

 **Съезд**
Congress



5-7 сентября 2018 / Санкт-Петербург
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Упрямова Е.Ю.

Ингаляционные методы обезболивания самопроизвольных родов





Только 14% рожениц не испытывают болей в родах

У 86% женщин роды
сопровождаются
СИЛЬНЫМИ
болевыми ощущениями



Влияние боли в родах на состояние матери и плода



Ингаляционные анестетики

- 1880: Закись азота (N_2O), Станислав Кликович
- 1961: 50/50 - N_2O : O_2 (Entonox) в одном баллоне
- 1965: одобрение Энтонокса (Entonox) центральным советом акушеров
- 1934: Дивинил-Эфир
- 1975: Изофлуран
 - 0,75% с O_2
 - 0,2% с Entonox (Isonox)
- 1984: 1% Энфлуран в воздухе
- 1995: Десфлуран - 1-4,5% в O_2
- 2003: Севофлуран 2-3% - 4-5% в O_2 /воздух
- 2007: Севофлуран 0,8% в O_2 /воздух (O_2 от 37% до 51%)

HISTORY



a short history of Obstetric Anaesthesia

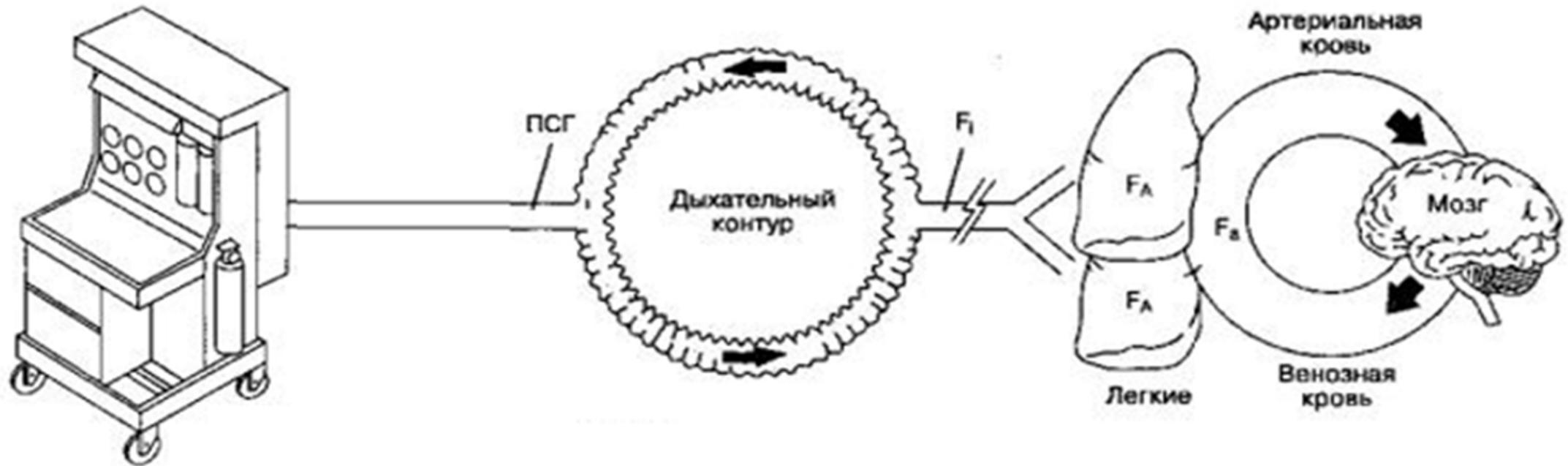
The pain of childbirth has afflicted women for generations and the quest to relieve such pain has been pursued throughout history. **Dr Ann Whitfield** relates the story of obstetric anaesthesia from its early beginnings in ancient times, the introduction of chloroform by Sir James Young Simpson in the 1800s, through to the present day and the controversy over natural childbirth.

The unique pain of childbirth has been recognised since time immemorial. There are numerous references in the Bible such as Genesis Chapter 3 and there are many other descriptions of attempts by previous civilisations to alleviate this torment. The Chinese gave their parturients opium and alcohol, while the Egyptians in Pharaonic times burnt turpentine near the labouring woman or concocted a vinegar and marble dust mixture to rub on her abdomen. Acknowledging childbirth to be painful and often dangerous, the Babylonians and Greeks before Christ practised goddess-worship and placation with sacrifices. Hippocrates noted that primipara suffer the most pain in childbirth. Many ancient methods were non-pharmacological and seem to us barbaric.

Witchcraft was practised in mediaeval times and in 1591 Eufame McCulzean was

attempting to cast her labour pains onto a dog. In the 18th century Mesmer induced a trance-like state in his patients, the forerunner of present-day hypnotism which is occasionally used in childbirth. The introduction of general anaesthesia in 1846 was immediately recognised by James Young Simpson as applicable to childbirth. Simpson was professor of obstetrics in Edinburgh (and senior president of the R.M.S. in 1835), a man of wide interests and with a great humanitarian desire to introduce some form of pain relief for his patients in labour (Figure 1). Hearing of Liston's success in London, using ether for an amputation, he at once obtained a small quantity and used it on January 1st 1847. On January 19th he gave the first obstetric anaesthetic. He continued to use ether during 1847 but was not satisfied with it and began searching for an alternative.

