


# 5-HT<sub>3</sub> blockade does not attenuate postspinal blood pressure change in cesarean section

## A case-control study

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### Abstract

Spinal anesthesia (SpA) for elective caesarean section (CS) is often accompanied by clinically relevant arterial hypotension. The Bezold-Jarisch reflex, causing postspinal hypotension, has been shown to be antagonized by serotonin type 3 (5-HT<sub>3</sub>) blockade. Our aim was to assess if routine prophylactic administration of the 5-HT<sub>3</sub> antagonist ondansetron (ODS) attenuates postspinal change in maternal blood pressure.

Elective CS under SpA were retrospectively analyzed. Eighty parturients having routinely received 8 mg ODS prior to SpA were compared with 80 patients having not (control group).

Mean arterial blood pressure significantly decreased from baseline to the postspinal period ( $P < .0001$ ) without differences in blood pressure decreases between the 2 groups. This also applied to the heart rate. Overall use of cafedrine/theodrenaline was higher in the ODS group (0.8 (0.4–1.6) mL vs 0.8 (0–1.0) mL in the control group,  $P = .01$ ). APGAR values showed a presumably clinically irrelevant decrease in control group compared with the ODS group.

Our results suggest that routine administration of ODS in a dosage of 8 mg does not effectively attenuate postspinal change in maternal blood pressure during CS in our setting. Given the wide variability of anesthetic techniques, only large prospective and randomized multicenter trials will ultimately serve to elucidate this issue.

**Abbreviations:** 5-HT = serotonin, 5-HT<sub>3</sub> receptor = serotonin receptor type 3, BJR = Bezold-Jarisch reflex, CS = cesarean section, HR = heart rate, MAP = mean arterial blood pressure, ODS = ondansetron, SpA = spinal anesthesia.

**Keywords:** 5-HT<sub>3</sub>, cesarean section, ondansetron, spinal anesthesia

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### 1. Introduction

According to current guidelines, elective cesarean section (CS) is usually performed under spinal anesthesia (SpA).<sup>[1]</sup> Arterial hypotension is one of the most common complications associated with this technique.<sup>[2]</sup> Besides maternal symptoms such as dyspnoea or nausea, impaired uteroplacental perfusion may seriously affect the fetal well-being, as evidenced by lowered umbilical cord blood pH or reduced APGAR scores.<sup>[3]</sup> A sympathetic vasomotor block is mainly responsible for the decrease in arterial blood pressure during the onset of SpA. Consequently, intravenous fluids and vasopressors are commonly administered to counteract this phenomenon.<sup>[2]</sup>

In addition to direct vasoplegia, hypotension may be aggravated by bradycardia and vasodilation induced by activation of mechanoreceptors in the left ventricle, thereby shifting the autonomic control toward a parasympathetic dysbalance. This depressor reflex is called the Bezold-Jarisch reflex (BJR).<sup>[4]</sup> Results from animal studies suggest that the BJR is mediated by the activation of serotonin (5-HT) type 3 (5-HT<sub>3</sub>) receptors located on intracardial endings of vagal afferent nerves and may consequently be blocked using 5-HT<sub>3</sub> antagonists.<sup>[5]</sup> However, results from a recent meta-analysis on studies assessing the effect of 5-HT<sub>3</sub> blockade to prevent or treat SpA-induced hypotension and bradycardia are inconclusive, suggesting rather moderate effects only in obstetric patients.<sup>[6]</sup> Moreover, validity of many trial results may be restricted due to limited patient numbers.

Thus, it was our aim to investigate whether 5-HT<sub>3</sub> blockade using prophylactic administration of ondansetron may reduce bradycardia as well as attenuate change in maternal blood pressure during CS performed under SpA in a larger patient cohort. Data were retrospectively analyzed following a change in periprocedural anesthesiological management in the obstetrical department of a German university medical center.

## 2. Patients and methods

### 2.1. Study design and oversight

Parturients who had undergone elective CS under SpA were included into the analysis. Due to the retrospective design of the study, patient consent was waived according to the approval of the institutional review board. An analysis of the impact of blockade of 5-HT<sub>3</sub> receptors with regard to change in blood pressure as well as incidence of bradycardia, vasopressor use, fluid intake, and maternal and infantile outcome was performed. The retrospective data evaluation was based on the patient files and electronic documentation of the anesthesia process. Only patients with complete datasets were included into the analysis.

