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IMPACT OF THE HYPITAT TRIAL ON DOCTORS’ BEHAVIOUR AND PREVALENCE OF ECLAMPSIA IN THE NETHERLANDS

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ABSTRACT

We questioned if participation in the HYPITAT trial (induction of labour versus expectant monitoring in women with gestational hypertension or pre-eclampsia at term) impacted implementation of its results and subsequently maternal health. We identified women with hypertensive disease from the Perinatal Registry, and distinguished the period before, during and after the trial. We included 43,641 women. Induction of labour increased from 58.3 to 67.1% (P < 0.001) and prevalence of eclampsia decreased from 0.85 to 0.19% (P < 0.001) before and after the trial. Concurrently, participation in the HYPITAT trial among others had immediate consequences for obstetric management and maternal health.
INTRODUCTION

The incidences of maternal mortality and eclampsia as the result of hypertensive disease have decreased over the past century in Western countries. In the Netherlands however, the Dutch Maternal Mortality Committee (MMC), stated that hypertensive disease in pregnancy was the leading cause of maternal morbidity and mortality up to 2008. The Maternal Mortality Ratio (deaths per 100 000 live births) from hypertensive disease in pregnancy increased from 2.7 per 100 000 live births in 1983–92 to 3.5 in 1993–2005. The conservative approach towards the management of pre-eclampsia in the Netherlands and substandard care are possible explanations for these results. In other developed countries more aggressive management has been advocated. This discrepancy regarding the treatment of women with hypertensive disease of pregnancy, gave us the opportunity to set up a randomized clinical trial in which induction of labour was compared with expectant monitoring.

In 2009, the HYPITAT trial, a multicenter nationwide randomized controlled trial comparing induction of labour with expectant monitoring in the management of gestational hypertension and mild pre-eclampsia at term, showed that induction of labour improved maternal outcome without increasing the caesarean section rate, and should therefore be the treatment of choice in these women.

We wondered whether participation of hospitals in the HYPITAT trial had an impact on the implementation of its results and subsequent consequences for maternal health.

METHODS

We studied data from the Perinatal Registry of the Netherlands from 2001 until 2009. The HYPITAT trial was performed between October 2005 and March 2008. We identified women with gestational hypertension or mild pre-eclampsia with a singleton pregnancy and a fetus in cephalic position beyond 36 weeks of gestation from our national database, and distinguished the period before the trial (January 2001–October 2005), the period during the trial (October 2005–March 2008) and the period after the trial (April 2008–December 2009). We studied trends in onset of labour and the occurrence of eclampsia, both in the 38 hospitals that participated in the HYPITAT trial and the 55 hospitals that did not.

RESULTS

Table 1 shows the distribution of spontaneous labour, induced labour and primary caesarean section in 22 830, 11 298 and 9 513 women with gestational hypertension or mild pre-eclampsia treated before, during and after the trial. The number of all women in whom labour was induced increased after the HYPITAT trial (58.3% before
versus 67.1% after the trial, $P < 0.001$). This change in management was mainly because hospitals that participated in the trial increased the number of inductions (12.1%; $P < 0.001$) compared with a 5.1% increase ($P < 0.001$) in non-participating hospitals. When comparing the hospitals that participated in the HYPITAT trial with the hospitals that did not participate we also found significant differences between induction of labour before the trial (53.5% versus 64.3%; $P < 0.001$) as well as after the trial (65.6% versus 69.4%; $P < 0.001$) even though the difference was much smaller after the trial than before.

Similarly, in women with a gestational age beyond 36 weeks, there was a decrease in the risk of suffering from eclampsia: .85% before the trial versus .19% after the trial ($P < 0.001$). This decrease was specifically observed in the hospitals that participated in the HYPITAT trial, where the prevalence decrease was from .95% to .13% ($P < 0.001$)