Фармакокинетика ингаляционных анестетиков



Десфлуран → 0,45

Закись азота → 0,47

Севофлуран → 0,65

Изофлуран → 1,4

Галотан → 2,5

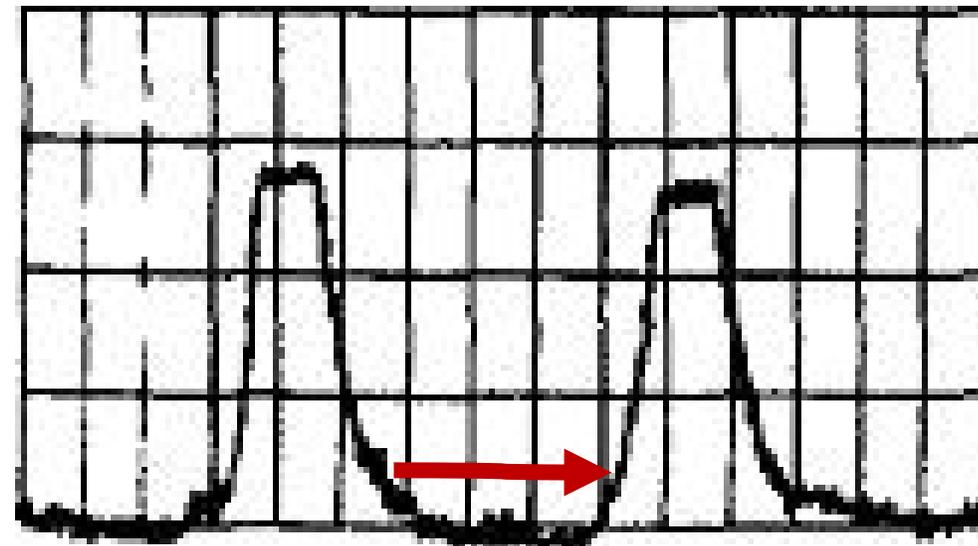
Метоксифлуран → 15



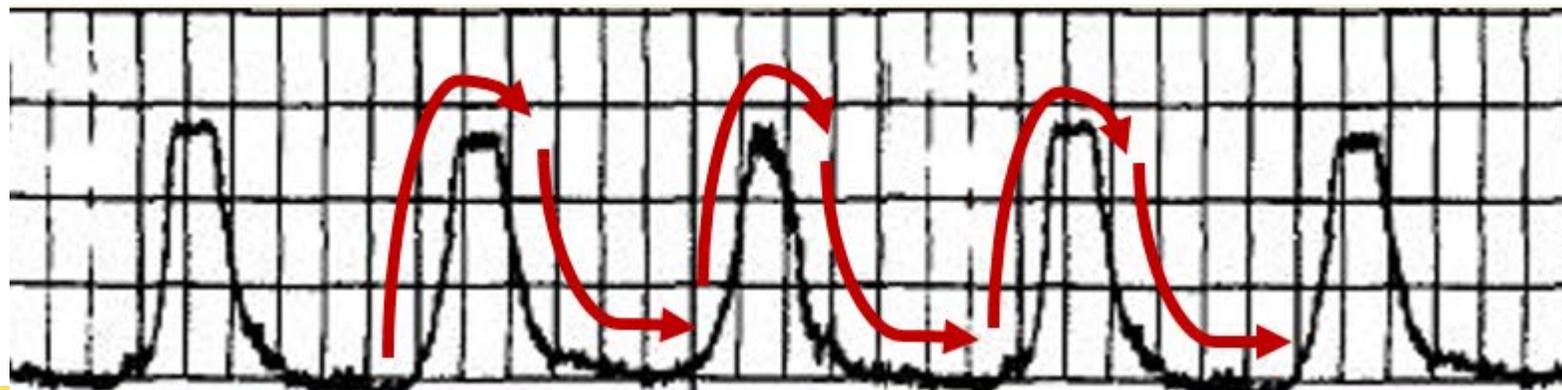
Режим введения (Entonox - N₂O/O₂ - 50/50)



- при продолжительных схватках (свыше 80-90")
- у повторнородящих



- при коротких энергичных схватках (60-70")
- у первородящих

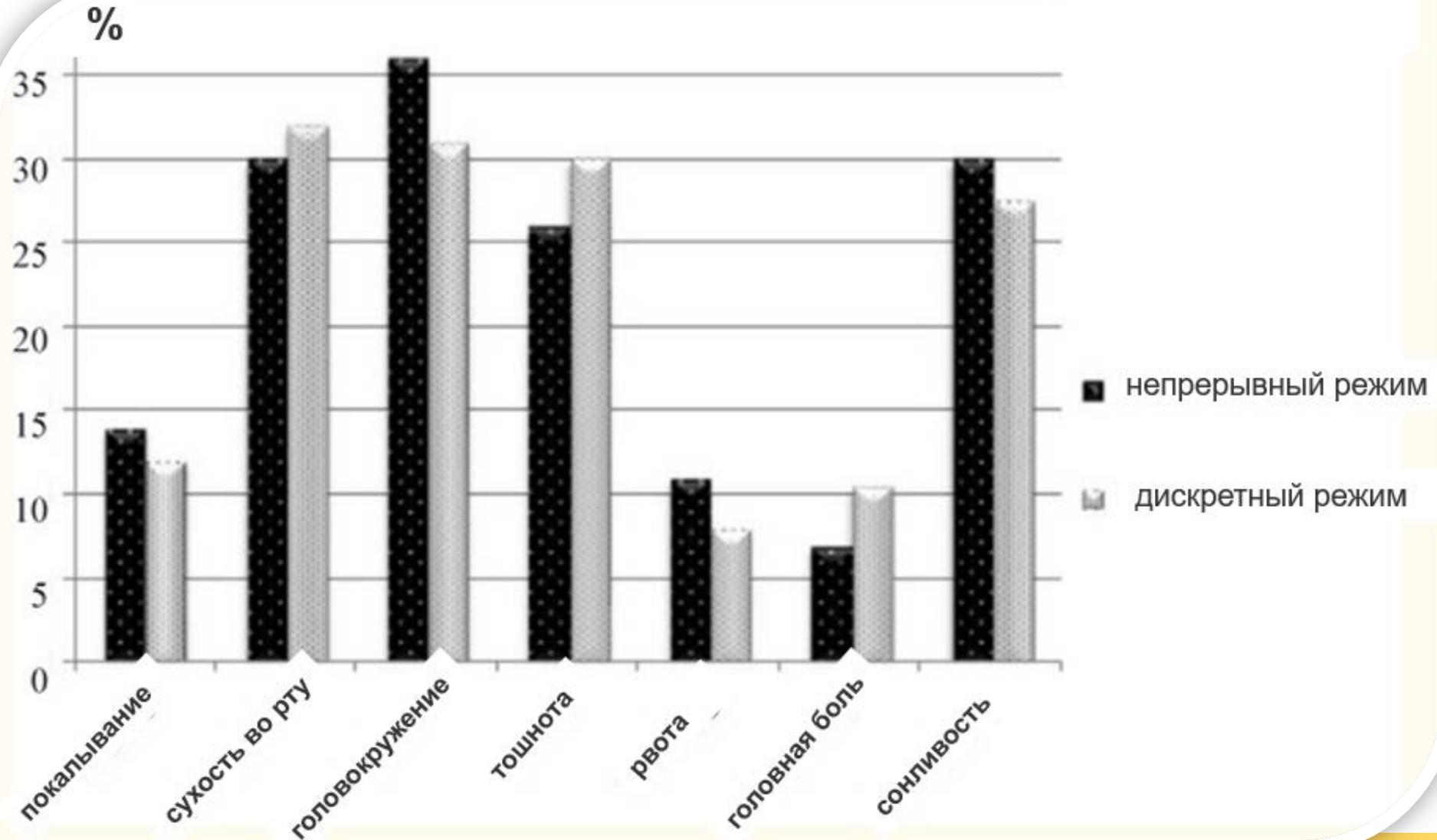


Побочные эффекты (закись азота)



Удовлетворенность обезболиванием (Entonox)

60



Iran J Pharm Res. 2016 Spring; 15(2): 641-646.

