WHO recommendation on the use of antispasmodic agents for prevention of delay in labour

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Recommendation

The use of antispasmodic agents for prevention of delay in labour is not recommended.

(Weak recommendation, very low quality of evidence)

Publication history

First published: May 2014

Updated: prioritized for updating in 2018

Assessed as up-to-date: May 2014

Remarks

- The GDG noted that the available data were too heterogeneous with respect to the participants and interventions to permit wide applicability of the results. The shortening in the length of the first stage of labour by one hour was considered clinically inconsequential, as it did not translate to improvement in the other critical maternal or infant outcomes. The GDG placed a high value on safety issues, which were poorly reported, and chose not to recommend the practice until new information demonstrating clinical benefits with minimal risks becomes available.

- The GDG considers the use of antispasmodic agents for treatment of delay in labour as a research priority.

Background

Difficult labour (or dystocia) is characterized by abnormally slow labour progress arising from inefficient uterine contractions, abnormal fetal presentation or position, inadequate bony pelvis or abnormalities of the pelvic soft tissues of the mother. (1, 2) Evidence suggests that up to one third of first-time mothers experience delay in the first stage of labour. (3)
Augmentation of labour is the process of stimulating the uterus to increase the frequency, duration and intensity of contractions after the onset of spontaneous labour. It has commonly been used to treat delayed labour when uterine contractions are assessed to be insufficiently strong or inappropriately coordinated to dilate the cervix. Labour augmentation has traditionally been performed with the use of intravenous oxytocin infusion and/or artificial rupture of amniotic membranes (amniotomy). The procedure aims to shorten labour in order to prevent complications relating to undue prolongation, and to avert caesarean section. There is evidence that a significant proportion of women with uncomplicated pregnancies are subjected to routine augmentation of labour with oxytocin. (4)

While augmentation of labour may be beneficial in preventing prolonged labour, its inappropriate use may cause harm. Augmentation with synthetic oxytocin may result in uterine hyperstimulation, with adverse effects such as fetal asphyxia and uterine rupture, and thus increase the risk of a cascade of interventions during labour and delivery. (5)

**Methods**

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach.(6) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on augmentation of labour (2014).(7)

A Cochrane systematic review was conducted, on the use of antispasmodics compared with placebo or no medication for shortening the duration of labour.(8) In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations on augmentation of labour in September 2013, where this recommendation was developed. The GDG comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

Further information on procedures for developing this recommendation are available [here](#).

**Recommendation question**

For this recommendation, we aimed to answer the following question:

- In pregnant women in labour (P), does use of antispasmodic agents for prevention of delay in labour (I), compared to no intervention (C), improve maternal and perinatal outcomes (O)?

**Evidence Summary**
Evidence on the use of antispasmodics compared with placebo or no medication for shortening the duration of labour was drawn from a Cochrane systematic review of 21 RCTs (3286 women). (8)

The review included heterogeneous groups of participants, interventions and outcomes. Ten trials included only primigravid women, one only multigravid women, nine included both and one did not specify the gravidity of participants.

One trial included only women with induction of labour, two included both women following induction or in spontaneous labour, 13 trials only included participants in spontaneous labour, and five trials did not specify whether participants were in spontaneous or induced labour.

Antispasmodics with musculotropic effects (drotaverine hydrochloride, rocurine and camylofin dihydrochloride) and those with neurotropic effects (valethamate bromide and hyoscine butyl-bromide) were reported separately. Most of the trials included in the review (14) used antispasmodics followed by a protocol of active management of labour, which included amniotomy, augmentation with oxytocin, or both, and only two trials avoided amniotomy and oxytocin augmentation, while five trials did not mention amniotomy or oxytocin. Antispasmodic drugs were administered intravenously, intramuscularly or per rectum.

All but one of the trials recruited women with low-risk pregnancies.

Evidence related to the duration of labour and the rate of cervical dilatation was extracted from trials that excluded data for women whose final mode of delivery was caesarean section.

