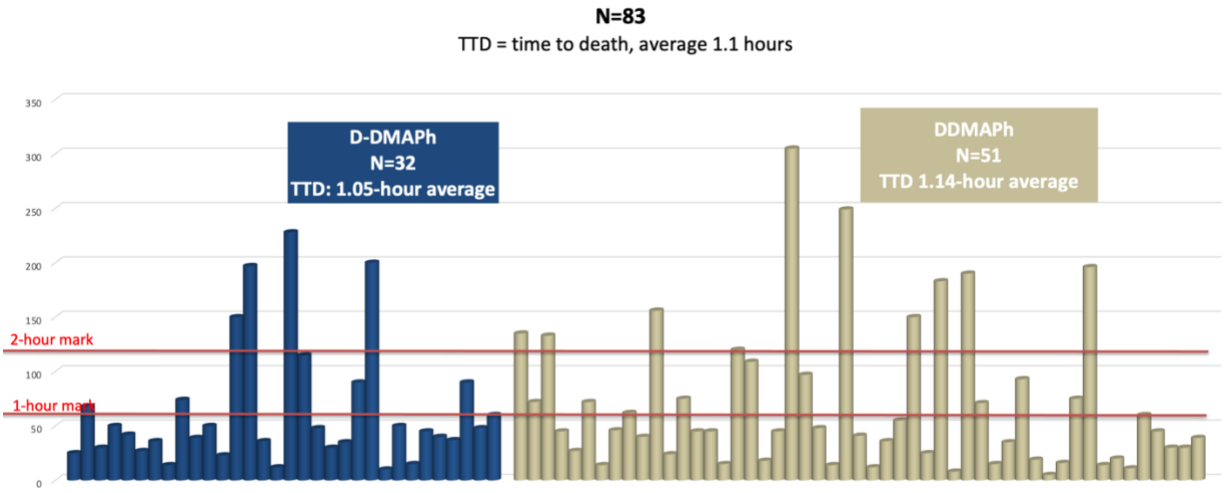
As many of you are aware, in January 2021, Carrol Parrot and I recommended adding 5gm of phenobarbital to the previously recommended two choices of D-DMA or DDMA (article from the Academy attached). This was based on data from 52 patients in 5 aid-in-dying states. We ended that article with the promise to continue monitoring the data to see if the impressive initial results held up.

Now, data from 83 patients confirms the initially observed benefit. However, we are recommending an important change in the aid-in-dying protocols:

The Academy now recommends one single protocol for all patients: DDMAPh.
Giving digoxin 30 minutes before the other medications (D-DMAPh) is no longer recommended. The rationale for this recommendation is discussed below.

NOTE: The Academy's recommendations are just that: *recommendations*. Every clinician is responsible for their own prescribing decisions. While the Academy's recommendations are based on significant data, each clinician is expected to use their own judgment for their patient care.

Previous data from non-phenobarbital protocols (D-DMP2 or D-DMA) had consistently shown a moderate advantage for patients who self-administered the digoxin 30 minutes before the other medications. But adding phenobarbital has resulted in faster times to death compared with all previous regimens. With D-DMAPh (added phenobarbital), the advantage of the early digoxin administration virtually disappears (only 9% faster than giving the digoxin with the other medications, DDMAPh). With a now average time to death of 1.1 hours, a 9% faster time to death by giving early digoxin has no significance at the bedside. (Though the maximum time to death is slightly higher in the DDMAPh group, the numbers are too small to consider this significant.)



There are many advantages to this new recommendation:

- Prescribers do not have to choose between two aid-in-dying protocols. Both yield similar clinical results.
- A one-size-fits all protocol has a significant advantage in teaching and recommending aid-in-dying medications.
- By not administering the digoxin separately, the protocol is simpler to follow for patients, families, and other bedside attendants.

NOTE: For prescribers who choose not to add 5gm of phenobarbital to their DDMA prescriptions, early digitalis (D-DMA) maintains a moderate advantage of some 20%, providing shorter average and maximum times to death.

Added phenobarbital, we believe, continues to have significant advantages:

- It is the only medication with gastric absorption, improving reliability in patients with gastroparesis or other causes of slow gastric emptying. Diazepam, morphine, digoxin, and amitriptyline must reach the duodenum for absorption to occur.
- If a patient has opiate and/or benzodiazepine tolerance, as is common in hospice patients, the phenobarbital acts on a different receptor.
- As a third class of sedative, phenobarbital works synergistically with the morphine and diazepam to increase respiratory suppression.
- Data has shown an overall improvement in time to death by adding phenobarbital.

On a more personal note: Four years ago, by monitoring EKG and pulse-oximeter data at the bedside and giving the digoxin 30 minutes before the other mixed powders, I saw an earlier and more robust digoxin effect on the EKG. And the data showed improved reliability and times to death compared to mixing digitalis with the other medications. “Pre-dig” is my baby. So I, with Carol’s agreement (and a bit of nostalgia), get to be the one to put this baby to sleep. By adding phenobarbital to the DDMA protocol, early digoxin no longer provides a significant benefit.

The Academy now recommends: DDMAPh

Digitalis 100mg (from powder, not crushed tablets); Diazepam 1,000mg; Morphine 15,000mg; Amitriptyline 8,000mg; Phenobarbital 5,000mg. These are dispensed to the patient as powder, to be mixed with water or clear apple juice shortly before the time of ingestion.

The Academy will continue to monitor results with this protocol. For those of you who aren't already submitting your aid-in-dying data, we hope you will do so at https://www.acamaid.org/datareport/. The more information clinicians provide, the better aid-in-dying pharmacology will become.

Thank you all, and your comments and suggestions are more than welcome.

Lonny

Lonny Shavelson, MD
Chair
American Clinicians Academy on Medical Aid in Dying
Donations to continue our essential work are gratefully accepted
at https://www.acamaid.org/donateonline/