Maternal Side-Effects of Continuous Labor: A Randomized Clinical Trial

Jila Agah,^{a,*} Roya Baghani,^b Yaser Tabaraei,^c and Ab

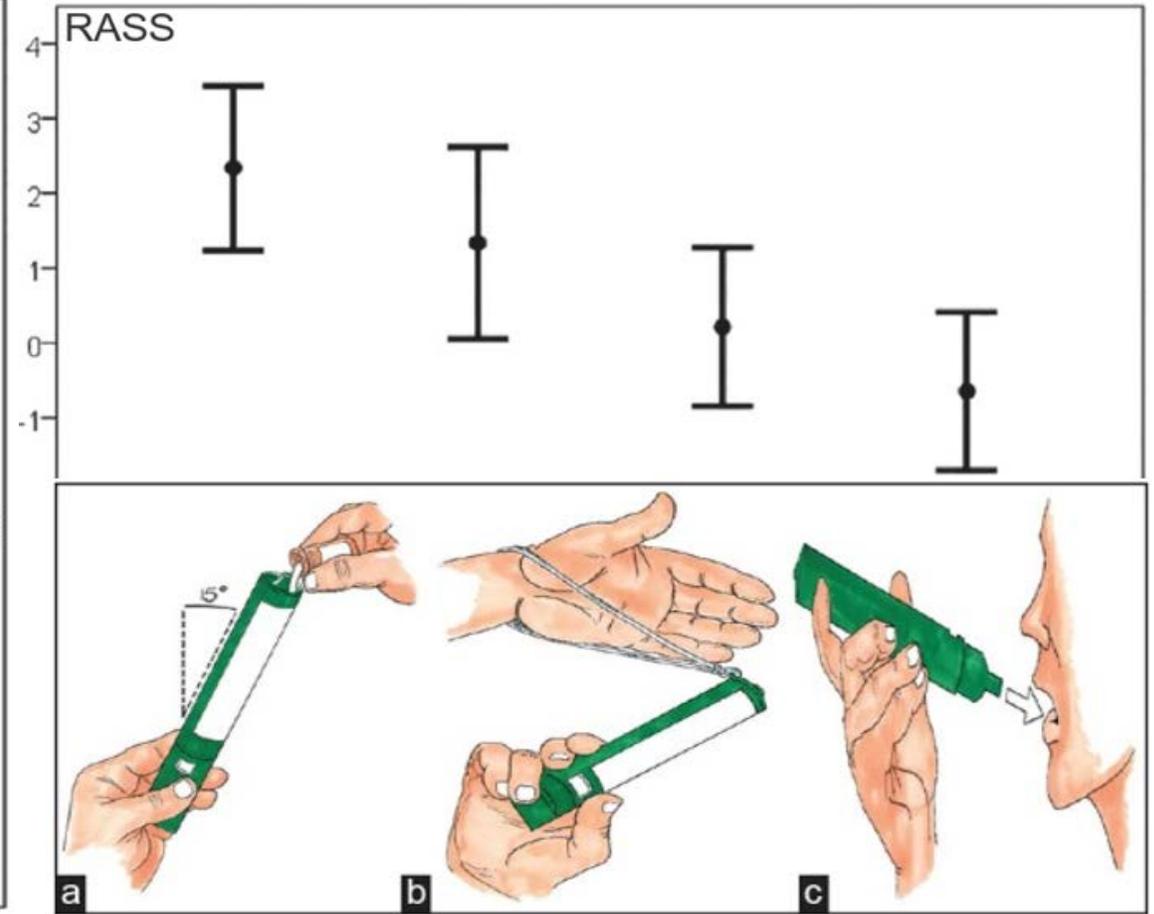
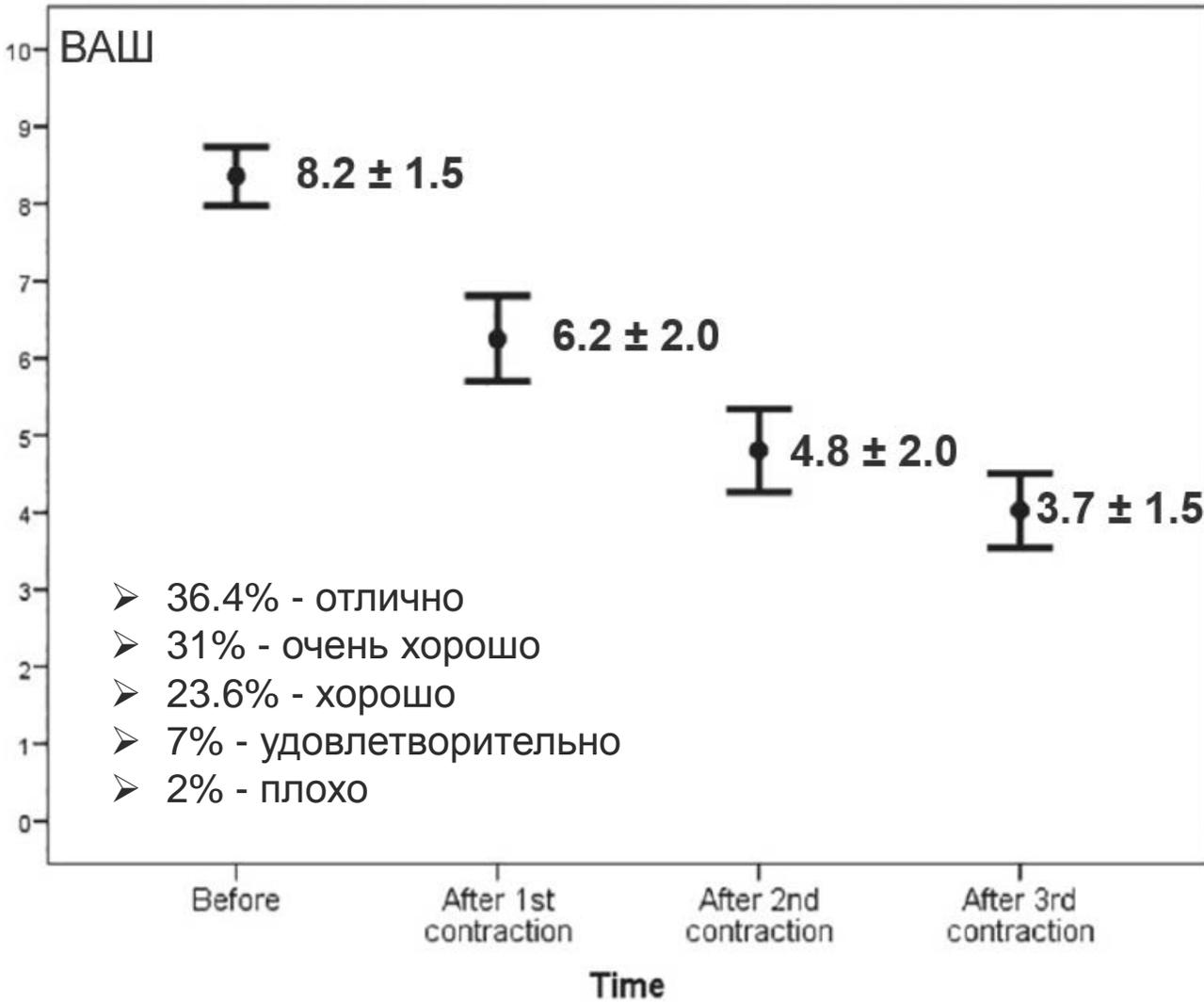
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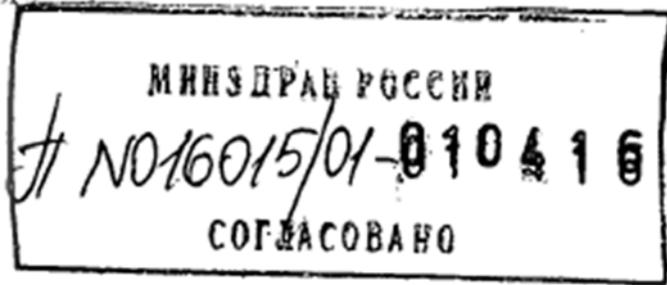
Abstract

