

Acupuncture *versus* pharmacological approach to reduce *Hyperemesis gravidarum* discomfort

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Aim. Several reports have suggested the use of acupuncture as a useful treatment for *hyperemesis gravidarum* (HG), in particular the effects on nausea intensity was underlined. The aim of this study was to compare the efficacy of acupuncture sessions plus acupressure with a metoclopramide/vitamin B12 treatment.

Methods. In this study we randomized 88 pregnant patients suffering from HG to receive either acupuncture sessions plus acupressure (acupuncture group) or metoclopramide infusion (metoclopramide group) supplemented by vitamin B12 complex. Somatic symptoms and the ability to achieve the daily routine activity (functioning) were evaluated. Acupuncture sessions were performed at the hospital twice a week for 2 weeks according to the traditional Chinese medicine criteria. Acupression was applied for 6-8 h/day. In the metoclopramide group, patients received at hospital metoclopramide infusion (20 mg/500 mL saline for 60 min) twice a week for 2 weeks. An oral supplementation with vitamin B12 complex (30 mg/day) was also prescribed.

Results. Both treatments reduced vomiting episodes and then nausea intensity with a consequent improvement in the rate of food intake. The effect of acupuncture seems to be progressive, increasing at the end of treatment whereas pharmacological approach has a prompt effect in responders remaining stable thereafter. Moreover, acupuncture was significantly more effective than drugs in improving functioning.

Conclusion. In our study for the first time acupuncture, applied accordingly to Chinese formula, was compared to drugs demonstrating the same effect of both treatments on HG symptoms. Interestingly, functioning was significantly improved just by acupuncture. Even if the effect of acupuncture on HG discomfort remains to be confirmed, the reports on the effect of acupuncture on psychosocial variables could represent a further advantage of acupuncture application and provide an incentive to widen the base of the research.

Key words: Acupuncture - Acupression - Hyperemesis gravidarum.

Hyperemesis gravidarum (HG) represents a discomforting condition which affects 50% to 80% of pregnant women.¹ Corticosteroids, anti-histamine medication, pyridoxine, metoclopramide are commonly utilized alone or in combination to reduce the symptoms of HG. In a recent review Mazzotta *et al.* considered several studies about the efficacy of such drugs concluding that none of them is able to afford complete relief from symp-

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toms.² The Cochrane review, including 20 trials about the use of pyridoxine, anti-histamine medication and a combination of them, concluded that pyridoxine is effective in reducing the symptoms of HG and, among the drugs analysed, it is the least likely to cause side effects.³

The poor efficacy showed by drugs stimulated the development of non-pharmacological approaches to HG. Indeed, several reports have proposed acupuncture or acupressure to relief nausea and vomiting. Indeed, Vickers *et al.* reviewed 33 studies on the stimulation of acupoint 6 of *Pericardium* (PC6, Neiguan) for nausea and vomiting induced not only by pregnancy, but also by drugs/chemotherapy. They concluded that any of the stimulation methods under evaluation (acupressure, acupuncture, electrostimulation) was able to significantly reduce symptoms.⁴ A further analysis, taking into account 7 studies restricted to nausea induced by pregnancy found a reduction of symptoms in 50% of cases. The authors concluded that methodological bias (namely, the lack of a randomization file and placebo arm) and the heterogeneity of the populations studied did not allow to consider acupuncture as a valid treatment of HG.⁵ Moreover, the Cochrane review, including the data of 4 trials published from 1988 to 1994, concluded that the effect of P6 acupressure on HG symptoms should be considered equivocal.³

In the present study we compare the efficacy of acupuncture sessions, including the stimulation of 5 acupoints according to the whole Chinese formula, plus acupressure, with metoclopramide infusion, the commonest pharmacological approach for hyperemesis in our country, supplemented with vitamin B12 complex. The efficacy was considered in terms of relief of not only somatic symptoms such as nausea intensity, episodes of vomiting and rate of food intake, but also their impact on the quality of life.