### 2.2. Patients and interventions

During the period from May 2017 to December 2018, the periprocedural management in our institution changed from no routine administration to routine 5-HT<sub>3</sub> blockade being administered prior to SpA. Elective CS during this period were checked for eligibility for retrospective analysis. Inclusion criterion was American Society of Anesthesiologists status I or II. Exclusion criteria were: pre-existing cardiovascular conditions, known contraindications to and prior medication with serotonin (ant-)agonists, emergency procedures, conversion to general anesthesia, additional sedation, use of combined spinal-epidural anesthesia, and procedures with a blood loss of >1000 mL (including multiple pregnancies). For retrospective analysis, sample size was calculated as follows: assuming an incidence of postspinal hypotension in obstetric patients of 55% and a reduction to 35% by prophylactic administration of ondansetron, both according to the recent literature,<sup>[6]</sup> we calculated a required size of 63 patients per group to obtain a statistical power of 90% at a probability of type I error (alpha level) of 0.05.<sup>[7]</sup> To account for possible dropouts, sample size was increased to 80 patients. We formed 2 patient cohorts of the same size according to the treatment regimen: 80 consecutive patients meeting the inclusion criteria following the change in management (each receiving 8 mg ondansetron as slow i.v. injection prior to SpA (ODS group)), and 80 consecutive patients before this change (having not received ODS and therefore being designated control group).

Patients arrived in the operation room on the operation table in supine position. Apart from ODS administration, all patients received 1000 mL crystalloid infusion solution (Jonosteril, Fresenius Kabi, Germany) as pressure infusion via peripheral i.v. line during administration of SpA (coload) over a time period of 10 to 15 minutes in accordance with our institutional standard procedure and recent recommendations. After change to the sitting position, standard monitoring comprising a 3-channel ECG, noninvasive blood pressure measurement, and pulse oximetry was installed. SpA was performed using hyperbaric bupivacaine 0.5% (dosage of 0.1 mL/10 cm body

height), supplemented with 5 µg sufentanil, at the level of lumbar vertebra 2/3 or 3/4 interspace, according to institutional standard. Blood pressure and heart rate (HR) measured immediately before SpA were termed baseline values.

Following administration of SpA, patients were placed in a left-lateral tilted position to avoid aortocaval compression. Correction of hypotension following onset of SpA using fluids and vasopressors was left to the attending anesthetist. In our department, Akrinor (Ratiopharm, Germany), a fixed mixture of cafedrine hydrochloride 200 mg and theodrenaline hydrochloride 10 mg in a volume of 2 mL, is routinely used to treat hypotension due to SpA for CS. According to recent recommendations, vasopressors are used to correct a systolic blood pressure decreasing below 100 mm Hg and not prophylactic. Norepinephrine is only administered in case of severe and life-threatening hypotension (e.g., due to massive blood loss, refractory aortocaval compression, high level of spinal block). The same applies to colloid infusion solutions, while crystalloid infusion solution is used as a routine fluid.

Blood pressure, administered dosage of Akrinor, volume replacement before and during CS, and HR were recorded and analyzed. In addition, all data relating to anesthesia and surgery were extracted from the electronic patient data management system.

### 2.3. Primary outcome

The primary outcome measure was the change in mean arterial blood pressure (MAP) following onset of SpA.

### 2.4. Secondary outcome

Secondary outcome parameters were the changes in HR following SpA, the number of administered vasopressors and crystalloid fluids, blood loss, and postnatal outcome of the newborn (APGAR score, cord blood pH, and base excess).