Labor pain is one of the most tiresome types of p now. Administration of a suitable agent such as I outcomes. Entonox can be administered in two v study is to demonstrate whether continuous meth clinical trial was performed in Mobini Hospital, delivery were included in this study. Fitted patie thorough training, the patients used Entonox dur intermittently and 50 others used it continuously progression were registered and compared in two software, t-test and chi square test. The maternal two groups ($p>0.05$). Mothers' satisfaction rate i significantly ($p<0.001$). Meantime of active phas

Метоксифлуран в акушерстве



Севофлуран в акушерстве



...имеющиеся данные подтверждают безопасность применения севофлурана для матери и ребенка при проведении планового кесарева сечения. Безопасность севофлурана при родоразрешении через естественные родовые пути не изучалась.

Кесарево сечение

Использование севофлурана для поддержания анестезии при кесаревом сечении не вызывало неблагоприятных эффектов у матери или новорожденного. Не обнаружено разницы между севофлюраном и изофлюраном по влиянию на новорожденного, что оценивалось по шкале Апгар (8-9) и неврологической и адаптационной шкалам (в среднем = 29,5). Безопасность севофлурана при самопроизвольных родах не оценивалась.



➤ **МАК** (минимальная альвеолярная конечная анестетическая сила ингаляционного анестетика при атмосферном давлении, необходимая для предотвращения двигательной реакции в ответ на болевой стимул у 50% субъектов.

➤ **МАК пробуждения (MAC awake)** — минимальная альвеолярная концентрация, при которой после прекращения продуктивного контакта с 50% пациентов. Она характеризует седативный эффект анестетика.

Sevoflurane	1 MAC	MACawake/MAC
20 лет	2,6%	0,34
40 лет	2,1%	
беременность	1,8-2,0%	

Pregnancy Decreases the Requirement for Inhaled Anesthetic Agents

Richard J. Palahniuk, M.D.,* Sol M. Shnider, M.D.,† E. I. Eger, II, M.D.‡

The effects of pregnancy on requirements for inhalation anesthetic agents were evaluated. The minimum alveolar concentrations (MAC) of halothane, methoxyflurane, and isoflurane needed to prevent movement in response to a standard stimulus were determined in six pregnant and six nonpregnant ewes. Pregnancy was associated with significant reductions in MAC of 32 per cent for methoxyflurane, 25 per cent for halothane, and 40 per cent for isoflurane. (Key words: Anesthesia, obstetric; Pregnancy; MAC; Potency, anesthetic; MAC.)

PHYSIOLOGIC CHANGES such as an increase in alveolar ventilation and a decrease in functional residual capacity explain in part the ease with which the parturient can be anesthetized with conventional doses of inhalation anesthetics.¹⁻⁴ There is, however, also the possibility that the anesthetic requirement might be reduced during pregnancy. We have studied the relative anesthetic potencies (as defined by MAC^{5,6}) of three inhalation anesthetics in pregnant and nonpregnant ewes.

Method

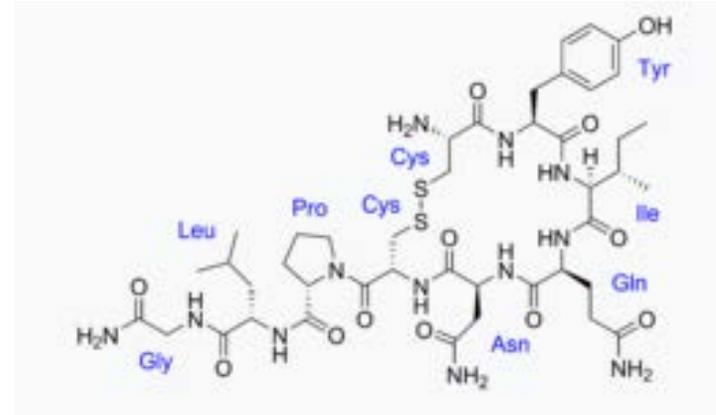
We determined MAC's in six pregnant ewes and compared the values obtained with MAC's in six nonpregnant ewes. Ewes were of mixed breeds but were obtained from the same flock. All pregnant ewes were within three weeks of term as determined by known breeding date and x-ray. Each animal was anesthetized in sequence with isoflurane (Forane®), halothane, and methoxyflurane. At least 48 hours elapsed between administrations. We gave no drug other than the anesthetic agent and oxygen. Anesthesia was administered by mask for induction and the trachea intubated. Ventilation was controlled with an Air-Shields Ventilator at 12 breaths/min at 7 to 10 ml/kg tidal ventilation. End-tidal gas samples were obtained through a nylon catheter inserted to near the distal end of the endotracheal tube. Isoflurane and methoxyflurane were analyzed with a Beckman LB-1 infrared Medical Gas Analyzer. Halothane was analyzed with an Analytic Systems ultraviolet analyzer. MAC was determined in triplicate as previously described.^{5,6}

Original Article

Effect of breastfeeding on haemodynamics and consumption of propofol and sevoflurane: A state entropy guided comparative study

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- Анальгетический эффект окситоцина реализуется посредством влияния на эндогенные опиоиды. Высвобождение опиоидных пептидов стимулируется нейротрансмиссией окситоцина
- Подтверждена кардиопротективная роль окситоцина, который может влиять на выраженность гемодинамических ответных реакций

Propofol and Sevoflurane usage	лактация	без лактации	контроль	P
Общая доза пропофола, мг (mean±SD)	74.13±6.97	102.88±5.30	95.25±8.00	<0.001**
Потребность в пропофоле, мг/кг (mean±SD)	1.22±0.05	1.73±0.04	1.58±0.08	<0.001**
Общая доза севофлурана, мл (mean±SD)	3.80±0.76	6.43±0.75	5.15±0.77	<0.001**
etSev,%	1.41±0.11	2.19±0.58	1.85±0.36	<0.001**

Севофлуран/сократительная способность миометрия

International Journal of Obstetric Anesthesia (2002) 11, 246–251
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 doi:10.1054/ijoa.2002.0963, available online http://www.idealibrary.com on IDEAL®

