Review Article

Perioperative fluid therapy and intraoperative blood loss in children

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ABSTRACT

Fluid and blood administration are required during surgery in children. The type, amount and tonicity of the intravenous fluids is an important aspect to be considered during anaesthesia management. The physiological differences between adults and children regarding the body water and blood volume needs to be understood. We performed a PUBMED search for English language articles using keywords including 'children', 'intravenous fluid therapy', 'crystalloids', 'colloids', 'fluid homeostasis', 'Starling equation', 'Donnan effect', 'blood loss', 'estimation of blood loss', 'blood management program'. This review discusses the physiological basis, historical background, risk of hyponatraemia, need of glucose in the intravenous fluids as well as the recent concepts in blood transfusion as related to children.

Key words: Blood loss, blood management program, children, colloids, crystalloids, Donnan effect, estimation of blood loss, fluid homeostasis, intravenous fluid therapy, Starling equation

INTRODUCTION

Children undergoing surgery require administration of intravenous (IV) fluids to meet the fluid requirement arising because of perioperative deficits (fasting, gastrointestinal, renal or cutaneous losses); haemorrhage and third space losses. Maintenance therapy represents the fluids and electrolyte requirements due to anticipated physiological losses from breathing, sweating and urine output in an average individual with normal intracellular fluid (ICF) and extracellular fluid (ECF) volumes over a 24 h period. Fluid is also required to maintain an adequate tissue perfusion as well to counteract the effects of anaesthetics.[1] Therefore, the objective of intraoperative fluid administration is to maintain or re-establish the child's normal physiological state of normovolaemia, normal tissue perfusion, normal metabolic function, normal electrolytes and normal acid–base status.[2] The type of fluid (crystalloids or colloids) and the composition (isotonic vs. hypotonic) of the fluid administered perioperatively has been extensively researched.[3]

Children may encounter intraoperative blood loss because of trauma, major surgery (cardiac, craniofacial, transplantation) and with use of extracorporeal membrane oxygenation (ECMO). Hypovolaemia due to blood loss is the most common reason for anaesthesia-related cardiac arrest in children.[4] The primary goal of managing a bleeding child intraoperatively is avoiding hypotension, maintaining adequate tissue perfusion and oxygenation and maintaining haemostasis. On the other hand, transfusion of autologous blood and its components, is associated with increased morbidity and mortality.[5]

This review discusses the current concepts of fluid and blood administration in children undergoing surgery. A thorough literature search was done up to May 2019 using databases/search engines (Medline, Scopus, PubMed, and websites of National Societies for IV fluid management). All the articles published

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in English were searched. The following keywords were used 'children', 'intravenous fluid therapy', 'crystalloids', 'colloids', 'fluid homeostasis', 'Starling equation', 'Donnan effect', 'blood loss', 'estimation of blood loss', 'blood management program'.

Physiological basis of fluid management in children

About 50–80% of human body is composed of water, the content varying with type of tissue. Total body water (TBW) is 80% of body weight (BW) in preterm neonate and it is 60% of BW in children after 6 months of age.[6] Total body water decreases with age because of loss of water, mainly from ECF compartment. ECF accounts for 1/3rd of TBW and is larger in children than adults. It is made up of 3 compartments (plasma, interstitial fluid and transcellular fluid).[7] The ICF compartment represents 2/3rd of TBW [Figure 1].

At all ages, sodium (Na^+) is the primary cation and chloride (Cl^-) the major anion in plasma and are predominantly extracelluar. The intracellular compartment primarily consists of potassium (K), magnesium (Mg), proteins and organic/inorganic phosphate. Interstitial fluid has a composition equivalent to ICF except a lower protein content [Table 1].[8]

The distribution of ions and fluids between the ECF and ICF compartment is governed by the Donnan effect and Starling forces.[9] According to the Donnan effect when a semipermeable membrane separates a solution of non-diffusible ions from another solution of diffusible ions, equilibrium is attained with unequal distribution of diffusible ions across the semipermeable membrane due to presence of proteins.[9] At equilibrium the product of molar concentration of diffusible ions on either side of membrane will be the same, maintaining the electrical neutrality on both sides of membrane.