### 2.5. Statistical analysis

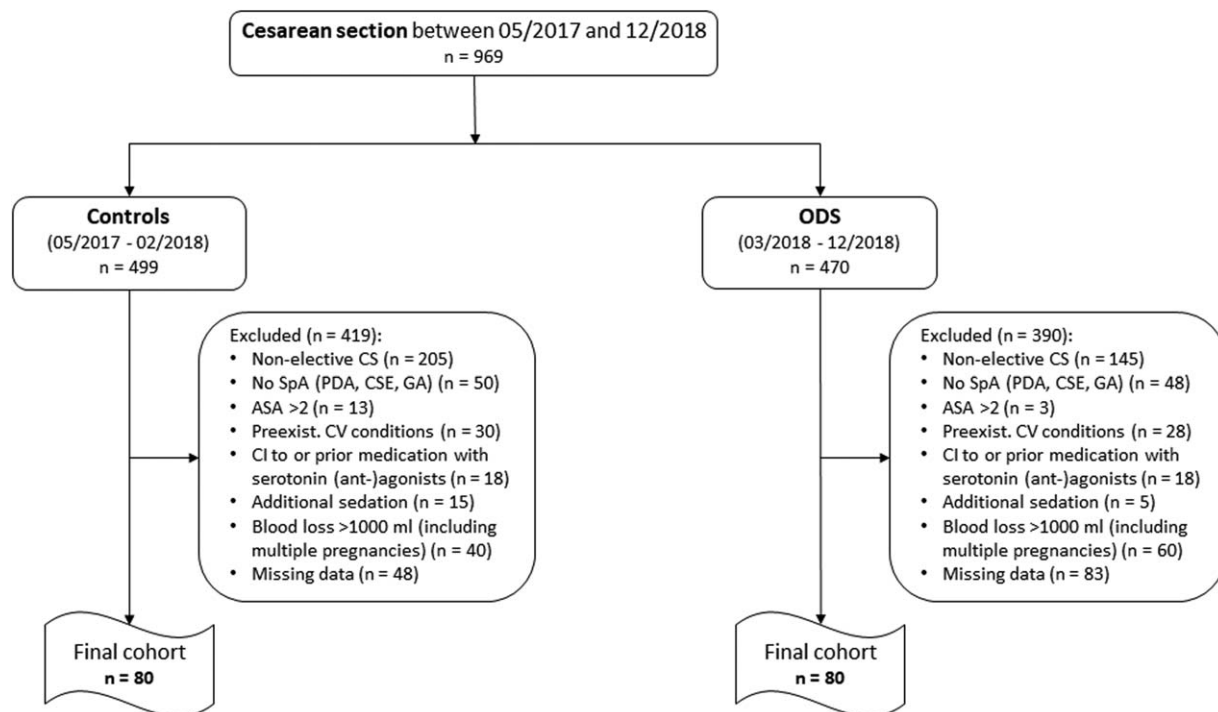
All data were transferred to Microsoft Excel (Version 16.16.11, 2018) and analyzed using IBM SPSS Version 23. Data are given as median values with 25 and 75 percentiles. They were analyzed using the Mann–Whitney *U* test for unpaired data, the Wilcoxon signed rank test for paired data, and the  $\chi^2$  test, respectively. The alpha level was set to 0.05. Graphical presentation was performed using Graphpad Prism 8.

All datasets generated for this study are available from the corresponding author on reasonable request.

## 3. Results

### 3.1. Patients

One hundred sixty patients undergoing elective cesarean section were retrospectively analyzed. While patients for the control group were recruited from the period between May 2017 and February 2018, that is, before the introduction of routine administration of ODS prior to SpA, the patients for the ODS group were recruited from the period between March 2018 and December 2018, that is, after this change in periprocedural anesthesiological management. Eighty of these patients had received 8 mg ondansetron (ODS group) prior to SpA, while



**Figure 1.** Retrospective study design and patient flow chart. CS = cesarean section, SpA = spinal anesthesia, PDA = peridural anesthesia, CSE = combined spinal-epidural anesthesia, GA = general anesthesia, ASA = American Society of Anesthesiologists physical status score, CV = cardiovascular, CI = contraindications.

the other 80 did not (control group). Figure 1 shows a flow chart of included and excluded patients.

There were no significant differences between the 2 groups in terms of age, weight, body mass index, baseline HR and blood pressure, and the duration of surgery (Table 1).<sup>[8,9]</sup>

### 3.2. Hemodynamics and vasopressor use

Neither patient received norepinephrine for blood pressure stabilization. There was no significant difference in terms of procedural blood loss between the groups (control group 500 (400–600) mL vs ODS group 500 (400–600) mL,  $P = .6$ ). However, patients in the control group received slightly more intravenous crystalloid fluids (2000 (1500–2000) mL) than those in the ODS group (1500 (1500–2000) mL,  $P = .039$ ).