ORIGINAL ARTICLE

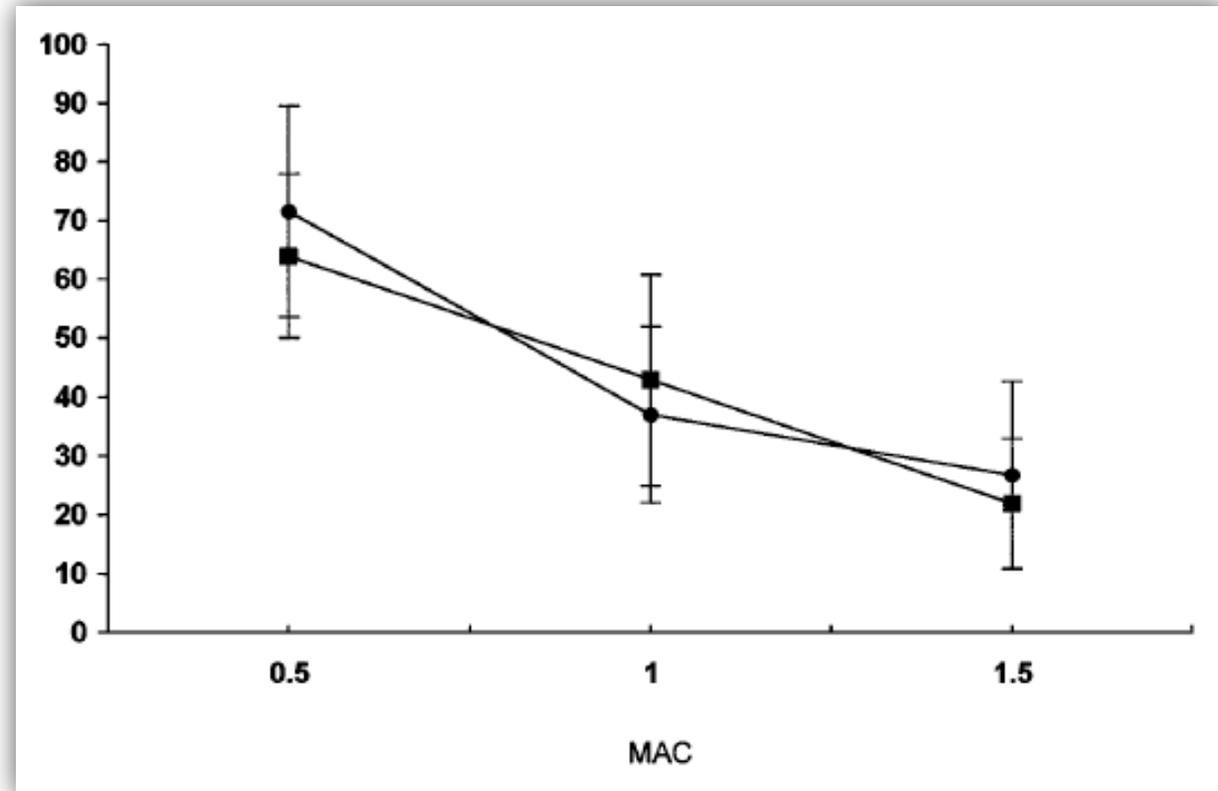
The in-vitro effects of sevoflurane and desflurane on the contractility of pregnant human uterine muscle

R. J. Turner, M. Lambros, L. Kenway, S. P. Gatt

Department of Anaesthesia, Prince of Wales Hospital, Randwick, NSW Australia

SUMMARY. The effect of desflurane and sevoflurane on the contractility of the uterus was examined *in vitro* on strips of human myometrium obtained at the time of elective cesarean section. Small strips (1 mm × 2 mm × 10 mm) of muscle were prepared and suspended in an organ bath containing oxygenated physiological saline. Force of contraction was recorded continuously using an isometric tension transducer. Following the onset of regular spontaneous contractions, baseline measurements were obtained and the strips were exposed to varying concentrations of sevoflurane or desflurane corresponding to 0.5, 1.0 and 1.5 minimum alveolar concentration (MAC). Sevoflurane depressed contractility to 72 ± 18% of control at 0.5 MAC, 37 ± 15% at 1.0 MAC and 27 ± 16% at 1.5 MAC compared with 65 ± 14 of control at 0.5 MAC, 43 ± 18% at 1.0 MAC and 22 ± 11% at 1.5 MAC for desflurane. The degree of depression of uterine muscle contractility produced by both these agents was significantly different from control at all concentrations. In conclusion, both sevoflurane and desflurane depress the contractility of isolated pregnant human myometrium at concentrations of 0.5, 1.0 and 1.5 MAC. These agents produce a similar degree of depression of uterine muscle contractility. © 2002 Elsevier Science Ltd. All rights reserved.

- Применение севофлурана более 1МАК/час в акушерстве чревато токолитическим эффектом и депрессией плода



	● Севофлуран		■ Десфлуран	
	сократительная способность	Частота	сократительная способность	Частота
0.5 MAC	72 ± 18%*	103 ± 20%	65 ± 14%*	99 ± 19%
1.0 MAC	37 ± 15%*	119 ± 34%	43 ± 18%*	128 ± 14%*
1.5 MAC	27 ± 16%*	119 ± 31%	22 ± 11%*	172 ± 41%*