The Starling hypothesis says that the fluid movement due to filtration across the capillary wall is dependent on the balance between the hydrostatic and the oncotic pressure gradient across the capillary wall (hydrostatic pressure in capillaries and interstitium and oncotic pressure in capillaries and interstitium). Under normal condition the amount of fluid filtering outward from the arterial ends of the capillaries equals almost exactly the fluid returned to the circulation by absorption. Based on this equation [Fluid movement = k [Pc + πi) − (Pi + πc)], k is the capillary filtration coefficient which is proportionate to the permeability of the capillary wall

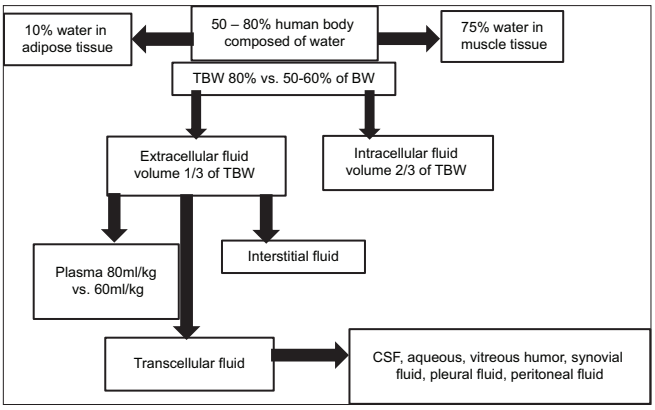

Figure 1: Water composition of the body and its distribution (Should be figure)

Table 1: Composition of ECF and ICF

	ECF	Interstitial fluid	ICF
Osmolality	290-310		190-310
Cations (meq/L)	155	-	-
Sodium (Na^+)	142	145	12
Potassium (K+)	4	4	156
Calcium (Ca+)	2.4	2.3	0.3
Magnesium (Mg+)	2	1-2	26
Anions (meq/L)	154		
Chloride (Cl-)	103	114	4
Bicarbonate (HCO3-)	27	31	12
Hydrogen phos (HPO4-)	2	-	-
Phosphate (PO4-)	1	-	-
Organic acids	5	-	-
Protein	16	-	55

and the area available for filtration. Oncotic pressure in interstitium is usually negligible so the osmotic pressure gradient (πc - πi) usually equals the oncotic pressure.

In a full-term neonate, the GFR increases to adult levels by 2 years of age. The low GFR is related to low systemic arterial pressure, high renal vascular resistance, low ultrafiltration pressure and decreased capillary surface area for filtration. However, capability for sodium conservation exists and so as the Na load and GFR increases, the ability of proximal tubules to absorb Na increases. The concentrating ability is low at birth and with water deprivation, urine concentrates to only 600–700 mOsm/kg because of hypotonicity of renal medulla. The tubular mechanisms for organic acids are poorly developed in neonates and increases to adult levels by 12–18 months.[6]

Historical basis of fluid management

Since the last decade the standard fluid management guidelines for hospitalised children have been based on the Holliday and Segar formula.[10] The 4/2/1

formula was based on the understanding that water maintenance needs parallel energy expenditure: 100 mL/100 kcal for the first 10 kg of body weight, 50 mL/100 kcal for 11–20 kg, and 20 mL/100 kcal for every kilogram of body weight above 20 kg. They also proposed 3 mEq/100 kcal sodium/day and 2 mEq/100 kcal potassium/day as maintenance electrolyte requirements based upon the electrolyte composition of breast and cow's milk. Based on this, hypotonic fluid (0.225% and 0.45% saline) was identified as the ideal maintenance fluid choice in hospitalised children.

In the past, several studies have reported hospital-acquired hyponatraemia in healthy children after elective surgery after the infusion of hypotonic solutions.[11-13] Administration of a hypotonic solution, particularly in hypovolemic children, decreases the serum sodium concentration and serum osmolality. This results in symptoms of headache, nausea, vomiting, weakness and lethargy, followed by seizures, cerebral edema, herniation of the cerebellar peduncles, aspiration and death in 30% of affected children.[14]

Antidiuretic hormone (ADH) and hyponatraemia

Various studies have reported 11–31% incidence of postoperative hyponatraemia and nearly all studies have shown that postoperative patients have an increased risk of developing hyponatraemia.[12,15,16] The increased risk of hyponatraemia in postoperative period is related to the release of antidiuretic hormone (ADH).[17] The primary stimulus for ADH release is an increase in osmolality, but many non-osmotic stimuli may also contribute [Table 2].[18] The ADH levels peak at 6 – 12 h after surgery and gradually taper off over the next 5 days. Kanda *et al.* in their study showed that hyponatraemia developed in patients who had both elevated ADH levels and received hypotonic 0.6% saline; elevated ADH levels alone or hypotonic saline alone were not associated with hyponatraemia.[19]