Materials and methods

From May 2001 to July 2002, 101 patients affected by HG and referred to the Depart-

ment of Obstetrics and Gynecology of the Universities of Modena-Reggio Emilia and Turin were deemed eligible for inclusion in the study. Inclusion criteria were: singleton pregnancy, gestational age lower than 12th week, diagnosis of HG following the commonly accepted criteria of nausea and severe vomiting leading to clinical symptoms of dehydration and >5% weight loss. Exclusion criteria were: maternal diseases, namely gastric ulcer and thyroid disorder as well as fetal malformations or chromosome abnormalities.

The protocol was approved by the Institutional Review Board and informed consent was signed before the allocation to receive acupuncture treatment (ACU group) or metoclopramide infusion (MCP group) took place. A computer-generated random list where odd and even numbers allocated patients to 1 of the 2 treatments was employed. The randomization file was held in Modena under the control of a midwife.

Out of the 101 eligible women, 88 agreed to participate in the study. Acupuncture sessions were performed at the hospital twice a week for 2 weeks. Each woman was treated using a so-called "formula acupuncture", receiving treatment always at the following acupoints: PC6 *Neiguan*, conception vessel 12 (CV12 *Zhongwan*), stomach 36 (ST36 *Zusanli*). The patients were also advised to wear a device giving acupressure at the PC6 point for 6-8 h/day at home (Sea-Band, P6 Nausea Control).⁶

The points were punctured with 0.3 mm diameter sterile disposable steel needles (length 52 mm), that were inserted to a depth of 10-30 mm and manipulated until the patient reported the characteristic irradiating sensation, said to indicate effective needling, that is commonly called *De Qi*.⁷ For needle manipulation the so-called "even" (intermediate) method was always used. After insertion needles were manipulated by raising and thrusting and twirling or rotating methods. The depth of insertion during raising and thrusting of the needle was intermediate, during twirling the needle was rotated mainly to the right. After obtaining the needle sensation the manipulation was stopped and the

TABLE I.—*The table shows the semi-structured interview utilized to collect clinical data.*

Score	0	1	2
Nausea	No nausea	Low intensity, no discomfort	High intensity, discomfort
Vomiting	No episodes	1-3/day	>3/day
Rate of food intake	Normal intake	Restricted intake	Fasting
Functioning	Unchanged daily activity	Stop work outside home	Difficult to achieve also house routine

needles were left *in situ* for 20 min without any further manually stimulation. Acupuncture was always performed with the same needle manipulation technique by 2 of the authors (I.N., G.A.), who are experienced and qualified acupuncturists.

Acupoints were located as follows:^{8,9} PC6 *Neiguan*: on the palmar side of the forearm, 2 inches above the transverse crease of the wrist, and between the tendons of the *flexor carpi radialis* and palmaris longus muscles; ST36 *Zusanli*: in the fossa 1 finger breadth lateral to the anterior margin of the tibia, and 3 inches inferior to the acupoint Dubi (ST 35), that is located at the lower border of the patella, in the depression lateral to the patellar ligament; CV12 *Zhongwan*: on the mid abdominal line, at the midpoint between the xiphisternal joint and the umbilicus.

In the MCP group the patients received metoclopramide infusion (20 mg/500 mL saline for 60 min) at the hospital, twice a week for 2 weeks. Oral supplementation with vitamin B12 complex (pyridoxine, hydroxycobalamine) (30 mg/day) (Benadol, Roche) was prescribed at home.

At the first examination and after each treatment session a senior midwife, appropriately trained by a physician, administered a semi-structured clinical ratings assessing intensity of nausea, episodes of vomiting and rate of food intake as well as the ability to achieve the daily routine activity expressed as functioning (Table I).

At the first examination the midwife also collected data on body weight, body mass index and weight loss occurred during pregnancy.

Statistical analysis

The analysis of the data was conducted by blind operators who did not know the be-

longing group of each patient. The data derived from the semi-structured interview were recoded as absent (value 0) or present (value 1 to 2). Comparison between the 2 groups was performed by the χ^2 test. Within-subjects evaluations were performed by Mc Nemar's χ^2 test. A value lower than 0.05 was considered as significant.

Results

In the ACU group 1 woman stopped treatment after 2 sessions because it proved ineffective. In the MCP group 4 women refused to be assigned to drug therapy and another 2 cases had a spontaneous abortion at the 10th week. Thus, the final analysis was carried out on 81 cases, 43 randomized to ACU and 38 to MCP.