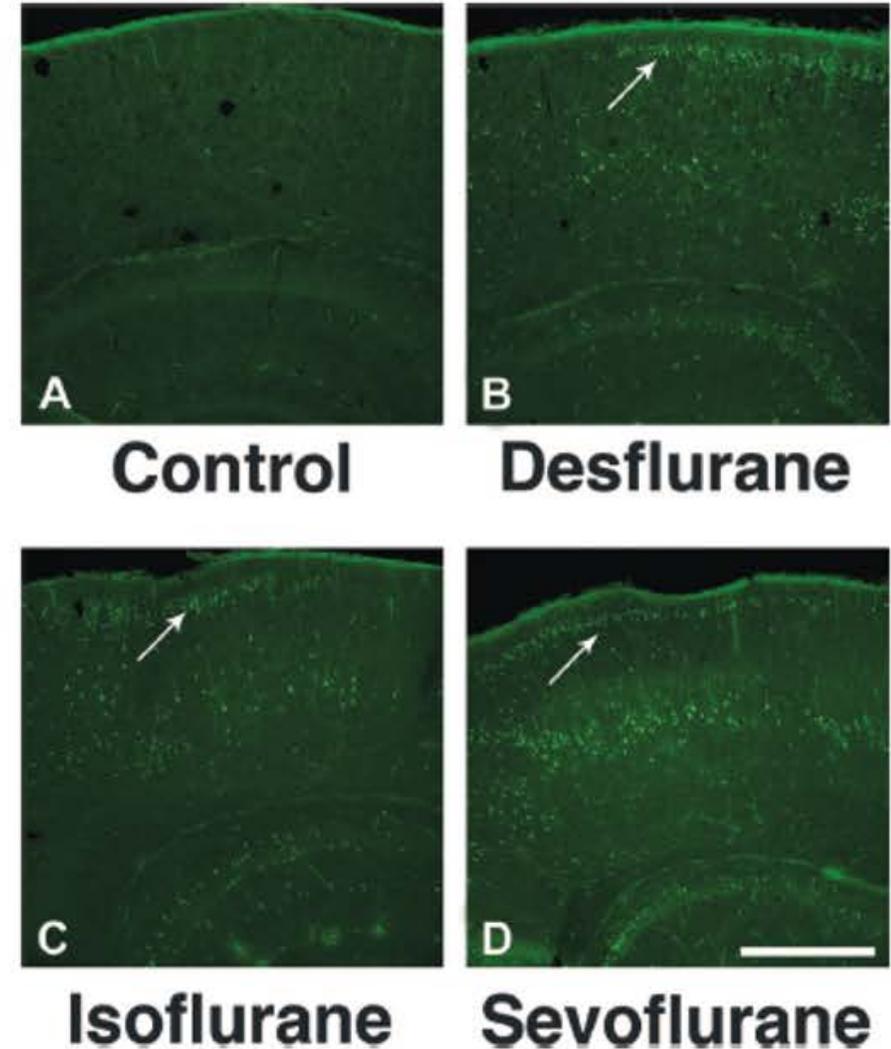
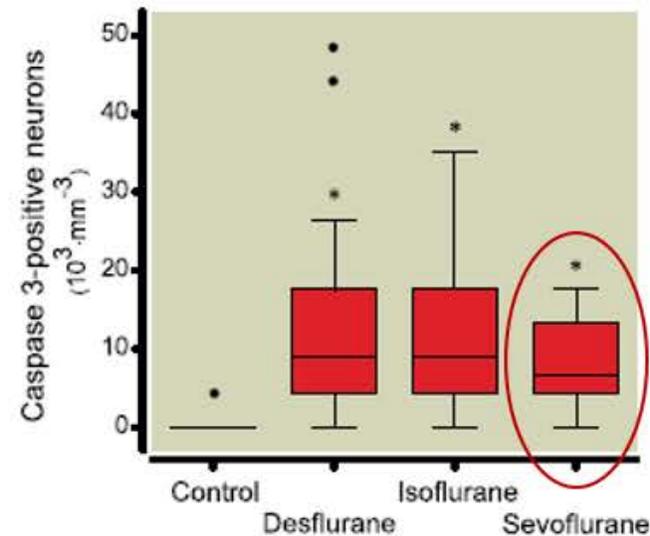
Anesthesiology 2011; 114:578-87

Comparison of the Neuroapoptotic Properties of Equipotent Anesthetic Concentrations of Desflurane, Isoflurane, or Sevoflurane in Neonatal Mice

George K. Istaphanous, M.D.,* Jennifer Howard, B.S.,† Xinyu Nan, B.S.,† Elizabeth A. Hughes, B.S.,† John C. McCann, B.S.,† John J. McAuliffe, M.D., M.B.A.,‡ Steve C. Danzer, Ph.D.,§ Andreas W. Loeperke, M.D., Ph.D.||

ABSTRACT

Background: Volatile anesthetics facilitate surgical procedures and imaging studies in millions of children every year. Neuronal cell death after prolonged exposure to isoflurane in developing animals has raised serious concerns regarding its safe use in children. Although sevoflurane and desflurane are becoming more popular for pediatric anesthesia, their cytotoxic effects have not been compared with those of isoflurane. Accordingly, using newborn mice, the current study established the respective potencies of desflurane, isoflurane, and sevoflurane and then compared equipotent doses of these anesthetics regarding their effects on cortical neuroapoptosis.





Концентрация севофлурана в молоке клинически не значима через 24 часа после анестезии. Вследствие быстрого вымывания концентрация севофлурана в молоке будет ниже, чем у других ингаляционных анестетиков.

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Safety of the breast-feeding infant after maternal anesthesia

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Keywords
breast feeding; anesthesia; infant

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Summary
There has been an increase in breast-feeding supported by the recommendations of the American Academy of Pediatrics and the World Health Organization. An anesthesiologist may be presented with a well-motivated breast-feeding mother who wishes to breast-feed her infant in the perioperative period. Administration of anesthesia entails acute administration of drugs with potential for sedation and respiratory effects on the nursing infant. The short-term use of these drugs minimizes the possibility of these effects. The aim should be to minimize the use of narcotics and benzodiazepines, use shorter acting agents, use regional anesthesia where possible and avoid agents with active metabolites. Frequent clinical assessments of the nursing infant are important. Available literature does suggest that although the currently available anesthetic and analgesic drugs are transferred in the breast milk, the amounts transferred are almost always clinically insignificant and pose little or no risk to the nursing infant.

Учитывая короткий период полувыведения севофлурана у матери, препарат не должен проникать к новорожденному.

Effects of different anesthesia protocols on lactation in the postpartum period

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Abstract

Objective: Many factors can influence the secretion of breast milk. Cesarean section is a risk factor for late onset of breastfeeding.

Material and Methods: In our study, we compared the lactation process by mothers who underwent elective cesarean section under general anesthesia, spinal anesthesia, epidural anesthesia, and normal birth; 84 patients between 18-40 years of age with a risk of ASA I-II were included. Randomly patients were divided into four groups: group G (general anesthesia, n:21), group S (spinal anesthesia, n:21), group E (epidural anesthesia, n:21), and group V (vaginal birth, without anesthesia, n:21). Oxytocin and prolactin values of all patients before and after operation or birth were recorded. In addition the initiation time of lactation after delivery or cesarean section were recorded.

Results: In all groups, there were no significant differences among hormone levels in the prepartum period ($p=0.350$). Prolactin levels in group G ($p=0.011$) and oxytocin levels in group V ($p=0.012$) in the postpartum period were significantly higher than in the other groups. The start of lactation was significantly delayed in group G ($p=0.003$).



	Общая анестезия	Спин/анестезия	Эпид/анестезия	Самопроизвольные роды	p value
Prolactin _{pre}	244.6±105.7	198.2±57.4	222.3±81.9	237.1±103.5	0.350
Prolactin _{post}	363.7±120.9	270.4±100.4 ^a	264.0±108.2 ^b	300.8±87.5	0.015
Oxytocin _{pre}	2.3±0.2	2.2±0.4	2.4±0.5	2.4±0.3	0.138
Oxytocin _{post}	2.3±0.3	2.2±0.5	2.6±0.7 ^c	2.8±0.4 ^c	0.012
Начало грудного вскармливания, ч	25.0±22.9 ^a	10.8±10.2	11.8±8.8	10.9±9.7	0.003

ORIGINAL ARTICLE

Sevoflurane analgesia in obstetrics: a pilot study ☆

A. Toscano, C. Pancaro, S. Giovannoni, G. Minelli, C. Baldi, G. Guerrieri,
J. A. Crowhurst,^a V. A. Peduto

Department of Anesthesia and Intensive Care, University Hospital, Perugia, Italy and ^aDepartment of Anaesthesia and Intensive Care, Queen Charlotte's Hospital, London, UK

SUMMARY. Continuous and intermittent administration of inhalational anesthetics has been successfully employed for treating pain during labor. We conjectured that intermittent sevoflurane administration would be effective for pain relief during labor without side effects to the mother or fetus. Fifty parturients breathed a mixture of 2–3% sevoflurane, oxygen and air before each uterine contraction began. The patients assessed the quality of analgesia by using a visual analogue scale (0–10) before the administration of sevoflurane and after each uterine contraction. All parturients but one were satisfied, demonstrating a mean visual analogue score before and after sevoflurane administration of 8.7 ± 1.1 and 3.3 ± 1.5 , respectively. Apgar scores at 1 and 5 min were 9 (range 5–9) and 10 (range 8–10), respectively. Our findings suggest that sevoflurane could be effective for the treatment of labor pain.