Fluid tonicity and hyponatraemia

Tonicity is a measure of effective osmolality. Solutes like sodium which have restricted cell-membrane permeability, remain in ECF compartment and create an osmotic pressure gradient which drives water movement from the ICF to the ECF compartment. Solutes which are freely permeable across cell membranes like dextrose distribute equally between the ECF and ICF compartments and do not create an osmotic pressure gradient or drive water movement.

Table 2: Non-osmotic stimuli of ADH release

Haemodynamic stimuli	Non-haemodynamic stimuli
Hypovolaemia	CNS disease
	Brain tumours
	Meningitis, encephalitis
	Head trauma
Decreased effective circulatory blood volume	Pulmonary disease
Cirrhosis	Pneumonia
Congestive heart failure	Bronchiolitis
Hypoalbuminaemia	Positive pressure ventilation
Hypotension	Hypoxia
	Oncological diseases
	Postoperative state
	Miscellaneous
	Pain
	Nausea vomiting
	Stress
	Medications
	Narcotics
	Vincristine
	Cyclophosphamide

Thus, the tonicity of an IV solution depends primarily on the content of its electrolytes. Normal plasma sodium concentration [Na] is 135–145 mEq/L, but the [Na] in the aqueous phase of plasma water is approximately 150 mEq/L; therefore, fluid with a tonicity (Na + K) of less than approximately 150 mEq/L is considered to be hypotonic.

Randomised controlled studies comparing hypotonic to isotonic IV fluids in paediatric surgical and medical patients have consistently shown that hypotonic IV fluids are associated with hyponatraemia.[12,13] A recent meta-analysis of studies including mostly surgical patients, demonstrated a higher risk of hospital-acquired hyponatraemia when hypotonic IV fluids were administered.[20] It has also been shown that hyponatraemia can occur even in patients receiving isotonic IV fluids, related to the presence of high circulating ADH levels.[19] ADH leads to the reabsorption of water in the collecting duct and the creation of concentrated urine with a urine osmolality of >100 mOsm/kg. Therefore, when the ECF compartment is expanded by isotonic fluids in the presence of high circulating ADH, sodium is excreted in the urine and free water is retained, leading to hyponatraemia.

The need for glucose during maintenance fluid therapy: Hypoglycaemia vs. hyperglycaemia

The need of glucose administration to compensate for preoperative fasting depends on the number of hours the child is kept fasting. The concentration of dextrose

in IV fluids utilised in surgical children has changed from the use of 5% dextrose solution in the past to use of 1–2% dextrose solutions in present day.[21,22] In the paediatric population both hypoglycaemia and hyperglycaemia is hazardous.

Hypoglycaemia

Glucose is essential for the normal brain to function. Severe hypoglycaemia, can adversely affect the central nervous system (CNS), especially in neonates. Depending on its degree, hypoglycaemia may provoke a counter-regulatory stress response (increase in plasma cortisol, epinephrine, glucagon and growth hormone); an increase in regional blood flow with a loss of cerebral vascular autoregulation and it may alter cerebral metabolism leading to a shift from glycolytic precursors to Krebs' cycle intermediates, alteration of ion homeostasis and acid–base abnormalities.[23] All these changes can lead to clinical symptoms and permanent neuronal damage.[24] Initial research had suggested that children become hypoglycemic under anaesthesia. However, it has now been shown in recent studies that the incidence of preoperative hypoglycaemia is between 0% and 2.5% and is usually associated with fast durations from 8 to 19 h.[21,22]

Hyperglycaemia

In the presence of ischaemia or hypoxia, it is speculated that the impaired metabolism of excess glucose causes an accumulation of lactate, a decrease in intracellular pH, and subsequently severely compromised cellular function that may result in cell death. Hyperglycaemia can also induce an osmotic diuresis that may lead to dehydration and electrolyte abnormalities. In children, hyperglycaemia, especially in the presence of an ischemic or hypoxic event, worsens neurologic outcomes as well as increases morbidity and mortality.[25] Studies have shown that the infusion of 2 or 2.5% dextrose solutions during surgery raises blood glucose levels to a lesser extent and keeps the sugars in the normal range (<8.3 mmol/l) than 5% solutions.[22]

