Clonidine Use for the Treatment of Sialorrhea Gravidarum
A Case Series

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BACKGROUND

Sialorrhea gravidarum (SG)
- occurs in 2.4% of pregnancies,
- it is often related to nausea and vomiting (NV) and/or gastroesophageal reflux (GER) although the origin is unknown,
- adverse perinatal outcomes have not been associated with SG,
- speech difficulties and sleep deprivation may cause social detachment for pregnant women.

Hypersalivation is promoted when
- muscarinic receptors M3 are blocked and/or M4 are stimulated,
- α1 or β1 adrenoreceptors are stimulated.

Clonidine is used to treat sialorrhea because
- it is a partial α-adrenergic agonist that stimulates the presynaptic α2 autoreceptors,
- it activates the negative feedback loop, and decreases noradrenaline concentrations

OBJECTIVES

✧ To describe the clinical experience with clonidine for the treatment of SG in our hospital.
✧ To review the literature on the use of clonidine during pregnancy .

METHODS

Retrospective case series
- was realized using the pharmacy software,
- identifed all hospitalized pregnant women with clonidine prescription to treat SG,
- at CHU Sainte-Justine between January 2010-February 2015.

Literature review
- was conducted using EMBASE/Pubmed with the followinfg MESH terms:“pregnancy”, “clonidine”, “sialorrhea”, “hypersalivation”, “ptyalism” , “hyperemesis gravidarum”.
- Articles written in French and English between 1974 and 2015 were used.
- Case reports and letters to the editor were included.

RESULTS

Retrospective case series
- Ten pregnant women (including 10 singletons) were treated with clonidine for SG
  - After failure of standard HG treatment and after an average of 2.6 hospital admissions for hyperemesis gravidarum (HG)
- The patients’ symptoms were considered to have improved enough for discharge after the addition of clonidine
  - Median duration of clonidine treatment before discharge: 2 days [1 to 5 days]
- Side effects: average SBP change of -15.7 ± 14.6 mmHg (median [min-max]: -15.0 [-46.0 – 7.0]) together with a DPB change of -11.2 ± 9.5 mmHg (median [min-max]: -8.0 [-24.0 – 2.0]). No other side effects were reported.
- Four exposures were between 4th to the end of 10th week and 6 during second trimester.
  - One birth defect reported was a simian crease dysmorphism in a newborn exposed after organogenesis.
- Regimen used: Initial: Clonidine 0.025 mg orally daily-0.05 mg 3x/day, Maintenance: 0.025-0.1 mg 2x/day (max. 0.2 mg/day)

TABLE 1 PREGNANCIES DATA

Pregnancy (#)	Nationality	Age (Years)	Hospital admissions for HG (#)	GA at start of clonidine treatment (Weeks)	BP change* – Systolic/ Diastolic (mmHg)
1	Iranian	36	3	$11^{3/7}$	-16/-9
2	Haitian	26	7	$9^{6/7}$	-46/-24
3	African	33	2	$11^{6/7}$	0/0
4	Honduran	24	1	$10^{0/7}$	-11/-14
5	Canadian	29	4	$16^{5/7}$	-21/-24
6	Haitian	38	4	$12^{0/7}$	-17/-22
7	Haitian	32	1	$9^{2/7}$	+7/+2
8	Canadian	38	2	$9^{5/7}$	-14/-7
9	Haitian	40	1	$23^{1/7}$	-11/-7
10	Nigerian	32	1	$15^{0/7}$	-28/-7
	Average	32.8	2.6	12.9	-15.7/-11.2
	St. dev.	5.3	2.0	4.3	14.6/9.5
	Median	32.5	2.0	11.7	-15.0/-8.0

* BP measured prior to 1st dose and during peak effect (2-4h)

TABLE 2 NEWBORNS DATA

Pregnancy (#)	GA at birth (Weeks)	Birth weight (Kg)	Sex	Apgar scores (at 1, 5, and 10 min)			Anomalies
1	$38^{2/7}$	2.73	F	9	9	9	Simian creases dysmorphism
2	$39^{4/7}$	2.70	M	9	9	9	Tremors at birth
3	$37^{2/7}$	2.70	F	7	8	9	None
4	$37^{1/7}$	2.99	F	9	9	9	None
5	$40^{0/7}$	3.36	M	8	9	9	None
6	$38^{6/7}$	3.25	F	4	7	9	None
7	$40^{2/7}$	3.46	F	3	6	9	None
8	$40^{0/7}$	3.16	M	9	9	9	None
9	$35^{3/7}$	2.91	M	9	9	9	Premature
10	$38^{4/7}$	2.95	F	9	9	9	None
Average	38.6	3.00		7.4	8.4	9	
St. dev.	1.57	0.28		2.4	1.1	0	
Median	38.8	3.0		9	9	9	

Literature review
- No data on the use of clonidine in SG has been found. Hypertension seems to be the only indication reported, when it is reported.
- From six studies, no reports linking the use of clonidine with birth defects have been located but only one publication reported exposure during first trimester (59 newborns).

DISCUSSION

Retrospective case series

Strengths:
- First case series on clonidine use for SG,
- Efficacy and maternal and newborns outcomes were analyzed.

Limits:
- Sample size too small to describe and to predict the population of women who will need or who will be good responders of clonidine for SG,
- Retrospective design,
- Compliance with medication therapy could not be monitored after discharge.

Literature review
- Although it seems to be safe, data is lacking regarding the use of clonidine during pregnancy.

CONCLUSION

- This case series adds the information available regarding clonidine use during pregnancy, after non-pharmacological measures and standard HG treatment.
- More data is needed to describe and to predict the population who will respond to clonidine for SG.

References

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