WEBVTT

1
00:00:00.130 --> 00:00:03.000
- This module will focus
on medication management

2
00:00:03.000 --> 00:00:04.728
of early pregnancy loss.

3
00:00:04.728 --> 00:00:08.020
Our aims here are to detail the efficacy

4
00:00:08.020 --> 00:00:09.740
of various treatment regimens

5
00:00:09.740 --> 00:00:12.170
and describe an evidence-based protocol

6
00:00:12.170 --> 00:00:14.080
for mifepristone and misoprostol

7
00:00:14.080 --> 00:00:16.224
to complete the miscarriage.

8
00:00:16.224 --> 00:00:19.190
We will cover evidence
that this combined regimen

9
00:00:19.190 --> 00:00:20.887
is the most cost-effective one,

10
00:00:20.887 --> 00:00:24.107
despite the higher cost of mifepristone.

11
00:00:24.107 --> 00:00:27.100
And we will also discuss considerations

12
00:00:27.100 --> 00:00:30.740

for integrating this care
into your clinical practice.

13
00:00:30.740 --> 00:00:34.070
Use of medications to expel
a non-viable pregnancy

14
00:00:34.070 --> 00:00:36.410
is just one of four options

15
00:00:36.410 --> 00:00:38.900
available to the
clinically stable patient.

16
00:00:38.900 --> 00:00:43.000
Evaluation of patients
for safe at-home EPL care

17
00:00:43.000 --> 00:00:45.530
and the use of a shared
decision-making model

18
00:00:45.530 --> 00:00:47.610
to choose treatment
are discussed in detail

19
00:00:47.610 --> 00:00:48.930
in separate modules.

20
00:00:48.930 --> 00:00:50.995
Research has consistently shown

21
00:00:50.995 --> 00:00:54.150
that patients are most
satisfied with their treatment

22
00:00:54.150 --> 00:00:57.303
when they can choose the type
of management they prefer.

23
00:00:57.303 --> 00:00:58.821
And a large number

24
00:00:58.821 --> 00:01:01.963
do have a preference for
medication management.

25
00:01:03.044 --> 00:01:06.750
A recent multi-site randomized
control trial in the US,

26
00:01:06.750 --> 00:01:07.836
the PreFaiR study,

27
00:01:07.836 --> 00:01:10.460
established that the
most effective regimen

28
00:01:10.460 --> 00:01:12.640
for medication management of EPL

29
00:01:12.640 --> 00:01:14.923
includes pre-treatment with mifepristone,

30
00:01:14.923 --> 00:01:17.684
followed by use of misoprostol.

31
00:01:17.684 --> 00:01:20.210
This combination was shown to be safe

32
00:01:20.210 --> 00:01:23.234
and more successful in
achieving timely completion

33
00:01:23.234 --> 00:01:25.638
and avoiding an aspiration procedure

34
00:01:25.638 --> 00:01:29.332

than protocols that use
misoprostol alone for EPL care.

35
00:01:29.332 --> 00:01:32.210
Misoprostol is the prostaglandin analog

36
00:01:32.210 --> 00:01:35.379
most commonly used for
miscarriage treatment.

37
00:01:35.379 --> 00:01:39.640
It stimulates uterine contractions
and softens the cervix

38
00:01:39.640 --> 00:01:42.123
for expulsion of the pregnancy tissue.

39
00:01:42.123 --> 00:01:45.960
It is very inexpensive and
stable at room temperature,

40
00:01:45.960 --> 00:01:48.320
this makes it simple to keep it stocked

41
00:01:48.320 --> 00:01:50.781
and dispense to patients for at-home use.

42
00:01:50.781 --> 00:01:53.840
Misoprostol is also more readily available

43
00:01:53.840 --> 00:01:55.692
in many settings than mifepristone

44
00:01:55.692 --> 00:01:58.550
and can be used alone for EPL treatment

45
00:01:58.550 --> 00:02:00.489
when mifepristone is not accessible.

46
00:02:00.489 --> 00:02:04.110
Mifepristone acts as a
competitive antagonist

47
00:02:04.110 --> 00:02:08.112
to both progesterone and
glucocorticoid receptors.