Based on above observations there is a growing consensus that intraoperative dextrose is selectively administered only in those patients at greatest risk for hypoglycaemia and where required one should consider the use of fluids with lower dextrose concentrations (e.g. 1% or 2.5%).[26,27] The populations at highest risk of hypoglycaemia include neonates, children receiving hyperalimentation, and those with endocrinopathies, in whom monitoring blood glucose levels and adjusting the rate of infusion is also recommended.[1] Routine dextrose administration is no longer advised for otherwise healthy children receiving anaesthesia.

However, neonates require dextrose-containing fluid during surgery because they require 4–8 ml/kg glucose for brain development. In addition, limited glycogen reserve makes the neonate susceptible to hypoglycaemia without glucose supply.[23,24] Association of Paediatric Anaesthetists of Great Britain and Ireland (APA) consensus guidelines and European consensus statement guidelines recommend intraoperative use of low dextrose (1–2.5%) containing isotonic fluids which have been shown to maintain acceptable blood glucose levels and prevent electrolyte imbalances during surgery.[2,28] Sumplemann *et al.* found that the intraoperative use of an isotonic balanced electrolyte solution with 1% glucose and a mean infusion rate of 10 ml/kg/h helps to avoid acid–base imbalance, hyponatraemia, hypoglycaemia, ketoacidosis and hyperglycaemia in surgical neonates.[26] Whether such low glucose-containing fluids maintain blood glucose levels by initiating catabolism of the body's own stores is unknown. Datta *et al.* found in their study that 1% dextrose-containing fluid promotes catabolism and insulin resistance, increases acidosis and may result in rebound hyperglycaemia in neonates. They therefore recommend 2–4% dextrose solution as metabolically suitable.[27]

Guidelines for intraoperative fluid therapy in children

Guidelines by various societies (APA,[28] NICE[29] and guidelines from Association of the Scientific Medical Societies of Germany[2]) have been proposed for calculating the volume of fluid to be administered during surgery.

Role of preoperative fasting

It was thought that children develop preoperative fluid deficit because of ongoing insensible fluid losses and urine output. Based on this Furman *et al.* proposed calculating preoperative deficit by multiplying the Holliday and Segar hourly rate by the number of hours the patient was NPO. Half of this amount was replaced during the first hour of surgery followed by other half over next 2 h.[30] Later Berry *et al.* suggested that children 3 years and younger should receive 25 mL/kg, whereas children 4 years and older should receive 15 mL/kg of basic salt solution over the first hour of surgery.[31] The methods of both Furman *et al.* and Berry were developed based on the assumption that patients

had been NPO for at least 6 to 8 hours. However, based on the liberalisation of fasting guidelines allowing clear fluids for up to 1–2 h, the amount of IV fluids required to cover for preoperative fluid deficit may be less. On the other hand, irrespective of the fasting recommendations of 2 h the child may be fasting for >6 h in certain situations.

The guidelines recommend that the perioperative fasting times for children should be as short as possible to prevent patient discomfort, dehydration and ketoacidosis. If preoperative and postoperative fasting times are short, perioperative IV fluid therapy is not required in children beyond neonatal age who drink sufficient volumes and undergo short procedures (<1 h) with a venous access in place.[2] If the child is fasting for >6 h appropriate volume of fluid can be administered based on the degree of dehydration (1% dehydration = 10 ml/kg fluid loss). For preoperative fluid resuscitation it is recommended that glucose free crystalloid containing sodium in the range of 131–154 mmol/L is administered in a bolus of 20 ml/kg over 10 min in children and 10 ml/kg over 10 min in neonates for a maximum of 40–60 ml/kg.[2]

Maintenance fluid therapy

The maintenance fluid requirements are calculated based on Holliday and Segar formula.[10] Both APA[28] and NICE[29] guidelines recommend maintenance fluid administration of isotonic fluids based on Holliday and Segar formula. However, in NICE guidelines it is recommended that fluids be restricted by 50–80% in view of risk of water retention based on non-osmotic ADH secretion.[29] The German guidelines recommend administration of balanced electrolyte solution with 1–2.5% dextrose at the rate of 10 ml/kg/h as an initial infusion followed by adjustment in rate based on requirement.[2]