**Table 1**

**Patients characteristics.**

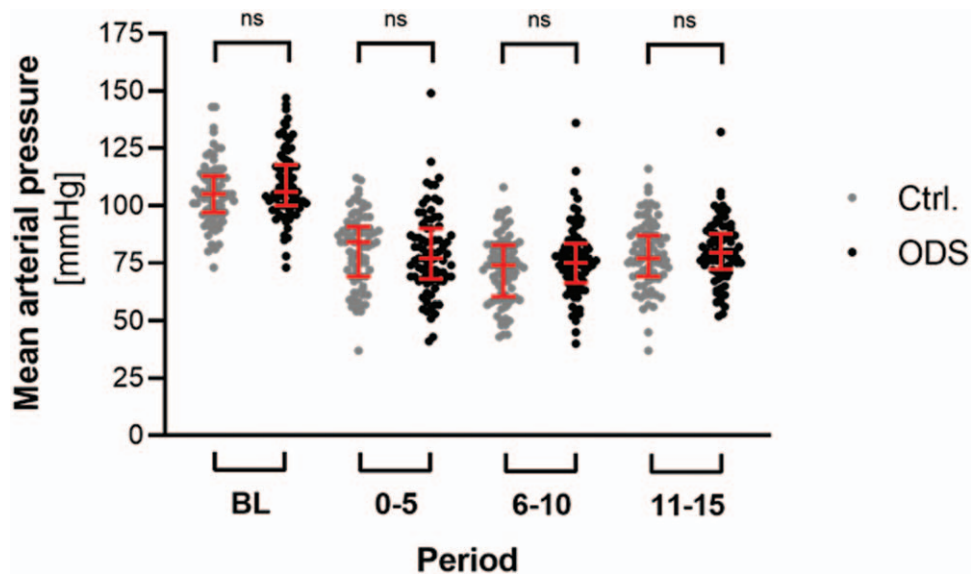
	Control group	ODS group	P value
Age (y)	34 (31–38)	34 (30–37)	.74
Weight (kg)	79 (68–88)	79 (71–92)	.62
BMI (kg/m <sup>2</sup> )	29 (26–33)	29 (26–33)	.98
HR (bpm)	91 (82–102)	94 (85–100)	.6
BP <sub>sys</sub> (mm Hg)	134 (126–144)	139 (128–146)	.11
BP <sub>mean</sub> (mm Hg)	105 (97–113)	106 (100–118)	.13
BP <sub>diast</sub> (mm Hg)	85 (77–91)	86 (80–96)	.18
Duration of surgery (min)	41 (33–50)	41 (34–52)	.64

N = 80 per group. Median (with 25 and 75 percentiles). Mann–Whitney U test. ODS = ondansetron, BMI = body mass index, HR = baseline heart rate, BP = baseline blood pressure (systolic, mean, diastolic).

To assess an effect of ODS administration on the postspinal change in blood pressure, the percentage drop in MAP from baseline MAP was analyzed. The characteristic depression in blood pressure usually occurs rapidly following SpA within the first 15 minutes.<sup>[10]</sup> These were divided into periods of 5 minutes and the lowest MAP value within each period was recorded. In both groups, MAP significantly decreased from baseline to the postspinal period ( $P < .0001$ , Wilcoxon signed rank test, Fig. 2). As given in Table 2, there were no significant differences in percentage MAP drops between the 2 groups. The distribution of the individual absolute MAP values is shown in Figure 2, likewise revealing no intergroup differences. Of note, systolic blood pressure behaved similarly without any intergroup differences (not shown).

In order not to miss potential severe hypotensive episodes beyond the time period of the first 15 minutes, the most pronounced percentage drop in MAP in every individual patient during the whole observation period (i.e., the whole procedure time) was compared. This revealed a slight but significant intergroup difference toward lower MAP values in the ODS group (55 (50–64) % vs 60 (51–68) % in the control group,  $P = .049$ ). However, this difference was not significant when calculating absolute values (control group 62 (56–71) mm Hg vs ODS group 60 (54–67) mm Hg,  $P = .28$ ). Furthermore, the time from administration of SpA until this most pronounced MAP drop occurred did not differ between the groups (control group 12 (6–33) minutes vs 19 (7–36) minutes,  $P = .34$ ).

