SERUM THYROID HORMONES CHANGES IN PATIENTS UNDERGOING CAESAREAN SECTION UNDER GENERAL OR REGIONAL ANAESTHESIA

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SUMMARY

The effects of anaesthesia on serum thyroid hormones were studied in 32 pregnant young women undergoing Caesarean section at term. Eighteen patients received general anaesthesia and 14 lumbar extradural blockade. Maternal serum concentrations of thyrotrophin (TSH), thyroxine (T4), triiodothyronine (T3) and reverse triiodothyronine (rT3) were measured using radioimmunoassay at 0, delivery and 24 h. There were no significant changes in TSH in the two groups. T4 concentrations decreased significantly at 24 h in the general anaesthesia group but regional anaesthesia produced a significant decrease only at the time of delivery. T3 concentrations decreased with both techniques. Reverse T3 increased markedly with general anaesthesia only at 24 h.

Thyroid function in pregnancy at term has been studied thoroughly (Selenkow, Birnbaum and Hollander, 1973), but the influence of anaesthesia on thyroid function at the time of birth has not been investigated in either the mother or the newborn. Early animal experiments suggested that barbiturates, especially thiobarbiturates, depressed acutely the uptake of radioactive iodine (Wase and Greenspan, 1953; Wase, Repplinger and Foster, 1953; Wase and Foster, 1956; Mitskevich, 1957), and similar changes have been noted with cyclopropane, diethyl ether and thiopentone anaesthesia (Oyama, 1957, 1959). When thyroid uptake of iodine-131, or the release of 131I-labelled hormone were measured in humans, both an increase and a decrease were observed following general anaesthesia (Engstrom and Markardt, 1955; Goldenberg, Rosenbaum and Hayes, 1955; Goldenberg et al., 1956; Brown et al., 1964; Fore, Kohler and Wynn, 1966). In contrast, regional analgesia did not produce any significant changes in these measurements (Greene and Goldenberg, 1959). Conflicting results have been obtained on the effects of general anaesthesia on the plasma concentrations of serum thyroxine (T4) (Oyama, Shibata and Matsuki, 1969; Oyama et al., 1969a, b). The use of lignocaine for spinal anaesthesia was associated with a decrease in serum T4 concentration (Oyama and Matsuki, 1971). In animal experiments, when pituitary thyrotrophic hormone (TSH) was measured following general anaesthesia, an increase or a biphasic response was noted (Männistö, Saarinen and Ranta, 1976). However, in human studies thiopentone, halothane, diethyl ether and methoxyflurane were associated with unchanged TSH concentrations (Oyama, Matsuki and Kudo, 1972a). These inconsistent results have prevented any conclusions on the effects of anaesthesia on thyroid function in either the mother or the infant. Among the possible reasons for this are: the lack of a sensitive and precise method for the determination of thyroid function, and at the time of these studies the lack of complete tests of thyroid function. Furthermore, the effect of surgery on thyroid function in the absence of anaesthesia has not been explored sufficiently.

We report some effects of anaesthesia on serum thyroid hormones in women undergoing Caesarean section.

METHODS

Thirty-two unselected women undergoing Caesarean section at term were studied. The procedure for the study was approved by the Research and Medical Ethics Committee of the Nassau County Medical Center. None of the subjects had a history of thyroid or other endocrine disease.

Eighteen patients received general anaesthesia, and 14 regional anaesthesia. General anaesthesia comprised induction with thiopentone 3.5 mg kg⁻¹ followed by suxamethonium 1.5 mg kg⁻¹, endotracheal intubation and artificial ventilation with...
oxygen until delivery of the baby. Thereafter, anaesthesia was maintained with diazepam or pethidine, or both, nitrous oxide in oxygen and neuromuscular blockade was maintained with an infusion of suxamethonium. Regional analgesia combined a lumbar extradural block with lignocaine, bupivacaine or 2-chloroprocaine, or a combination of these agents. Venous blood samples for hormone analysis were collected just before anaesthesia, at the time of delivery and 24 h thereafter.

All hormone measurements were made by radioimmunoassay techniques. Thyrotrophin (TSH), thyroxine (T4), L-3,3',5-triiodothyronine (T3), L-3, 3',5'-triiodothyronine (reverse T3, rT3) and the resin uptakes of T3 (RUT3) and rT3 (RUrT3) were measured in every sample using commercially available kits.* For rT3 resin uptake assay, the kit was the same as for RUT3 with replacement of $^{125}$I-T3 with $^{125}$I-rT3.

All these methods have been tested for specificity, sensitivity, accuracy and reproducibility.