Replacement fluid therapy

According to the APA guidelines, replacement for intraoperative losses is with isotonic solutions and colloids or blood based on the child's hematocrit.[28] The 3rd space loss (its existence is a matter of debate) due to sequestration of fluid from vascular space into tissues around the surgical site is difficult to quantify and is roughly estimated as 2 ml/kg/h for superficial surgery, 4–7 ml/kg/h for thoracotomy and 5–10 ml/kg/h for abdominal surgery. The NICE guidelines only mention replacement of ongoing losses with isotonic saline without mentioning the rate of fluid administration.[29] Sumplemann *et al.* recommend that in patients with circulatory instability balanced isotonic electrolyte solutions without glucose can be given as repeat-dose infusions of 10–20 ml/kg until desired effect is obtained.[2] A normal BV is an important prerequisite for adequate venous return, CO and sufficient tissue perfusion. A decrease in BV shifts interstitial fluid towards intravascular space. An initial step is to stabilise the circulatory system by infusion of balanced salt solution to maintain ECFV and BV. If the volume of crystalloids exceeds then to avoid interstitial fluid overload, leading to haemodilution and decrease in oxygen supply, colloids like albumin, gelatin, HES 130 are used as repeat dose infusions. However, the total dose should not exceed 10–20 ml/kg (not to exceed 50 ml/kg dose).

Which type of isotonic solution is preferred?

Various types of isotonic solutions are available for administration and the most commonly used are normal saline (NS), Ringer lactate (RL) and Plasmalyte™ (acetate). Normal saline has an osmolality of 286 mOsmol/kg H_2O whereas RL has an osmolality of 273 mOsmol/kg H_2O (mildly hypotonic). The amount of Cl in these solutions is very high (156 mmol/L) and administration of large volumes of these solutions can cause chloride overload with suppression of renal blood flow and renin-angiotensin aldosterone system leading to hyperchloremic acidosis.[32] Also, acetate in the solutions is quickly metabolised by the liver compared to lactate without interfering with the diagnostic use of lactate as a marker of tissue perfusion. Therefore, balanced electrolyte solutions are recommended for intraoperative infusion.[33,34]

Role of colloids

The intraoperative use of colloids in children is still debatable and sparsely studied.[35,36] Most of the research studies have been done in adult patients which have shown renal failure in patients with sepsis. However, in paediatric animal studies, as well as in children undergoing major cardiac surgery no renal failure has been seen with use of moderate and high doses of HES 130. A meta-analysis opined that intravascular volume expansion with low molecular weight 6% HES did not appear to modify renal function, blood loss or transfusion when administered to children during the peri-operative period.[37] However, since the quality of evidence was low, the authors recommended conduct of high-quality RCTs to study their effect in children.

Blood loss and need for transfusion

Blood administration is commonly required during the perioperative period especially during major surgeries in children. Therefore, assessment of the need and utility of blood transfusion is an integral part of anaesthesia management. It is also important to understand that the administration of blood in children carries significant morbidity and mortality issues because of transfusion related acute lung injury, circulatory overload and haemolytic transfusion reactions.[38] Based on these, patient blood management (PBM) programs have been implemented providing an evidence-based care in which optimal transfusion therapy leads to an improved outcome. Although these programs have been successfully used in adult population it is not yet well established in neonates, infants and children.[5,39] Various practice guidelines and recommendations for perioperative blood management in adults[40,41] as well for neonates, infants and children have been published.[42,43]

Basis of blood transfusion in paediatrics

The requirement of blood transfusion depends on many factors like age, quantity of blood loss, the baseline haemoglobin concentration and different blood physiology. Neonates and infants have higher blood volume per weight [Table 3] but are less tolerant of the loss. Also, the metabolic rate and baseline oxygen demands are greater than adults. Preoperative iron deficiency anaemia is more prevalent in this population and increases the risk of blood transfusion requirement intraoperatively. Neonatal haemoglobin (Hb) is more than 70% foetal Hb in term neonates compared to 90% in preterms implying decreased oxygen delivery to the tissues.