Next, we explored the use of the vasopressor Akrinor within the first 15 minutes following SpA. Since Akrinor, which is a fixed mixture of 2 drugs with different concentrations, cannot be given in milligram, its use was calculated in milliliters. Prior to SpA, 4 patients in the control and 3 in the ODS group had to be



**Figure 2.** Changes in mean arterial blood pressure (MAP) following spinal anesthesia. Figure shows the distribution of individual absolute MAP values prior to (BL) and over 15 min (split in periods of 5 min each) following spinal anesthesia. There were no significant differences between the control (gray dots) and the ODS group (black dots). N=80 per group. Median (with 25 and 75 percentiles). Mann–Whitney *U* test. ODS = ondansetron.

administered Akrinor due to hypotension assumed being clinically relevant, resulting in nonsignificant intergroup differences ( $P = .97$ ). As shown in Table 3, patients in the ODS group tended to receive more Akrinor during the first 15 minutes following administration of SpA. When the total use of Akrinor during the whole anesthesia time was calculated and compared between the groups, the ODS patients received significantly more Akrinor than those in the control group.

We analyzed the course of heart rate following SpA during the whole procedure. Baseline median HR was comparable in both groups (Table 1, Fig. 3). As with MAP, the first 15 minutes were divided into periods of 5 minutes, followed by recording of the lowest HR value within each period. HR significantly decreased in the postspinal period in the control as well as in the ODS group to 90 (82–97) and 86 (79–93) % of the respective baseline ( $P < .0001$  vs baseline, Wilcoxon signed rank test). The distribution of the individual absolute HR values during the first 15 minutes is shown in Figure 3, revealing no significant intergroup differences. In contrast to the blood pressure, this also applied for the most pronounced drop in HR in every individual patient during the whole procedure time (control group 66 (59–79) % of baseline vs ODS group 68 (60–75) %,  $P = .94$ ). Expressed in absolute values, this difference was likewise not significant (control group 62 (55–68) bpm vs ODS group 61 (56–68) bpm,  $P = .94$ ). Moreover, the time from administra-

tion of SpA until this most pronounced HR drop occurred did not differ between the groups (control group 17 (12–32) min vs 15 (11–30) min,  $P = .42$ ). In each of the groups, 2 patients were administered atropine due to HR drops that were assumed being clinically relevant.

No significant side effects of ODS such as dysrhythmia, headache, or rigor occurred in any of the patients in the respective group.

### 3.3. Postnatal outcome of the newborn

To assess any effects of ODS on the postnatal outcome of the newborn, we analyzed APGAR scores and the cord blood pH as well as BE. While the latter showed no significant intergroup differences (Table 4), APGAR values 5 minutes following delivery were significantly lower in control group than in ODS group (Table 5). However, these differences were only transient and were not observed 10 minutes after delivery.

## 4. Discussion

With this study we sought to assess whether routine administration of 8 mg ondansetron prior to SpA for elective CS attenuates

**Table 2**  
Changes in mean arterial blood pressure (MAP) following spinal anesthesia.

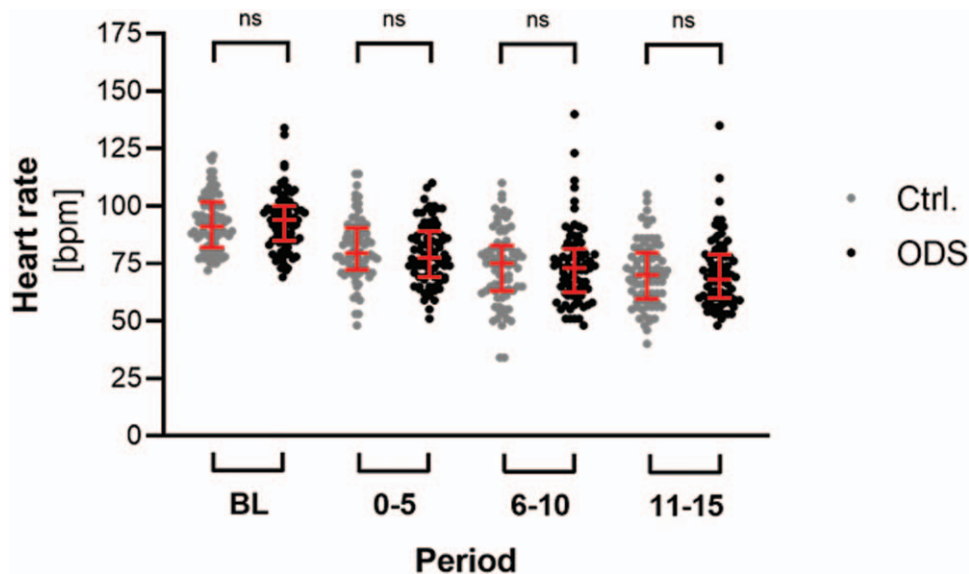
	Control group	ODS group	<i>P</i> value
MAP drop 0–5 min (%)	78 (68–88)	74 (61–85)	.08
MAP drop 6–10 min (%)	72 (59–80)	69 (63–77)	.92
MAP drop 11–15 min (%)	75 (62–85)	74 (66–84)	.92

