Feticidal digoxin injection before dilation and evacuation abortion
Evidence and ethics

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Feticidal injection of digoxin before dilation and evacuation (D&E) abortion has become common in recent years and is now a standard policy at some abortion clinics. The procedure entails amniocentesis and administration of digoxin into the amniotic fluid or fetus before uterine evacuation. Two new reports in this issue of the journal present conflicting views about its safety [1,2].

An invasive procedure, amniocentesis causes pain and incurs cost, inconvenience and risk. Hence, clear justification is needed for it to be used routinely. Several rationales, discussed below, have been invoked for digoxin injection before D&E.

1. Facilitation of D&E abortion

Some clinicians claim that fetal death makes D&E technically easier by allowing fetal maceration and cervical priming before evacuation. However, no Level I evidence supports this hypothesis. To date, only one randomized trial has tested this hypothesis (Table 1) [3]. This trial randomized women to receive either intra-amniotic digoxin or placebo before D&E. The anticipated reductions in operating time and operative difficulty did not materialize. Instead, five times as many women vomited after receiving digoxin as after receiving placebo. A second trial [4] that randomized women to receive four different regimens of digoxin was not informative because it lacked a control group not exposed to digoxin.

Level II studies have a control group and thus allow comparisons. The most rigorous such study about digoxin before D&E is the new report by Dean et al. [2]. This natural experiment at one large facility provided a unique opportunity to assess safety. Compared with the unexposed, women given digoxin were more likely to abort outside the facility, and they had more intrauterine infections as well. The difference in all complications was more than threefold, large enough to suggest causation, not bias, as the explanation. For every 20 women given digoxin, one experienced a preventable complication as a result.

Level III evidence includes case–series reports without control groups. In the absence of controls, no comparisons can be made [10]; one cannot determine whether the exposure (digoxin) influenced important patient outcomes. Thus, although the new report by Steward et al. [1] found complications with digoxin to be rare, the complication rate without digoxin is unknown. The three prior case–series reports without controls [5–7] also could not address comparative safety.

Published data (Table 1) provide no support for the hypothesis that digoxin injection facilitates D&E. On the other hand, it is associated with more vomiting, chorioamnionitis and extramural abortion. Moreover, digoxin injection may fail to achieve its primary objective: from 0% to 70% of first injections are unsuccessful in causing fetal demise, depending on dose and route of administration [11].

2. Patient preference

When queried, women in several studies have reported a preference for feticide before evacuation [3,4]. However, this
preference is often based on misinformation [11]. In one randomized trial, 29% of women who said they might want digoxin before a future D&E thought (incorrectly) that it would make the procedure easier and 19% thought (incorrectly) that it would reduce their pain [3]. In addition, some women are inappropriately concerned about the potential for fetal pain, a biological impossibility at these gestational ages [12]. Correcting these misconceptions will likely reduce patients’ interest in digoxin injection.

3. Avoiding extramural abortion with signs of life

After laminaria placement, spontaneous abortion occasionally occurs outside the abortion facility; if the fetus has signs of life, this can pose difficult questions about appropriate care of the abortus in a local hospital [11]. Although feticidal injection may skirt this problem, large numbers of women must be treated needlessly to serve the rare patient who might benefit. An alternative is to provide a 24-h number where outside physicians and emergency personnel can call for information and advice should this situation arise. Another is to provide an information sheet that the patient could carry to any outside provider with ultrasound documentation of gestational age and directions not to resuscitate a previable abortus. Ironically, feticidal injection of digoxin may increase the risk of extramural abortion, although with a dead abortus [2].

4. Avoiding prosecution

Another rationale is self-serving: to avoid running afoul of the Partial-Birth Abortion Ban Act of 2003 [13]. This Act outlaws a procedure termed “partial-birth abortion,” which is defined as an abortion in which:

- the person performing the abortion deliberately and intentionally [emphasis ours] vaginally delivers a living fetus until, in the case of a head-first presentation, the entire fetal head is outside the body of the mother, or, in the case of breech presentation, any part of the fetal trunk past the navel is outside the body of the mother for the purpose of performing an overt act that the person knows will kill the partially delivered living fetus.

Influenced by defense lawyers intent on protecting their clients rather than patients, some organizations and hospitals responded to the Act by mandating digoxin injection to ensure fetal death before D&E [13–15]. However, an irrational law does not merit an irrational reaction. Since the Act clearly hinges on intent [11], a more reasonable approach is simply to document intent. Intent to perform a “traditional” or “standard” D&E can easily be written in the preoperative evaluation and again afterward in the operative note [11]. In 2007, the Supreme Court specifically ruled that “standard” D&E by definition does not involve delivery of a live fetus and therefore is not prohibited by the Act [Gonzalez v. Carhart, 550 U.S. 124 (2007)]. Wording such as “piecemeal” or “multiple passes” used in the operative

### Table 1

Summary of recent evidence, feticidal digoxin injection before dilation and evacuation abortion, by level of evidence