No differences were observed between ACU and MCP groups as far as body weight (60.6 ± 11.1 vs 57.9 ± 13.2 kg), body mass index (22.7 ± 4.7 vs 22.5 ± 4.5) and weight loss during pregnancy (-3 ± 1.9 vs -3.8 ± 1.9 kg). Similarly no differences were observed between ACU and MCP group in nausea intensity, vomiting episodes, rate of food intake.

In the ACU group nausea intensity diminished after the second session in the 25% of the population and at the end of treatment such positive effect involved half of the patients. Vomiting episodes, and consequently the rate of food intake, responded sooner to treatment, 16.2% of the patients showing an improvement after the first session. Similarly, as observed for nausea intensity, at the end of treatment the effect involved half of the population (Table II).

In the MCP group, nausea intensity diminished after the second session in 23.6% of the patients, the effect remaining stable

TABLE II.—The table shows the number of cases improved at each session, percentage was reported in brackets. The asterisks indicate a significance in respect to baseline value: * $P<0.05$ and ** $P=0.001$.

	ACU (n. 43)	MCP (n. 38)	P>
<i>Nausea intensity</i>			
1 st	1 (2.3)*	1 (2.6)*	0.3
2 nd	11 (25.5)**	9 (23.6)**	0.6
3 rd	19 (44.1)**	12 (31.5)**	0.2
<i>Vomiting episodes</i>			
1 st	7 (16.2)**	4 (10.5)**	0.4
2 nd	15 (34.8)**	12 (31.5)**	0.5
3 rd	24 (55.8)**	14 (36.8)**	0.07
<i>Rate of food intake</i>			
1 st	7 (16.2)**	2 (5.2)*	0.2
2 nd	15 (34.8)**	10 (26.3)**	0.2
3 rd	21 (48.8)**	14 (36.8)**	0.2

throughout the observation period. Vomiting episodes also disappeared after the second session in 31% of the cases, with a consequent improvement in the rate of food intake, the effect persisting until the end of treatment (Table II).

The impact of acupuncture on the patients' functioning seemed to take longer to make itself felt, not becoming apparent until the third session. MCP treatment produces a slight effect on improving functioning in the 20-30% of the cases after the second session of treatment. The comparison between the treatments showed that acupuncture was significantly more effective than pharmacological approach (Figure 1).

As far as the fetal outcome was concerned no differences were observed between ACU and MCP groups for age at delivery (39.2 ± 1.7 vs 40.2 ± 1.1 weeks), birth-weight ($3\,123\pm 329$ vs $3\,425\pm 450$) and rate of cesarean section (10% vs 15%).

Discussion and conclusions

In the present study we compare acupuncture, performed using a formula taking into consideration some principles of the traditional Chinese Medicine plus acupressure, with a pharmacological treatment employing metoclopramide plus vitamin B12 com-

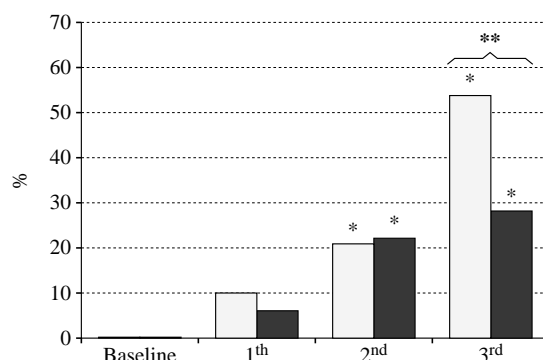


Figure 1.—The figure shows the percent of subjects improved at each session. White bars indicate the ACU group, black bars indicate the MCP group. The single asterisk indicates the significance of the within-group comparison (*) ($P<0.05$) and the double asterisk indicates the significance of the between group comparison (**) ($P=0.01$) (Mc-Nemar χ^2 Test).

plex. Both treatments reduced vomiting episodes and then nausea intensity with a consequent improvement in the rate of food intake. The effect of acupuncture seems to be progressive, involving at the end of treatment whereas pharmacological approach has a prompt effect in responders remaining stable thereafter. However, since the power of the study was not calculated before starting, it is correct to state that nothing can be concluded about the comparative efficacy of the 2 methods of treatment.