Percentage of lowest MAP drop from baseline MAP within periods of 5 min. N=80 per group. Median (with 25 and 75 percentiles). Mann–Whitney *U* test. ODS = ondansetron.

**Table 3**  
Use of the vasopressor Akrinor following spinal anesthesia.

	Control group	ODS group	<i>P</i> value
Akrinor 0–5 min (mL)	0 (0–0.36)	0 (0–0.4)	.047
Akrinor 6–10 min (mL)	0 (0–0.4)	0 (0–0.4)	.30
Akrinor 11–15 min (mL)	0 (0–0)	0 (0–0.4)	.24
Akrinor 0–15 min (mL)	0.4 (0–1.0)	0.6 (0–0.8)	.14
Akrinor overall (mL)	0.8 (0–1.0)	0.8 (0.4–1.6)	.01

Use of the vasopressor Akrinor before and up to 15 min following spinal anesthesia and overall use during whole anesthesia time. N=80 per group. Median (with 25 and 75 percentiles). Mann–Whitney *U* test. ODS = ondansetron.



**Figure 3.** Changes in heart rate following spinal anesthesia. Figure shows the distribution of individual heart rate values prior to (BL) and over 15 min (split in periods of 5 min each) following spinal anesthesia. There were no significant differences between the control (gray dots) and the ODS group (black dots). N=80 per group. Median (with 25 and 75 percentiles). Mann-Whitney U test. ODS = ondansetron.

the postspinal depression in arterial blood pressure. The results of our retrospective analysis on 160 patients question that arterial hemodynamics as well as heart rate drops are significantly influenced by ODS premedication. Overall use of the vasopressor Akrinor was significantly higher when ODS had been administered. No clinically relevant side effects on the postnatal outcome of the newborn were observed.

It was in the early to mid-nineties of the last century that the involvement of peripheral 5-HT<sub>3</sub> receptors being located in intracardiac endings of the vagal nerve in the autonomous circulatory control first had been described in animals.<sup>[11]</sup> Yamano et al<sup>[5]</sup> demonstrated in rats that the Bezold-Jarisch reflex could effectively be antagonized using 5-HT<sub>3</sub> receptor blockade. This reflex is supposed to contribute to the development of arterial hypotension following SpA by decreasing the heart rate, with numerous reports of severe bradycardic events and even asystole requiring resuscitation during or following CS under SpA.<sup>[12–15]</sup> The occurrence of cardiac arrest during shoulder surgery in the sitting position under interscalene nerve block is explained by the same mechanism.<sup>[16]</sup> Consequently, prophylactic 5-HT<sub>3</sub> blockade prior to administration of SpA is supposed to prevent postspinal hypotension by antagonizing the BJR. In the perioperative setting, 5-HT<sub>3</sub> antagonists are usually administered for effectively avoiding postanesthesia nausea and vomiting.<sup>[17]</sup> While there exist a number of different substances, ODS is most widely used for this purpose. Although generally

well tolerated, described side effects comprise anaphylactic reactions, migraine and dizziness, constipation as well as QT time prolongation, bradycardia, and hypotension.