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>Exposure</th>
<th>Control</th>
<th>Sample size</th>
<th>Benefits</th>
<th>Harms</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I evidence</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Jackson et al. [3]</td>
<td>Randomized trial</td>
<td>Digoxin 1 mg intra-amniotic</td>
<td>Saline (same volume) intra-amniotic</td>
<td>126</td>
<td>None</td>
<td>Significantly more vomiting with digoxin; number needed to harm=8</td>
<td>No reduction in operating time (a priori hypothesis)</td>
</tr>
<tr>
<td>Nucatola et al. [4]</td>
<td>Randomized trial</td>
<td>Digoxin 1 or 1.5 mg intra-amniotic</td>
<td>Digoxin 1 or 1.5 mg intrafetal</td>
<td>52</td>
<td>None</td>
<td>Cannot be determined</td>
<td>Underpowered pilot study; no unexposed treatment arm</td>
</tr>
<tr>
<td>Level II evidence</td>
<td>Before–after study</td>
<td>Digoxin 1 mg intra-amniotic or intrafetal</td>
<td>No digoxin</td>
<td>1079</td>
<td>None</td>
<td>Significantly more complications (spontaneous abortion and infection) with digoxin; number needed to harm=20</td>
<td>Use of historical controls</td>
</tr>
<tr>
<td>Level III evidence*</td>
<td>Case–series report</td>
<td>Digoxin 1 mg intra-amniotic or intrafetal</td>
<td>N/A</td>
<td>4906</td>
<td>Cannot be determined</td>
<td>Cannot be determined</td>
<td>Lack of control group precludes causal inferences</td>
</tr>
<tr>
<td>Borgatta et al. [5]</td>
<td>Case–series report</td>
<td>Digoxin 1.5 mg intra-amniotic</td>
<td>N/A</td>
<td>22</td>
<td>Cannot be determined</td>
<td>Cannot be determined</td>
<td>Lack of control group precludes causal inferences</td>
</tr>
<tr>
<td>Molaei et al. [6]</td>
<td>Case–series report</td>
<td>Digoxin 0.125 to 1 mg intrafetal or intra-amniotic</td>
<td>N/A</td>
<td>1795</td>
<td>Cannot be determined</td>
<td>Cannot be determined</td>
<td>Lack of control group precludes causal inferences</td>
</tr>
<tr>
<td>Drey et al. [7]</td>
<td>Case–series report</td>
<td>Digoxin 1 mg intra-amniotic</td>
<td>N/A</td>
<td>8</td>
<td>Cannot be determined</td>
<td>Cannot be determined</td>
<td>Lack of control group precludes causal inferences</td>
</tr>
</tbody>
</table>

* Two case–series reports [8,9] that included intrafetal digoxin before abortion are omitted from this table because the abortion technique involved labor induction in addition to D&E or assisted delivery.
report provide corroboration that the preoperative intent was accomplished during the procedure. However, should a living fetus be delivered unintentionally, no violation has occurred.

Alternatively, the surgeon can transect the umbilical cord and document asystole before removing the fetus. After fetal death, the Act does not apply.

5. Ethics

The three guiding principles of bioethics are beneficence (or nonmaleficence), autonomy and justice. Based on the published evidence (Table 1), routine use of feticidal digoxin injection before D&E violates the first two principles.

Beneficence (or nonmaleficence) requires that what we do for patients is in their best interests; stated alternatively, we must not harm patients knowingly. Since the published evidence indicates net harm, expense and pain to women from this procedure, it should not be offered routinely. Similarly, we cannot do things to patients that are solely for our benefit (e.g., avoiding running afoul of an unethical law). The latter course would pit our interests against those of our patients, an untenable ethical position.

Autonomy stipulates that women choose treatment options freely and after receipt of full informed consent. This information must now include the statement that feticidal digoxin injection has no known benefits and several documented harms. Clinical protocols that require routine use of digoxin injections at specific gestational ages are inconsistent with beneficence and patient autonomy.

6. Other opinions

In 2010, the Society of Family Planning found insufficient evidence to support the practice of pre-D&E digoxin injection [11]. A published Clinical Guideline noted that, “to justify the harm of the documented increase in spontaneous labor and extramural delivery, along with an increase in vomiting seen in the one blinded digoxin RCT, in addition to any more infrequent risks,” new research would be needed to show some benefit of the procedure, in particular “a significant increase in D&E safety.” The comparative study [2] published in this issue supports this assessment.

7. Clinical implications

Obstetrics and gynecology has a checkered history of uncritical adoption of worthless and harmful practices. In recent decades, these have included a shave and enema before delivery, urinary estriol determinations to predict fetal well-being, routine episiotomy, prostaglandin F2α abortion, mandatory X-ray pelvimetry before cesarean delivery for cephalopelvic disproportion, home ureteric activity monitoring, laser conization and intravenous ethanol as a tocolytic agent [16]. These procedures all “overgrazed” on the medical commons too long [17]. As a result, women suffered needlessly, and resources were wasted.

The risk/benefit equation argues against routine feticidal digoxin injection. Hence, its advocates [1] are now ethically obliged to demonstrate its merit by performing and publishing randomized controlled trials or prospective cohort studies sufficient to shift the risk/benefit equation in favor of fetocide. Until its putative advantages have been established, the procedure must remain experimental [18]. Thus, feticidal injection of digoxin should be offered only in the context of a formal research study. This entails a written proposal, approval by an Institutional Review Board and informed consent acknowledging that the procedure has known harms but no countervailing benefits.

We have the tools at our disposal to determine what therapies we should offer [16,19,20]. What remains unresolved is whether we as a profession have the moral courage to use them [21]. Women deserve no less from us.

References