| Table 1. Onset of delivery in women with a singleton pregnancy in cephalic position after 36 weeks of gestation with gestational hypertension or mild pre-eclampsia |
| Onset of labor | Spontaneous | Induction of labour | Primary caesarean section | Missing | Prevalence of eclampsia |
| | n | % | n | % | n | % | n | % | n |
| All woman | | | | | | | | | |
| Before the trial (n=22 830) | 9 002 | 39.4 | 13 313 | 58.3 | 474 | 2.1 | 41 | 0.2 | 193 | .85 |
| During the trial (n=11 298) | 4 712 | 41.7 | 6 345 | 56.2 | 208 | 1.8 | 33 | 0.3 | 34 | .30 |
| After the trial (n=9 513) | 2 976 | 31.3 | 6 385 | 67.1 | 134 | 1.4 | 18 | 0.2 | 18 | .19 |
| $P<0.001$ | $P<0.001$ | | | | | | | | |
| Women who delivered in hospitals that participated in HYPITAT | | | | | | | | | |
| Before the trial (n=12 663) | 5 608 | 44.3 | 6 772 | 53.5 | 249 | 2.0 | 34 | 0.3 | 120 | .95 |
| During the trial (n=6 571) | 3 048 | 46.4 | 3 406 | 51.8 | 90 | 1.4 | 27 | 0.4 | 14 | .21 |
| After the trial (n=5 475) | 1 797 | 33.2 | 3 593 | 65.6 | 67 | 1.2 | 18 | 0.3 | 7 | .13 |
| $P<0.001$ | $P<0.001$ | | | | | | | | |
| Women who delivered in hospitals that did not participate in HYPITAT | | | | | | | | | |
| Before the trial (n=10 167) | 3 394 | 33.4 | 6 541 | 64.3 | 225 | 2.2 | 7 | 0.1 | 73 | .72 |
| During the trial (n=4 727) | 1 664 | 35.2 | 2 939 | 62.2 | 118 | 2.5 | 6 | 0.1 | 20 | .42 |
| After the trial (n=3 945) | 1 143 | 29.0 | 2 738 | 69.4 | 64 | 1.6 | 0 | 0.0 | 11 | .28 |
| $P<0.001$ | $P=0.002$ | | | | | | | | |
compared with a decrease from 0.72% before the trial to 0.28% after the trial (P = 0.002) in hospitals that did not participate.

DISCUSSION

In the Netherlands the optimal treatment for pregnant women at term with hypertensive disease was not clear before the HYPITAT trial, and a conservative approach, that is expectant management until spontaneous onset of labour, was not uncommon. The HYPITAT trial showed that in women with gestational hypertension or mild pre-eclampsia at term, induction of labour reduced the risk of maternal complications, decreased the caesarean section rate, was cost effective, and should therefore be the treatment of choice in these women. We found an increase in induction of labour and a decrease in women with eclampsia in all hospitals in the Netherlands, specifically in hospitals that participated in the trial.

Several remarks can be made on these apparent consequences of the trial. First, the number of women who were randomized in the HYPITAT trial (n = 756) or who were asked to take part in the study but refused (n = 428) was only 18% of all women with hypertensive disease at term. Apparently, the trial did not only affect the women who participated, but also those women who did not participate but who were treated in hospitals participating in the trial. Second, before the trial, the number of inductions for hypertensive disease at term was higher in the hospitals that did not participate in the HYPITAT trial. Apparently, those hospitals that had a conservative approach before the study were more often willing to participate in the HYPITAT trial than hospitals that already had a more aggressive approach. Third, implementation of induction of labour after the trial was better in hospitals that had participated in the HYPITAT trial. This was associated with a stronger decrease of eclampsia.

The changes we observed over time might be attributable to the trial results but they could also be the result of ongoing changes in practice. For example, because of the efforts of the Dutch Maternal Mortality Committee or the results of the LEMMoN trial (a nationwide population-based cohort study).5 In addition, the introduction of maternal morbidity audits in the Netherlands may have contributed to increased awareness.

Our report shows that a nationwide trial can change practice already before its results are translated into guidelines, and before specific implementation measures are taken. Whereas the UK National Institute of Clinical Excellence (NICE) adapted their guidelines on ‘Hypertension in Pregnancy’ immediately, the revision of the Dutch guideline is expected for the end of 2011.6
CONCLUSION

We showed that participation in a multicenter trial improves doctors’ awareness on the clinical problem, and had immediate consequences for maternal health.

REFERENCES