Despite that a number of studies already addressed the use of 5-HT<sub>3</sub> antagonists for the prevention of postspinal hypotension and a recent meta-analysis suggests positive effects,<sup>[6]</sup> the design of the included trials is very heterogeneous (heterogeneity index I<sup>2</sup>=87%) and the results are therefore inconclusive. By this reason, routine administration of 5-HT<sub>3</sub> antagonists for this purpose is not mentioned by recent guidelines for obstetric anesthesia.<sup>[1]</sup> Change in MAP following SpA onset was defined as being the primary outcome parameter of our analysis. It seems likely that in daily hospital routine, there exist a variety of definitions of postspinal hypotension to trigger vasopressor administration, ranging from absolute threshold values of systolic or mean arterial pressure to percentage decreases. Therefore, we decided to focus on the change in blood pressure instead of the incidence in hypotension based on a predefined threshold value, to provide meaningful results for the various clinical settings. Furthermore, we chose to focus on MAP since this has been shown to better reflect uteroplacental perfusion than systolic blood pressure.<sup>[18]</sup> The results from our retrospec-

**Table 4**  
Cord blood values.

	Control group	ODS group	P value
Cord blood pH	7.35 (7.32–7.7.37)	7.33 (7.29–7.37)	.29
Cord blood BE	–0.95 (–1.7–0.275)	–1.2 (–2.4––0.1)	.19

N=80 per group. Median (with 25 and 75 percentiles). Mann-Whitney U test. BE=base excess.

**Table 5**  
APGAR score values.

APGAR scoring	Score value	Control group	ODS group	P value
1 min	<10	75	75	>.99
	<8	9	7	.60
5 min	<10	34	19	.01
	<8	2	2	>.99
10 min	<10	12	8	.48
	<8	1	1	>.99

Distribution of APGAR score values among the newborn (ODS group vs control group). N=80 per group.  $\chi^2$  test. ODS = ondansetron.

tive analysis revealed that 8 mg ODS, given intravenously prior to administration of SpA, was not effective to avoid the postspinal decrease in maternal arterial blood pressure in our setting. We rather found a slight, most likely clinically irrelevant trend toward the most pronounced percentage drop in MAP during the whole procedure time in the ODS group. Accordingly, the use of the vasopressor Akrinor to stabilize blood pressure was marginally but significantly increased in the ODS group when analyzing the whole study period. This fixed 20:1 mixture of cafedrine (covalently linked norephedrine and theophylline) and theodrenaline (covalently linked norepinephrine and theophylline) is used since both substances complement one another. While theodrenaline increases vascular resistance, cafedrine exhibits an inotropic effect, resulting in an optimal pharmacodynamic potential of the combination.<sup>[19]</sup> Cardiac effects of cafedrine/theodrenaline are mediated by  $\beta$ -adrenoceptors, while arterial resistance is largely controlled via  $\alpha$ -receptors. In addition, inhibition of phosphodiesterase is thought to be a further mode of action, since both substances contain the nonselective phosphodiesterase inhibitor theophylline. While Akrinor has been demonstrated to induce an increase in cardiac preload, stroke volume, and cardiac output, its precise effect on  $\alpha$ -receptors is still under debate. Clinically, it evokes a rapid increase in mean arterial blood pressure with at most a very mild decrease in heart rate (compared with, e.g., phenylephrine). In recent studies on the use in parturients, no negative impact on umbilical cord pH or APGAR score had been observed.<sup>[19,20]</sup>

Overall, patients in the ODS group were administered slightly less intravenous fluids in total than those in the control group, but considering a number of 80 patients per group, we assume that this small difference highly likely would have no impact on the incidence of postspinal maternal hypotension.

Choice of substance might be one factor influencing the observed results. While the effect of ODS seems to be (if any) rather moderate,<sup>[6]</sup> results from Eldaba and Amr suggest a pronounced positive influence on postspinal hypotension as well as on the use of vasopressors during CS when granisetron is used instead of ondansetron.<sup>[21]</sup> While most studies assessed the effects of ODS, alternative 5-HT<sub>3</sub> antagonists need to be further investigated for their potential to reduce postspinal hypotension.

5-HT<sub>3</sub> blockers are supposed to exert effects on hemodynamics via antagonizing the BJR, resulting in stabilization of the heart rate. However, we found differences neither in percentage postspinal HR decreases nor in the extent of the absolute lowest HR values between the 2 groups. This is in accordance with the results from Ortiz-Gómez et al.<sup>[22]</sup> Moreover, we would like to stress that, besides HR decrease, other factors may also have a relevant pathogenetic impact on the emergence of postspinal hypotension, namely vasodilation due to sympathetic blockade.