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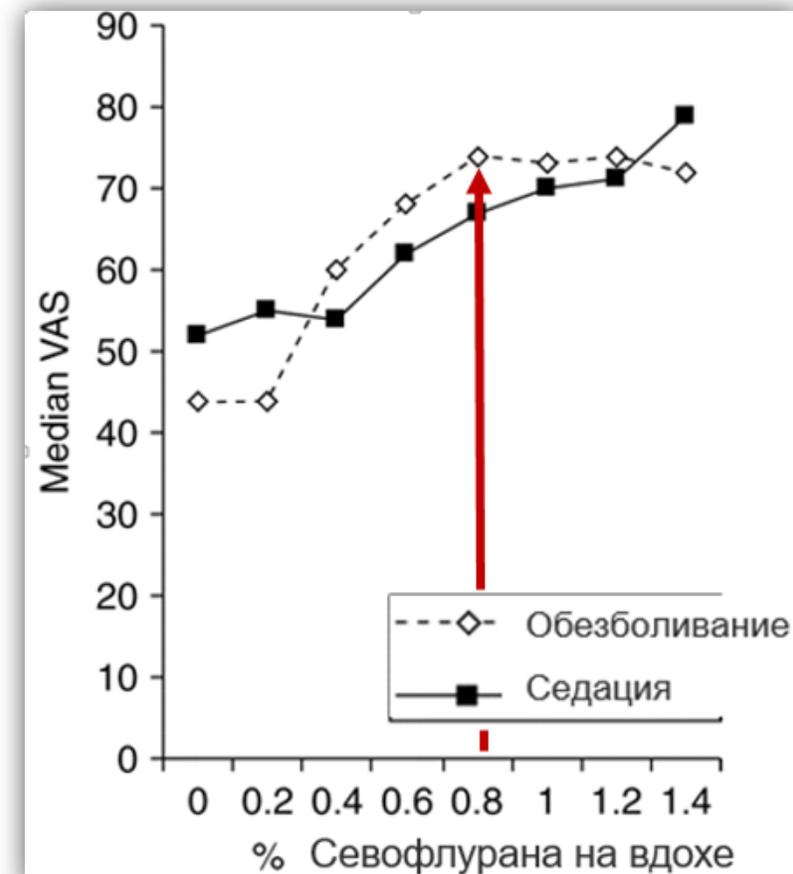
- n=50, ОМЗ 5см (3-9).
- система Mapleson, лицевая маска
- поток 6л/мин, FiO₂ 0,5 + Севофлуран
- дискретный режим введения: за 60" до схватки севофлуран в концентрации 2-3 об% добавляли к кислород-воздушной смеси до достижения концентрации на выдохе etSev 1-1,5 об%. При внеочередном маточном сокращении концентрация увеличивалась до 4-5 об% в течении 3-х вдохов, а затем снижалась до 2 об% до достижения etSev 1-1,5 об%.
- Для определения эффективной концентрации севофлурана применяли метод Диксона¹
- Среднее время экспозиции 119±75мин,
- ВАШ 8,7±1,1 → 3,3±1,5
- Апгар 9-10, кровопотеря 245±97мл
- Осложнения: сонливость (4), эпизодов десатурации, нарушения ЧСС плода не зафиксировано.

**Не подобрана эффективная концентрация
Расход анестетика!**

Analgesia with sevoflurane during labour: I. Determination of the optimum concentration^{†‡}

S. T. Yeo^{1,3*}, A. Holdcroft¹, S. M. Yentis¹ and A. Stewart²

- n=22, ОМЗ > 3см
- мини-испаритель (Penlon Ltd, Oxford, UK), лицевая маска
- поток 4л/мин, кислород - воздух, концентрация O₂ от 37% до 51% + Севофлуран
- Для определения эффективной концентрации севофлурана применяли метод Диксона (0,2 об%)
- Осложнения: 4 – чрезмерная седация (при 1,2 об%)



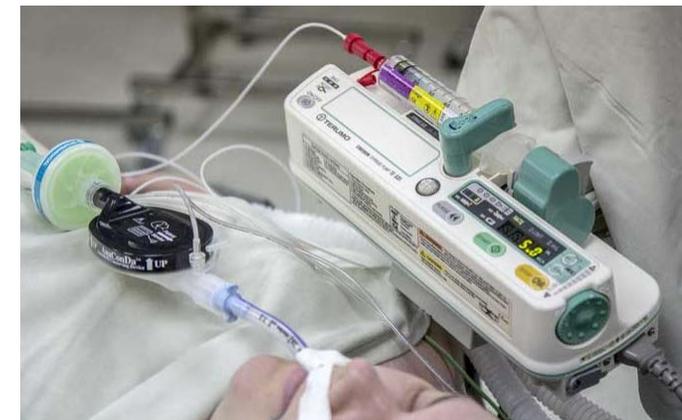
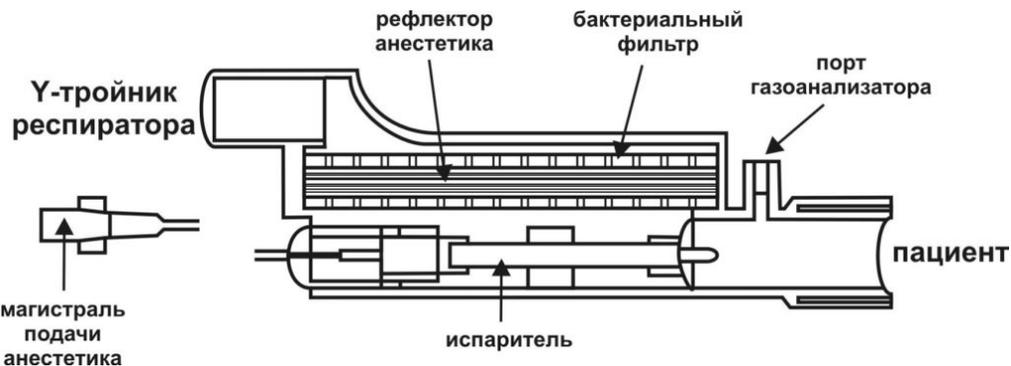
Концентрация Севофлурана 0,8 об% является оптимальной для обезболивания самопроизвольных родов