Student's t tests were performed on basic and logarithmic data for paired samples, together with one-sample tests on percentage changes; 5% was chosen as the level of statistical significance.

RESULTS

TSH

There were no significant changes in the concentrations of TSH at the three sampling times and there was no difference between the two groups (fig. 1).

T4

There were no differences in the mean values of serum concentrations of T4 observed at the three sampling times between the subjects receiving general and those receiving regional anaesthesia. A significant decrease was observed at 24 h after delivery in the general anaesthesia group ($P<0.02$). In the regional anaesthesia group a sharp decrease was observed at

* The human TSH kit (hTSH; Nuclear Medical Systems Inc.) uses anti-hTSH rabbit serum and a second antibody which is goat-anti-rabbit gamma globulin, together with hTSH $^{125}$I-labelled thyrotrophin. The T4 and T3 kits (Diagnostic Products Corporation) and the rT3 (Serono Laboratories Inc.) were similar, using $^{125}$I-labelled antigens, ANS (8-anilino-1-naphthalene sulphonic acid) and goat-anti-rabbit gamma globulin. For RUT3, the kit was from Nuclear Medical Laboratories Inc. and used inorganic silicate as the binder. In this determination, the two hormones are used as reagents to demonstrate the number of available binding sites on serum thyroglobulin (TBG) by saturating serum TBG with the $^{125}$I-labelled hormone.
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the time of delivery ($P < 0.01$) but there was no further decrease at 24 h (fig. 2).

$T3$

A significant decrease occurred with anaesthesia, continuing after anaesthesia ($P < 0.01$). There were no differences between the two groups at all times (fig. 3).

$rT3$

A pattern similar to that for $T3$ was found for all samples except at 24 h with general anaesthesia (fig. 4). The significant decrease ($P < 0.01$) in serum concentrations of $rT3$ with general anaesthesia from zero time to delivery was followed by a marked increase at 24 h ($P < 0.01$). Regional analgesia was associated with a sudden decrease ($P < 0.01$) at the time of delivery which continued for 24 h, similar to the changes occurring in $T3$. The significant differences in serum $rT3$ concentrations between the general and regional anaesthesia groups at 24 h reflected primarily this increase in $rT3$ with general anaesthesia at that time.

DISCUSSION

We have demonstrated that changes in thyroid function occur at the time of delivery and in the period after delivery in women at term undergoing Caesarean section with general or regional anaesthesia.

Our data are in agreement with studies showing that anaesthesia does not influence serum thyrotrophin concentrations (Charters, Odell and Thompson, 1969; Oyama, Matsuki and Kudo, 1972a, b; Kirby, Clark and Johnston, 1973; Männistö, Saarinen and Ranta, 1976). There were no significant differences between the effects of general and regional anaesthesia on this pituitary hormone. There was an early sudden decrease in serum $T4$ concentrations following regional anaesthesia and a later decrease after general anaesthesia. This decrease in serum $T4$, observed with both anaesthetic techniques, may have been produced by: an acute decrease in the secretion of $T4$ by the thyroid, an accelerated hepatic or renal catabolism of the circulating hormone, a redistribution of the hormone between the vascular, extracellular or intracellular compartments (Oyama, Shibata and Matsuki, 1969; Oyama et al., 1969a, b); or a perin-operative expansion of the vascular space. The long half-life of $T4$ in the circulation and the absence of changes in thyrotrophic hormone make a decrease in $T4$ secretion unlikely to account for the observed changes.

The absence of changes in the resin uptake of $T3$ or $rT3$ from times of sampling before to after delivery almost precludes the possibility of a decrease in the thyroid hormone–plasma binding proteins. Such a change could lead to a shift of thyroxine from the vascular space. Although no measurements of blood volumes have been carried out in this study, a decrease in this compartment at the time of delivery and in the postpartum period has been reported by other investigators. In addition, in this study the peri-operative hydration regimen was very similar and dilutional hypoproteinaemia and resulting decreased hormone concentration was unlikely to occur.

Of considerable interest were the observations that the two thyroid hormones, $T3$ and $rT3$, which are derived primarily from the metabolic conversion of $T4$ in the liver and kidney (fig. 5), decreased throughout the study with one sample time exception. This suggests that both general and regional anaesthesia

![Fig. 4. Serum reverse triiodothyronine ($rT3$) concentrations (mean ± SEM) in patients undergoing Caesarean section under general or regional anaesthesia.](image_url)

![Fig. 5. Triiodothyronine and reverse triiodothyronine.](image_url)
may interfere with mono-deiodination of T4 to its metabolic products T3 and rT3. However, other explanations, such as hormone redistribution and circulatory changes, may be possible. In addition, these data suggest that regional and general anaesthesia differ in their effect on the overall metabolic transformation of T4 in the period after anaesthesia. The increase in rT3 which was seen only at 24 h after general anaesthesia remains unexplained. An increase in rT3 when T3 decreases has been observed in a variety of clinical situations (Chopra et al., 1975).