No clinically relevant side effects were observed in our patients. In particular, prophylactic administration of ODS did not seem to have a relevant impact on the postnatal outcome of the newborn, as revealed by unremarkable results of the cord blood analysis as well as the APGAR scoring. In this regard, our results are in line with that from others.<sup>[23]</sup> However, due to potentially life-threatening cardiac arrhythmias potentially being associated with the use of ODS,<sup>[24]</sup> risks and benefits should always carefully be weighed against each other. Our data, revealing that an assumed prophylactic effect against postspinal change in blood pressure does not seem to be that pronounced or even does not exist at all, may help the clinician in doing so.

With regard to hypotension, our results are in contrast to that from Owczuk et al.<sup>[25]</sup> that revealed positive effects on systolic blood pressure decreases when administering ODS in the same dosage as we did. However, the results of our as well as of any of the referenced studies have to be interpreted considering the respective individual local standards and particularly anesthetic techniques. While Owczuk et al used a fixed dosage of 20 mg of bupivacaine without opioid supplementation irrespective of the patients' heights and avoided to administer more than 200 mL crystalloid infusion during the whole procedure, we individually titrated the dosage of the local anesthetic, added sufentanil to reduce the amount of bupivacaine, and performed coloadung with 5 times the volume of crystalloid infusion solution. It is obvious that the hemodynamic response of the patients and therefore the possible influence of 5-HT<sub>3</sub> blockade on this response will likewise differ considerably, resulting in divergent study results. This is illustrated by the work from Karacaer et al that revealed, in accordance with our results, no effect of prophylactic administration of 8 mg ODS on incidence of hypotension following SpA for CS.<sup>[23]</sup> Patients in that study received almost the same SpA regimen as ours (coloadung with crystalloid, not more than 10 mg bupivacaine, supplemented with opioid).

Choice of dosage might be another influencing factor. When Wang et al<sup>[26]</sup> compared 4 different dosages of prophylactic ODS prior to SpA for CS, they found positive significant effects on hypotension only when 4 or 6 mg had been administered, suggesting that at higher dosages of 8 mg, adverse side effects might outweigh a positive influence. In accordance with that, in the study from Sahoo et al, demonstrating that the most pronounced positive effects on maternal hypotension among all the studies included into the meta-analysis from Heesen et al, 4 mg of ODS were used, similar to a study from Rashad and Farmawy.<sup>[6,27,28]</sup> Therefore, our results might be explained by dose effects. However, Ortiz-Gómez et al,<sup>[22]</sup> who performed a randomized and placebo-controlled study on parturients receiving SpA for elective CS and included ODS in different dosages (2, 4, and 8 mg), found that neither dosage of prophylactic administration of ODS had any clinically relevant influence on maternal postspinal hypotension.

Obviously, our report has limitations. First, due to the retrospective design, unobserved differences between the control and the ODS group influencing the results cannot be excluded. Moreover, no placebo substance was administered in the control group, and of course the personnel was not blinded for any intervention. Second, ODS was given prior to SpA, but the exact timing of its administration was not standardized. Third, interventions to counteract hypotension during CS were not strictly standardized a priori but were left to the hand of the attending anesthetist.

## 5. Conclusion

The results of our analysis suggest that routine administration of ODS in a dosage of 8 mg does not effectively attenuate postspinal change in maternal blood pressure during CS in our setting. Given the heterogeneity of the present literature assessing the effects of 5-HT<sub>3</sub> blockade for this purpose with a wide variability of anesthetic techniques, only large prospective and randomized multicenter trials will ultimately serve to elucidate this issue.

## Author contributions

**Conceptualization:** Claudia Neumann, Markus Velten, Sven Klaschik.

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**Validation:** Brigitte Strizek, Maria Wittmann, Sven Klaschik.

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**Writing – original draft:** Claudia Neumann, Cornelia Heik-Guth.

**Writing – review & editing:** Markus Velten, Brigitte Strizek, Maria Wittmann, Tobias Hilbert, Sven Klaschik.

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