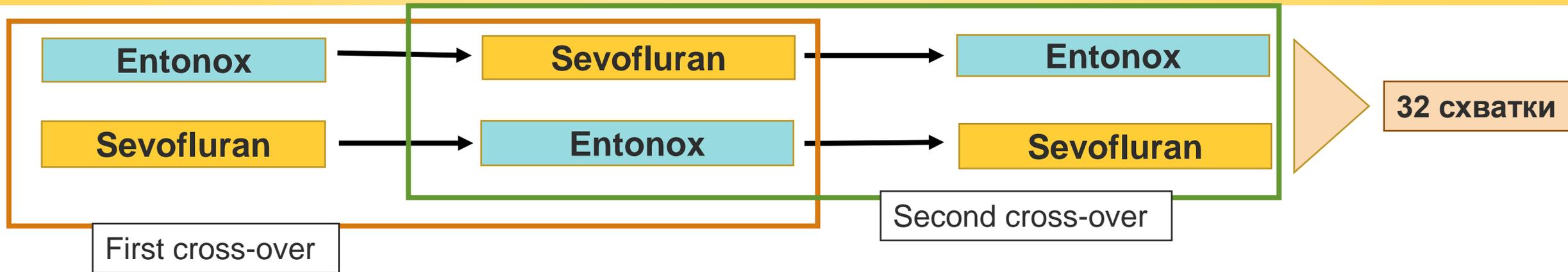


- меньшая точность при прерывистом режиме подачи газовой смеси
- концентрация анестетика в контуре была заметно выше, чем установленная на циферблате, особенно при высоких температурах окружающей среды

	20 °C	25 °C	30 °C
OMV	-0.51	+0.19	+0.5
DDV	-0.44	-0.3	-0.1

AnaConDa (The Anaesthetic Conserving Device - ACD)





Результаты исследования
n=32(16-16)

E-S-E

S-E-S

Выбыло 8 рожениц:
 2 - отказались от SeV
 4 - попросили ДЭА (3-7 схватка)
 1 - после 6 схватки - II п-д

самопроизвольные роды	21 (68%)
вакуум-экстракция плода	6 (19%)
кесарево сечение	4 (13%)
кровопотеря, мл	225 (150-500)

Выбыло 2 роженицы:
 после 7 схватки – ДЭА
 после 4 схватки - II п-д

Результаты исследования

VAS	P-values	Statistical significance	Comparison of VAS between agents	Mean difference, confidence interval
<u>Pain relief</u>				
First cross-over	0.0115	Significant	<u>Sevoflurane>Entonox</u>	MD 12 mm, 95% CI 3–21 mm
Second cross-over	0.0006	Significant	<u>Sevoflurane>Entonox</u>	MD 18 mm, 95% CI 9–28 mm
<u>Sedation</u>				
First cross-over	0.0001	Significant	<u>Sevoflurane>Entonox</u>	MD 21 mm, 95% CI 12–31 mm
Second cross-over	0.0001	Significant	<u>Sevoflurane>Entonox</u>	MD 29 mm, 95% CI 16–41 mm

- Севофлуран продемонстрировал лучший анальгетический эффект;
- Севофлуран связан с большей степенью седации, чем Entonox;
- Ни одна из рожениц не испытывала выраженную сонливость, все были в состоянии выполнить команды на протяжении всего периода исследования;
- Одна роженица испытала тошноту в группе Севофлурана, рвоты не зарегистрировано; В группе Entonox частота тошнота/рвота составила 8/4

Inhaled analgesia for pain management in labour (Review)

Klomp T, van Poppel M, Jones L, Lazet J, Di Nisio M, Lagro-Janssen ALM



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2012г.

26 исследований
2959 женщин
производные флурана (13)
N=18-509

Энфлуран 0,25-1,25%(Abboud 1981; McGuinness 1984; Stefani 1982)

Десфлуран 1,4-5% (Abboud 1995; Swart 1991)

Метоксифлуран 0,3-0,8% (Bergsjö 1971; Belfrage 1974; Jones 1969)

Севофлуран 0,8% (Yeo 2007)

Изофлуран 0,2-0,75% (McLeod 1985; Cheng 2001)

Изофлуран 0.2%-0.25%/ N₂O 50% (Arora 1992; Wee 1993)

Постоянный режим (Abboud 1981; Abboud 1995; Jones 1969; Stefani 1982)

Дискретный режим (Arora 1992; Bergsjö 1971; Cheng 2001; Jones 1969a; McGuinness 1984; McLeod 1985; Wee 1993, Yeo 2007)

Сравнение N₂O/производные флурана

Критерии оценки	Кол-во исследований	Кол-во пациентов	Результаты исследования		Статистический метод
Интенсивность боли (ВАШ, I период)	3	70	ПФ < N ₂ O	14.39 [4.41, 24.37]	MD (Random, 95% CI)
Обезболивание (ВАШ, I период)	2	70	ПФ > N ₂ O	-16.32 [-26.85, -5.79]	MD (Random, 95% CI)
Удовлетворенность обезболиванием	2/4	98/323	нет различий	0.98 [0.80, 1.18]	RR (Fixed, 95% CI)
Вакуум-экстракция плода	5	371	нет различий	0.71 [0.44, 1.15]	RR (Random, 95% CI)
Кесарево сечение	1	98	нет различий	0.0 [0.0, 0.0]	RR (Fixed, 95% CI)
Амниоцизия	2	245	нет различий	0.26 [0.02, 0.29]	RR (Random, 95% CI)

Отсутствие влияния:

- первый контакт в течение 1 часа
- грудное вскармливание
- необходимости в ИТ
- одинаковая выживаемость



MD (Fixed, 95% CI)

RR (Fixed, 95% CI)

RR (Fixed, 95% CI)

MD (Fixed, 95% CI)

RR (Fixed, 95% CI)

PR210
SEVONOX STUDY: A COMPARISON OF 0.8% SEVOFLURANE & ENTONOX FOR LABOUR ANALGESIA



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Background & Objectives: Labour epidural remains the gold standard for analgesia but is rarely available in developing countries. Parenteral opioids and Entonox (nitrous oxide 50%:

Parameter	Sevoflurane N=24	Entonox N=24	P Value
Среднее значение (МКИ* [интервал])			
Общая оценка боли	4.5 (2.5-9.0 [0.0-10.0])	5.0 (2.0-9.5 [1.0-10.0])	0.908
Оценка боли в течении 1-го часа	5.5 (4.0-7.0 [2.0-10.0])	6.0 (4.0-7.8 [0.0-10.0])	0.950
Оценка боли в течении последнего часа	8.0 (8.0-10.0 [2.0-10.0])	9.0 (8.0-10.0 [5.0-10.0])	0.616
Пациенты (%)			
Инструментальные роды	1.0 (4.2%)	5.0 (20.8%)	0.097
Кесарево сечение	6.0 (25.0%)	2 (8.3%)	0.121
Тошнота/рвота	1.0 (4.2%)	4.0 (16.7%)	0.156

Концентрация 0,8 об% Севофлурана сопоставима с Энтоноксом по анальгетической активности и аналогична по профилю безопасности

 **Съезд**
Congress



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Спасибо за внимание!
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