In a bleeding child the intraoperative goal should be to maintain normovolaemia but avoiding hypervolaemia to minimise swelling, edema and haemodilution. Initially, fluids can be administered to replace blood loss by administration of crystalloids or colloids in a 2:1 ratio of estimated blood loss. The preferred fluids are Ringers Lactate (273 mOsm) and Plasmalyte (294 mOsm) as they are associated with less severe acidosis than isotonic saline. In case of rapid blood loss and haemodynamic instability, administering colloids in a 1: 1 ratio may be required.

Table 3: Normal blood volume in neonates and children

Age	Blood volume
Preterm neonate	90 ml/kg
Full term neonate - 3 months	80-90 ml/kg
Above 3 months	70-80 ml/kg
Above 2 years	70 ml/kg

The decision on time to administer blood to children depends on the maximum allowable blood loss (MABL) calculated as: MABL = EBV × (H0 – H1)/ H0 (EBV = estimated blood volume; H0 = starting Hct; H1 = lowest acceptable Hct). Trigger for blood transfusion depends on age, Hb level and associated disease states. The required transfusion volume of packed red blood cells in children can also be calculated as follows: body weight (kg) X desired increment in haemoglobin (g/dl) ×5.[44]

Based on the PBM programs restrictive haemoglobin thresholds may be indicated in infants and children (target of 7 g/dL for haemodynamically stable patient). Current evidence for optimum haemoglobin threshold in neonates is controversial and evolving (12 g/dL). Red blood cell transfusion if indicated should be single donor, leucocyte depleted, irradiated and fresh.

SUMMARY

Many guidelines are available for fluid and blood administration in children. Research has proven that in children undergoing surgery the preoperative fasting period should be minimal and fluid administration should be with isotonic balanced salt solution. Administration of blood in children should be based on the preoperative Hb and type of surgery taking into consideration the problems associated with allogenic blood transfusion. Paediatric Blood Management programs show promise and can be implemented.

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Conflicts of interest

There are no conflicts of interest.

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Announcement

CALENDAR OF EVENTS OF ISA 2019

The cut off dates to receive applications / nominations for various Awards / competitions 2019 is as below. Please visit isaweb.in and log in with your ISA Regd. E Mail ID & Password and submit application with all documents as attachment. Mark a copy of the same by E Mail to secretaryisanhq@gmail.com. Write the name of Award applied as subject. Link will be sent to judges for evaluation. No need to send hard copy. Only ISA members are eligible to apply for any Awards / competitions. The details of Awards can be had from Hon. Secretary & also posted in www.isaweb.in

Cut Off Date	Name of Award / Competition	Application to be sent to
30 June 2019	Bhopal Award for Academic Excellence	Hon. Secretary, ISA (by log in & E Mail)
30 June 2019	Late Prof. Dr. A .P. Singhal Life Time Achievement Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2019	Rukmini Pandit Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2019	Dr. Y. G. Bhoj Raj Award	Hon. Secretary, ISA (by log in & E Mail)
30 June 2019	Mrs. Shashi & Dr. P Chandra Award	Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2019	Kop's Award	Chairperson, Scientific Committee ISACON 2019 copy to Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2019	ISACON Jaipur Award	Chairperson, Scientific Committee ISACON 2019 copy to Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2019	Prof. Dr. Venkata Rao Oration 2019	Hon. Secretary, ISA (by log in & E Mail)
30 Sept 2019	Ish Narani Best poster Award	Chairperson, Scientific Committee ISACON 2019
30 Sept 2019	ISA Goldcon Quiz	Chairperson, Scientific Committee ISACON 2019
10 Nov 2019	Late Dr. T. N. Jha Memorial Award & Dr. K. P. Chansoriya Travel Grant	Hon. Secretary, ISA, (by log in & E Mail) copy to Chairperson Scientific Committee ISACON 2019
20 Oct 2019	Bidding Application for ISACON 2021	Hon.Secretary, ISA by log in, E Mail & hard copy
20 Oct 2019	Awards (01 Oct 2018 to 30 Sept 2019)	Hon. Secretary, ISA (by log in & E Mail)

(Report your monthly activity online every month after logging in using Branch Secretary's log in ID)

1. Best City Branch
2. Best Metro Branch
3. Best State Chapter
4. Public Awareness – Individual
5. Public Awareness – City / Metro
6. Public Awareness - State
7. Ether Day (WAD) 2019 City & State
8. Membership drive
9. Proficiency Awards

Send hard copy (only for ISACON 2021 bidding) to

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