48
00:02:08.112 --> 00:02:11.430
These effects enhance the
activity of prostaglandins

49
00:02:11.430 --> 00:02:13.531
on the myometrium and the cervix,

50
00:02:13.531 --> 00:02:16.789
rendering the misoprostol more effective.

51
00:02:16.789 --> 00:02:20.297
While mifepristone remains
highly regulated in the US

52
00:02:20.297 --> 00:02:21.730
in that it requires

53
00:02:21.730 --> 00:02:25.370
a Risk Evaluation and
Mitigation Strategy, or REMS,

54
00:02:25.370 --> 00:02:28.740
and it is priced higher than misoprostol,

55
00:02:28.740 --> 00:02:31.800
currently at a cost of $54 per pill,

56
00:02:31.800 --> 00:02:35.598
an economic evaluation
alongside the PreFaiR trial

57
00:02:35.598 --> 00:02:40.350
demonstrated it is highly cost
effective to add mifepristone

58
00:02:40.350 --> 00:02:43.629
to a regimen of misoprostol
for EPL management.

59
00:02:43.629 --> 00:02:46.900
Only six patients need
to take mifepristone

60
00:02:46.900 --> 00:02:50.232
in order to gain one
more treatment success,

61
00:02:50.232 --> 00:02:53.320
yielding a low number needed to treat

62
00:02:53.320 --> 00:02:55.210
compared to misoprostol alone.

63
00:02:55.210 --> 00:02:57.970
The PreFaiR trial randomized 300 patients

64
00:02:57.970 --> 00:03:00.851
with an ultrasound diagnosis
of non-viable pregnancy

65
00:03:00.851 --> 00:03:04.225
between five and 12
completed weeks gestation,

66
00:03:04.225 --> 00:03:06.760
to either mifepristone pre-treatment

67
00:03:06.760 --> 00:03:11.246
followed by misoprostol or
misoprostol alone for treatment.

68
00:03:11.246 --> 00:03:14.853
The primary outcome to
define treatment success

69
00:03:14.853 --> 00:03:18.865
was gestational sac expulsion
at the first follow-up visit,

70
00:03:18.865 --> 00:03:22.294
which was scheduled for one
day after misoprostol use,

71
00:03:22.294 --> 00:03:24.650
and then, no additional interventions

72
00:03:24.650 --> 00:03:26.830
within the 30-day study period.

73
00:03:26.830 --> 00:03:28.770
There were only three participants

74
00:03:28.770 --> 00:03:31.310
not included in the analysis
for the first follow-up.

75
00:03:31.310 --> 00:03:34.940
This table shows the higher
success rate of mifepristone

76
00:03:34.940 --> 00:03:38.710
in combination with misoprostol
over misoprostol alone,

77
00:03:38.710 --> 00:03:43.710
84% compared to 67%, at
the first follow-up visit.

78
00:03:44.649 --> 00:03:48.190

Participants without success
were then given the option

79
00:03:48.190 --> 00:03:50.610
of either expectant
care or an intervention,

80
00:03:50.610 --> 00:03:53.291
with additional misoprostol or aspiration,

81
00:03:53.291 --> 00:03:57.513
before the second follow-up
visit at day eight.

82
00:03:57.513 --> 00:04:01.539
Overall, aspiration
was utilized by only 9%

83
00:04:01.539 --> 00:04:03.180
in the mifepristone group,

84
00:04:03.180 --> 00:04:07.488
compared to 24% in the
misoprostol-only group.

85
00:04:07.488 --> 00:04:10.050
Side effect rates were similar,

86
00:04:10.050 --> 00:04:12.790
with only vomiting
significantly more common

87
00:04:12.790 --> 00:04:13.973
in the mifepristone group.

88
00:04:13.973 --> 00:04:16.350
Mifepristone pre-treatment was not studied

89
00:04:16.350 --> 00:04:17.980

for incomplete miscarriages,

90
00:04:17.980 --> 00:04:21.248
as misoprostol alone has a high efficacy.