The 21 trials were conducted in India (nine trials), Iran (three), Saudi Arabia (two), Turkey (two) and Italy, Nepal, Kenya, Jamaica and the USA (one each).

**Antispasmodics versus control: maternal outcomes**

- No trials reported on maternal mortality.

- Using findings from trials that excluded data for women who had caesarean section when estimating mean duration of labour, there was a significant reduction in the duration of the first stage of labour (MD –59.10 min, 95% CI –95.81 to –22.38; seven trials, 1051 women) but no significant reduction in the length of the second stage of labour (MD 0.51 min, 95% CI –3.04 to 4.06; six trials, 753 women). There was a significant reduction in the total duration of labour for vaginal births in the antispasmodic group (MD –102.60 min, 95% CI –164.12 to –41.08; three trials, 392 women). This reduction was significant overall, and for neurotropic agents (MD –80.78 min, 95% CI –153.81 to –7.75; three trials, 244 women), but did not reach statistical significance for musculotropic agents (MD –138.21 min, 95% CI –291.51 to 15.09; two trials, 148 women).

- The rate of cervical dilatation for vaginal births was significantly faster with antispasmodics compared with control (MD 0.67 cm/hr, 95% CI 0.39 to 0.95; four trials, 553 women).

- The rate of caesarean section or instrumental vaginal birth was not reported in the review. However, no significant difference was observed in the rate of normal vertex deliveries between antispasmodics and control (RR 1.02, 95% CI 1.00 to 1.05; 16 trials, 2319 women).

- With respect to adverse events, no significant differences were observed in the incidence of cervical laceration between antispasmodics and control (RR 0.79, 95% CI 0.20 to 3.12), although few trials addressed this outcome and the number of events was small.
Overall, there was no difference observed in the incidence of PPH (blood loss > 500 ml) (RR 2.46, 95% CI 0.20 to 30.17), but one trial (100 women) showed a marginal increase in PPH risk for drotaverine hydrochloride, a musculotropic agent (RR 9.00, 95% CI 1.18 to 68.42). There was no significant difference in PPH observed between neurotropic agents and the control group (RR 0.75, 95% CI 0.13 to 4.26; one trial).

The incidence of maternal tachycardia was significantly higher for antispasmodic agents compared with control (RR 4.54, 95% CI 2.53 to 8.16). This effect was significantly different for neurotropic agents whereas it was similar between comparison groups for musculotropic agents. Similar effects were observed for mouth dryness and flushing of the face.

There were no significant differences between antispasmodic agents and control in the occurrence of maternal adverse events such as headache, nausea, vomiting, dizziness and giddiness.

**Antispasmodics versus control: infant outcomes**

- No trials reported data for perinatal death.

- Overall, there were no significant differences between groups for admission to NICU (RR 0.84, 95% CI 0.34 to 2.05).

- One trial reported fetal distress, with no significant difference between comparison groups (RR 0.50, 95% CI 0.10 to 2.61).

- One trial reported fetal bradycardia, with no significant difference between groups (RR 0.67, 95% CI 0.12 to 3.86).

- Two trials reported fetal tachycardia for neurotropic agents, with no significant difference between groups (RR 3.40, 95% CI 0.85 to 13.67).

- One trial reported meconium-stained liquor. However it was a small sample, there were few events, and the difference was not significant (RR 2.04, 95% CI 0.54 to 7.73).

Further information and considerations related to this recommendation can be found in the WHO guidelines, available at: [http://apps.who.int/iris/bitstream/handle/10665/112826/WHO_RHR_14.15_eng...](http://apps.who.int/iris/bitstream/handle/10665/112826/WHO_RHR_14.15_eng...)

**Implementation considerations**

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.

- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.

- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations (including, for example, the availability of augmentation agents and monitoring capacity), and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

Research implications

The GDG identified that further research on the following high-priority questions is needed:

- What are the effects of antispasmodic agents when used as treatment for confirmed delay in the first stage of labour?

Related Links

WHO recommendations for augmentation of labour (2014) –full document and evidence tables

Supporting systematic review:


References


Citation