Our data are in agreement with the study of Burr and others (1975) who demonstrated a decrease in serum T3 after surgery. Since the major source of T3 in plasma is from the peripheral mono-deiodination of thyroxine and both surgery and anaesthesia may decrease this process, no conclusion can be reached from this study concerning which of the two factors was primarily responsible for the observed effect. Burr and colleagues (1975) also reported an increase in serum reverse T3 following surgery, but without specific reference to the type of anaesthesia. We observed an increase in serum rT3 concentrations only after 24 h with general anaesthesia. The peripheral metabolism of T4 by mono-deiodination can yield rT3 as well as T3 (Chopra, 1974). During surgery, systemic illness, fasting and in the newborn there is stimulation of the T3 pathway of T4 catabolism coincidental with a decrease in the T3 catabolic pathway similar to that observed with general anaesthesia in the present study. No increase in rT3 occurred when T3 concentrations were decreased during regional anaesthesia. It is known that this latter anaesthetic technique has minimal effects on hepatic and renal function. Therefore, the “expected” change in the T3/rT3 ratio at 24 h after general anaesthesia can be explained by a direct hepatic or renal effect of the systemically administered anaesthetic agent. These effects of general anaesthetics are well documented in the literature. The observation of an alteration in the T3/rT3 ratio may provide another index of alterations in hepatic and renal function produced by general anaesthesia.

It is possible that the hormone changes in maternal blood following anaesthesia occur also in the foetus. Indeed, the effect may be more pronounced since foetal liver and kidney function is immature at term. Recent reports noting a frequency of neonatal hypothyroidism as large as 1 in 4000 live births (La Franchi et al., 1977) suggest that a reduction in serum T3 following anaesthesia in the newborn may worsen neonatal hypothyroidism where this condition exists.

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REFERENCES


**VARIATIONS DES HORMONES DE LA THYROIDE DANS LE SERUM SUR DES FEMMES SUBISSANT UNE OPERATION CESARIENNE SOUS ANESTHESIE GENERALE OU SOUS ANESTHESIE REGIONALE**

**RESUME**

Les effets de l'anesthésie sur les hormones de la thyroïde se trouvant dans le sérum ont été étudiés sur 32 jeunes femmes enceintes devant subir une opération césarienne une fois arrivées à terme. Dix-huit d'entre elles ont été placées sous anesthésie générale et 14 ont subi un blocage lombaire extradural. Les concentrations de thyrotrophine (TSH), de thyroxine (T4), de triiodothyronine (T3) et de triiodothyronine inversée (rT3) dans le sérum maternel ont été mesurées par essai de radiorésistances à 0, au moment de l'accouchement, et 24 h après. Il n'y a eu aucun changement sensible dans la TSH des deux groupes. Les concentrations de T4 ont baissé d'une manière significative après 24 h dans le groupe soumis à une anesthésie générale, mais l'anesthésie régionale n'a produit une diminution sensible qu'au moment de l'accouchement. Les concentrations de T3 ont diminué avec les deux techniques. Les concentrations de T3 inversée ont notablement augmenté avec l'anesthésie générale, mais seulement 24 h après.

**CAMBIOS EN LAS HORMONAS TIROIDES DEL SUERO EN PACIENTES SOMETIDOS A CESAREA BAJO ANESTESIA GENERAL O REGIONAL**

**SUMARIO**

Se estudiaron los efectos ejercidos por anestesia sobre las hormonas tiroides del suero en 32 mujeres jovenes embarazadas sometidas a cesárea al final de su periodo de embarazo. Dieciocho pacientes recibieron anestesia general y 14 bloqueo extradural lumbar. Las concentraciones en el suero materno de tirotropina (TSH), tiroxina (T4), triyodotironina (T3) y triyodotironina inversa (rT3) fueron medidas valiéndose de pruebas radioinmunológicas tomadas a 0, durante el parto y 24 horas despues. No se produjeron cambios significativos en el TSH de los dos grupos. Las concentraciones de T4 disminuyeron significativamente al cabo de 24 horas en el grupo de anestesia general, pero la anestesia regional produjo una significativa disminución solamente en el momento del parto. Las concentraciones de T3 disminuyeron con ambas técnicas. El T3 inverso aumentó notablemente con la anestesia general solo al cabo de 24 horas.