91
00:04:21.248 --> 00:04:25.180
Prior research has established
that incomplete miscarriages

92
00:04:25.180 --> 00:04:29.030
respond well to either
400 micrograms sublingual

93
00:04:29.030 --> 00:04:33.354
or 600 micrograms oral misoprostol.

94
00:04:33.354 --> 00:04:38.354
The PreFairR study regimen is
200 milligrams of mifepristone

95
00:04:38.663 --> 00:04:43.103
given 24 hours prior to 800 micrograms

96
00:04:43.103 --> 00:04:45.256
of vaginal misoprostol.

97
00:04:45.256 --> 00:04:49.058
This regimen is now regarded
as the most effective,

98
00:04:49.058 --> 00:04:52.749
evidence-based regimen for
all other types of EPL,

99
00:04:52.749 --> 00:04:57.749
namely anembryonic gestations
and embryonic or fetal demise.

100
00:04:57.771 --> 00:05:01.870

Importantly, this study did
not find any differences

101
00:05:01.870 --> 00:05:03.998
in success by type of EPL.

102
00:05:03.998 --> 00:05:06.760
When using a misoprostol only regimen,

103
00:05:06.760 --> 00:05:10.010
the initial dose of 800
micrograms vaginally

104
00:05:10.010 --> 00:05:12.672
can be repeated one to two days later.

105
00:05:12.672 --> 00:05:15.168
When mifepristone is not available,

106
00:05:15.168 --> 00:05:19.020
two doses of misoprostol
can increase success rates.

107
00:05:19.020 --> 00:05:21.960
Notably, recent research
around medication abortion

108
00:05:21.960 --> 00:05:23.570
for gestations over nine weeks

109
00:05:23.570 --> 00:05:25.720
can be applied and should be considered

110
00:05:25.720 --> 00:05:27.189
for EPL treatment also.

111
00:05:27.189 --> 00:05:30.880
Evidence supports an increase
in successful abortion

112
00:05:30.880 --> 00:05:33.803
after the standard
mifepristone/misoprostol regimen

113
00:05:33.803 --> 00:05:37.510
when a second dose of
misoprostol is routinely given

114
00:05:37.510 --> 00:05:39.720
four hours after the first.

115
00:05:39.720 --> 00:05:41.510
There are important considerations

116
00:05:41.510 --> 00:05:43.760
prior to implementing
medication management

117
00:05:43.760 --> 00:05:45.441
into your practice.

118
00:05:45.441 --> 00:05:47.814
These questions include,

119
00:05:47.814 --> 00:05:51.120
will you dispense misoprostol
directly from your clinic

120
00:05:51.120 --> 00:05:52.880
or write a prescription?

121
00:05:52.880 --> 00:05:56.130
Fortunately, misoprostol is
widely available in pharmacies,

122
00:05:56.130 --> 00:05:59.267
but due to its association
with induced abortion,

123
00:05:59.267 --> 00:06:01.530
it's recommended to clearly indicate

124
00:06:01.530 --> 00:06:03.420
that it is for miscarriage treatment

125
00:06:03.420 --> 00:06:05.160
to avoid potential obstruction

126
00:06:05.160 --> 00:06:06.970
of the prescription being filled.

127
00:06:06.970 --> 00:06:09.170
Will you register as a REMS provider

128
00:06:09.170 --> 00:06:11.704
to dispense mifepristone from your clinic?

129
00:06:11.704 --> 00:06:16.181
This can be an intimidating
but not insurmountable barrier.

130
00:06:16.181 --> 00:06:18.535
To become certified with the FDA

131
00:06:18.535 --> 00:06:21.600
to dispense mifepristone
from your own office,

132
00:06:21.600 --> 00:06:24.053
you must meet certain qualifications,

133
00:06:24.053 --> 00:06:26.730
complete a one-time prescriber agreement,

134
00:06:26.730 --> 00:06:30.729
oversee all mifepristone

dispensing under your certificate,

135
00:06:30.729 --> 00:06:33.609
and have patients sign an
agreement form before use.