The studies considered in the most relevant reviews ³⁻⁵ take into account the acupression alone without needles insertion and the sole use of PC6 acupoint, as opposed to the complete chinese formula which would include more acupoints for the current treatment of HG.

Recently, Smith *et al.* published a single blind randomized controlled trial on the use of traditional acupuncture vs acupressure vs sham acupuncture on reducing the symptoms of HG in a sample of 593 pregnant women.¹⁰ The authors concluded that traditional acupuncture represents the more effective treatments for women who experienced nausea and dry retching, whereas none of the treatments were able to affect episodes of vomiting. Conversely, a subject- and observer-masked, randomized, controlled trial on 55 pregnant women affected by HG

demonstrated no differences between traditional acupuncture formula and sham acupuncture on improving nausea.¹¹ Their conclusion were biased, however, by the small size of the sample and by the sole outcome considered which was nausea intensity.

In our study for the first time acupuncture, applied accordingly to the Chinese formula, was compared to pharmacological approach demonstrating that acupuncture shows the same effect of drugs in improving symptoms of HG.

Interestingly, functioning was significantly improved just by acupuncture. However, it has been recently demonstrated that acupuncture is useful to improve the quality of life of patients undergoing the treatment.¹² Even if the effect of acupuncture on HG discomfort remains to be confirmed, the reports on the effect of acupuncture on psychosocial variables could represent a further advantage of acupuncture application and provide an incentive to widen the base of the research.

Riassunto

Iperemesi gravidica: confronto tra approccio farmacologico e agopuntura

Obiettivo. Numerosi studi hanno suggerito un possibile uso dell'agopuntura in caso di iperemesi gravidica, sottolineando in particolare gli effetti sulla riduzione della nausea. Lo scopo di questo studio era confrontare l'efficacia del trattamento agopuntura/agopressione con quella del trattamento con metoclopramide.

Metodi. In questo studio 88 pazienti gravide affette da iperemesi sono state randomizzate a ricevere un trattamento di agopuntura/agopressione (gruppo agopuntura) oppure un trattamento farmacologico a base di metoclopramide/vitamine del complesso B12 (gruppo metoclopramide). Sono stati valutati sia i sintomi fisici, sia la capacità delle pazienti di attendere alle attività quotidiane («functioning»). L'agopuntura è stata praticata secondo i criteri e le prescrizioni della medicina tradizionale cinese: 2 sedute in ospedale a settimana per 2 settimane. Le pazienti sono state, inoltre, invitate a indossare a domicilio per 6-8 h al giorno i dispositivi Sea-Band in grado di esercitare agopressione. Il gruppo randomizzato a ricevere il trattamento farmacologico ha invece eseguito infusioni di metoclopramide (20 mg/500 fisiologica/60 min) sempre a cadenza bisettimanale per 2 settimane. Alle

pazienti è stato, inoltre, consigliato di assumere a domicilio un complesso vitaminico B12 (30 mg/die).

Risultati. I 2 tipi di trattamento si sono dimostrati ugualmente efficaci nel ridurre gli episodi di vomito e l'intensità della nausea con un conseguente aumento della quantità di cibo ingerito. L'effetto dell'agopuntura si è manifestato progressivamente con il raggiungimento dell'efficacia massima a fine trattamento, mentre la terapia farmacologica ha mostrato un effetto più immediato ma stabile nel tempo. Per quanto riguarda il functioning, l'agopuntura si è rivelata maggiormente efficace nel migliorare l'attività sia lavorativa che famigliare.

Conclusioni. Per la prima volta l'effetto dell'agopuntura è stato comparato a quello dei farmaci nel ridurre la sintomatologia in corso di iperemesi gravidica dimostrando che, per quanto riguarda i sintomi fisici, l'effetto dei 2 trattamenti è simile. L'agopuntura mostra, invece, una capacità superiore nel migliorare l'impatto della sintomatologia sulla vita famigliare e lavorativa.

Parole chiave: Agopuntura - Agopressione - Iperemesi gravidica.

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