136
00:06:33.609 --> 00:06:36.116
ACOG and reproductive health advocates

137
00:06:36.116 --> 00:06:39.719
are calling on the FDA to
remove the REMS designation,

138
00:06:39.719 --> 00:06:43.590
which would greatly benefit
access for all pregnant people

139
00:06:43.590 --> 00:06:47.030
to comprehensive and highly
effective miscarriage care.

140
00:06:47.030 --> 00:06:50.690
Do your patients have access
to a 24-hour call service,

141
00:06:50.690 --> 00:06:53.749
should they be alarmed by
any symptoms or side effects?

142
00:06:53.749 --> 00:06:56.450
Having a reliable clinician to reach

143
00:06:56.450 --> 00:06:58.240
can often alleviate concerns

144
00:06:58.240 --> 00:07:01.470
and prevent unnecessary
emergency room visits.

145

00:07:01.470 --> 00:07:04.140
What is the backup plan
for uterine aspiration,

146
00:07:04.140 --> 00:07:06.310
should the miscarriage be incomplete

147
00:07:06.310 --> 00:07:08.803
or an emergent need arise?

148
00:07:08.803 --> 00:07:12.640
Not having the option of an
in-office uterine aspiration

149
00:07:12.640 --> 00:07:15.972
should not be a barrier to
offering medication management,

150
00:07:15.972 --> 00:07:19.100
but it is wise to establish relationships

151
00:07:19.100 --> 00:07:21.210
with local hospitals or providers

152
00:07:21.210 --> 00:07:24.652
who can offer an aspiration if needed.

153
00:07:24.652 --> 00:07:27.960
Complications or need
for emergent aspirations

154
00:07:27.960 --> 00:07:29.284
are rare events.

155
00:07:29.284 --> 00:07:32.320
Follow-up and confirming
completion of the miscarriage

156
00:07:32.320 --> 00:07:35.064

are discussed in the
at-home management module.

157
00:07:35.064 --> 00:07:38.420
One of the greatest advantages
of using mifepristone

158
00:07:38.420 --> 00:07:40.472
in addition to misoprostol for EPL

159
00:07:40.472 --> 00:07:44.598
is the reduced need for repeated
follow-ups or aspiration.

160
00:07:44.598 --> 00:07:46.540
Mifepristone pre-treatment

161
00:07:46.540 --> 00:07:49.660
was found to be more cost-effective
than misoprostol alone

162
00:07:49.660 --> 00:07:51.852
due to this superior efficacy,

163
00:07:51.852 --> 00:07:55.850
even up to a cost of $293 per pill

164
00:07:55.850 --> 00:07:57.739
in a sensitivity analysis.

165
00:07:57.739 --> 00:08:01.480
The researchers performing
the economic evaluation

166
00:08:01.480 --> 00:08:03.520
determined that adding mifepristone

167
00:08:03.520 --> 00:08:05.580
was a "good value for patients"

168
00:08:05.580 --> 00:08:09.289
from both the healthcare sector
and societal perspectives,

169
00:08:09.289 --> 00:08:13.040
which did include taking into
account costs of childcare,

170
00:08:13.040 --> 00:08:15.538
transportation and lost productivity

171
00:08:15.538 --> 00:08:18.470
due to ongoing EPL-related care.

172
00:08:18.470 --> 00:08:21.950
Integration of either medication protocol

173
00:08:21.950 --> 00:08:23.701
for miscarriage management

174
00:08:23.701 --> 00:08:27.034
expands access for patients
choosing this option

175
00:08:27.034 --> 00:08:29.140
and is essential to offering

176
00:08:29.140 --> 00:08:33.010
a truly comprehensive
approach to EPL care.

177
00:08:33.010 --> 00:08:36.502
Addition of mifepristone
increases efficacy,

178
00:08:36.502 --> 00:08:39.057
thereby reducing need for follow-up

179
00:08:39.057 --> 00:08:42.986
or additional interventions,
and is cost effective,

180
00:08:42.986 --> 00:08:44.730
significant benefits

181
00:08:44.730 --> 00:08:48.193
which favor widespread
practice integration.